ATTACHMENT G1 (continued)
Exhibits to Comment Letter I14

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EXHIBIT A

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January 25, 2013

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Oakland, CA 94607

Subject: ***Casa Diablo IV Geothermal Energy Project Environmental Impact Report Geology and Water Resources Comments***

Dear Ms. Caro,

Thank you for the opportunity to comment on the Draft Joint Environmental Impact Statement and Environmental Impact Report Environmental Impact Report (EIR/EIS) for the Casa Diablo IV Geothermal Development Project (Project). The CD-IV Project includes the construction, operation, maintenance and decommission of a 33 net megawatt binary power plant and an expanded geothermal well field with an additional 16 geothermal resource wells, the construction of pipelines and an electric transmission line to interconnect to the Southern California Edison (SCE) Substation at Substation Road. Already existing in this area are three geothermal energy plants: MP I project (also called G-1) is a 10 MW plant and PLES 1 and MP 11 are both 15 MW plants for a total of 40 MW of existing net geothermal energy production in the Casa Diablo area. Please find my comments below on the Casa Diablo IV Geothermal Development Project.

I) The EIR/EIS fails to thoroughly analyze impacts to local groundwater resources

According to Section 3.7.1.3 of the EIR/EIS, the Mammoth Groundwater Basin, drained by the upper reaches of the Mammoth Creek, supplies the Mammoth Lakes community with groundwater for potable purposes with a total average production of 1.3 cubic feet per second (CFS). The shallow groundwater system is separated from the underlying geothermal reservoir by either intense alteration of thick ash-rich Early Rhyolite units in the western caldera or low permeability rocks from a landslide which occurred in the south-central portion of the caldera from a catastrophic collapse approximately 760,000 years ago. The Mammoth Community Water District extracts groundwater from nine municipal wells, which are located primarily to the west and south of the project site. The groundwater depths in the wells range from 10 feet below ground surface (bgs) to 400 feet bgs.

The risk to the potable groundwater source from the proposed project lies in several areas. The first is that hazardous materials used in geothermal energy production are at risk of being released by accidents and man-made or natural disasters (i.e. earthquakes) into the shallow groundwater system. This can happen in multiple ways; either by an accidental release at the surface, by the contamination of injection fluids or by leaks within the extraction and injection system causing geothermal fluids and their associated chemicals to be released directly into the subsurface and underlying groundwater aquifer. The project area lies within and adjacent to the Hilton Creek fault – an Alquist Priolo Earthquake Fault Zone which defines known active faults, making the subsurface and groundwater vulnerable to accidental releases and contamination. Section 4.8.2 in the EIR/EIS indicates

I14-71

that mitigation GEO-6: "The CD-IV power plant and pipelines will be designed and constructed to reasonably minimize the potential for failure or rupture in the event of fault offset in these zones" is proposed to accommodate small to moderate level earthquakes but moderate to large earthquakes could result in serious groundwater impacts. It is proven that geothermal extraction systems do increase the occurrence of earthquakes in the vicinity of injection wells for geothermal systems (Majer and Peterson, 2008) and (Nicholson and Wesson, 1990). Sanyal (2005) stated that "Prolonged, high pressure injection may induce seismic activity at a geothermal site, particularly if the fluid pressure is increased beyond the original pore pressure and if there are subsurface zones of weakness or active faults near the injection area. While the occurrence of microearthquakes near injection sites have been documented in several geothermal fields, such as The Geysers in California, no major earthquakes due to injection in a geothermal field has yet been reported." However Sanyal (2005) continues to state that major earthquakes have been documented as being induced by the petroleum and waste injection industries. Although only smaller earthquakes have been noted thus far resulting from the existing geothermal plants in California, larger earthquakes have occurred in other geothermal areas and have been linked to the geothermal injection process (Majer and Peterson, 2008). **I14-71 cont.**

Another risk of injection is that there exists a decent connection between the geothermal reservoir and the shallow groundwater system and that mixing may occur to some extent. Well P-17, located west of the project site, has already shown evidence of mixing according to section 4.7.4.1 of the EIR/EIS. The extraction and injection of geothermal fluids can deflate or inflate the reservoir and this can increase the risk of mixing. In addition, when geothermal reservoirs are depleted they can leave behind interstitial spaces **I14-72**

elevated in heavy metals and elevated concentrations could impact the groundwater source if a pathway exists or is later formed. When groundwater comes in contact with geothermal fluids or former geothermal-extraction areas it is often removed as a beneficial use for human consumption and deemed non-potable. According to Section 3.19.2 of the EIR/EIS, such is the case with the groundwater located in the southeast portion of the project area where the lines of mixing are too close and the water is not suitable for consumption. The impacts to the overlying shallow groundwater systems show early signs of mixing and the impacts to the environment and natural resources with a 50% increase in production of geothermal fluids in this area has not adequately been addressed in the EIR/EIS for this project. I14-72 cont.

Furthermore, as stated in section 4.7.4.1 of the EIR/EIS the models used are proprietary and as such the results and reports could not be vetted by the public. To date the EIR/EIS fails to include a thorough and public review of the subsurface hydrologic processes for the proposed project and fails to adequately analyze how the geothermal reservoir is connected to the overlying strata and groundwater systems that could be impacted by this project. I14-73

II) The EIR/EIS fails to adequately address the impacts from the project to surface water quality

II.a) Impacts from the injection of hazardous substances into the subsurface

Surface water quality is critical to down river systems from the project area because these waters serve as important ecological and recreational resources. These resources are vulnerable to impacts from the existing and proposed project. For instance, according to Section 3.7.1.2 of the EIR/EIS in 1993 a leak of spent isobutene fuel in the existing Casa Diablo geothermal plant was accidentally released into the injection piping located above grade I14-74

and the contaminated injection water was injected into the geothermal reservoir at approximately 1900 feet bgs. This chemical was subsequently detected up to 5 years later and 2 miles away at Hot Creek Gorge. Given the detection limits of isobutene and the distance the chemical travelled in the subsurface, in order to detect these chemicals up to 2 miles away and 5 years later the size of the leak had to have been more than a minor leak. The exact quantity accidentally injected was not indicated in the EIR/EIS. This accident demonstrated that a connection exists between the deeper reservoir and the shallow surface water systems and also indicates the continued and long-lasting impacts of mismanaged chemicals used in process operations at geothermal energy plants. As shown in Section 4.7.1 of the EIR/EIS the shallow geothermal system mixes with surface water in the area of Hot Creek and the presence of chemicals in these waters can have adverse impacts on the biological resources. Although the EIR/EIS addresses spill prevention problems it did not specifically detail how a future release of working fuel (isobutene or the equivalent) will be avoided in the future. The amount of geothermal energy being processed by the CD-IV project will increase production in this area 50% and therefore the risk and mitigations of a repeated release needs to be addressed. **I14-74 cont.**

II.b) Impacts from storm water run off on surface water quality

The Basalt Canyon drainage originates north and west of the project area and traverses the project area towards Mammoth Creek. With the addition of numerous new well pads, roads, and equipment comes an increase in storm water run off and thus an increase in total dissolved solids along with an increased potential for contaminated run-off from added vehicle and equipment loading. Although the EIR/EIS in Section 4.8.2 proposes mitigation HYD-1: "Appropriate erosion control measures will be used to control any offsite discharges, and the Project will adopt any relevant LRWQCB and **I14-75**

USFS best management practices to prevent soil erosion, including the preparation of a SWPPP" the EIR/EIS fails to adequately address the impacts of this added construction on Mammoth Creek. Mammoth Creek is already listed as an impaired water-body on Regional Water Quality Control Board's Clean Water Act Section 303(d) list for TDS and metals (RWQCB, 2013). The pattern of sheet flow in this area traverses the extensive project area directly and as such it should be thoroughly analyzed and the current EIR/EIS fails to do this. Furthermore, because existing facilities already increase run-off in the project area the combined impacts from the proposed and existing facilities needs to be taken into account and the EIR/EIS fails to accomplish this. **I14-75 cont.**

II.c Increased risk to surface water quality from hazardous material releases

The surface waters are also at risk from a release of hazardous materials from chemicals used on the project site. As noted in Section 2.2.7.6 of the EIR/EIS there will be large amounts (9,000 – 12,000 gallons) of n-pentane used in the proposed CD-IV process as well as other hazardous chemicals such as fuel, lubricants, transformer oil and other chemicals. These chemicals, even if properly contained, can be mismanaged as demonstrated above or be released in to the environment in the event of a large earthquake. The EIR/EIS does not adequately study nor address the risk of these releases to the receiving water-bodies. The EIR/EIS does not discuss the risk to these water-bodies in event of a serious ground-shaking event, which could occur in this tectonically active area. Because of the sensitive nature of the down river habitats the study of the impacts of a release of these specific chemicals into the surface water-bodies should be included in the EIR/EIS. **I14-76**

III) The EIR/EIS does not provide a thorough review of the risks to geothermal resources from the project

The proposed CD-IV project has the potential of impacting and irreversibly altering the natural geothermal features such as hot springs and pools, fumaroles (steam vents) and steaming ground in the vicinity of the project. As shown in Section 4.7.4.1 of the EIR/EIS water quality chemistry and temperatures indicate a clear connection from the Casa Diablo well field to the shallow geothermal features down flow from the site including Hot Creek Springs, Hot Bubbling Pool and Hot Creek Fish Hatchery. Reduction in temperatures of geothermal features can negatively impact the ecosystem and community resources. The rate of temperature decline (thermal drawdown) from the geothermal extraction/injection process in the reservoir exceeds the rate of recovery (Sutter, Fox et al., 2011) and although the process of geothermal energy is considered renewable reservoirs need "breaks" from extraction processes so that temperatures and pressures have time to recover to initial or close-to initial conditions. The decline in temperatures in a given system during the extraction and injection period will manifest themselves not only in the reservoir itself but also in the shallow geothermal features connected within the exploited reservoir. For this reason, as indicated in Section 4.7.4.1 of the EIR/EIS temperature declines are expected in the areas of concern for this project such as Hot Creek Springs, Hot Bubbling Pool, Hot Creek Fish Hatchery. **I14-77**

As mentioned in Section 4.7.4.1 of the EIR/EIS the Applicant had a proprietary numerical model developed to simulate geothermal production and reservoir response, yet this model has not been reviewed by the public

and thus the data cannot be validated. In addition, the mass balance equations used in the Section 4.7.4.1 of the EIR/EIS using Monitoring Well MBP-3 and Monitoring Well 44-16 seem to include only one sampling event from each well. The data is typically more reliable when data sets include more than one data point for each hypothesis, which this does not. The EIR/EIS in Section 4.7.4.1 indicates that at the lower forecast temperature slightly lower inflow temperatures are expected at the major surface manifestations. Again, since the data is proprietary and not available to analyze this cannot be confirmed. The term "slightly lower" is not quantified. The EIR/EIS in Section 4.7.4.1 indicates that the thermal discharge at the Hot Creek Fish Hatchery is forecast to be reduced by 0.85% and that the thermal outflow to Hatchery Springs will be reduced by about 17%. Thus, this area appears sensitive to changes in thermal inflow from the Casa Diablo reservoir and this area and the ecosystem it supports relies on adequate thermal input to survive. The EIR/EIS does not seem to adequately study the impacts of these lowered temperatures on the surrounding resources and furthermore what studies were done are not available for public review. Due to the importance of these geothermal resources to the community and the ecosystems the EIR/EIS process should demand a thorough study of these impacts and the current one fails to supply this. I14-77 cont.

IV) The EIR/EIS fails to adequately address the impacts from project-related subsidence

Subsidence is the sinking of the Earth's surface in response to geologic or human-induced causes. The scientific data as noted in Section 4.8.4 of the EIR/EIS shows that this area has undergone naturally occurring uplift in the resurgent dome and also subsidence. Subsidence was measured in this area, I14-78

and although it is difficult to distinguish naturally occurring subsidence from those associated with geothermal extraction it is indicated in the EIR/EIS that subsidence does occur in isolated areas around the production wells. As noted in Section 4.8.4 on the EIR/EIS the USGS observed that the apparent amount of subsidence was limited and spatially related to the producing area around Casa Diablo. The subsidence totaled 310mm since 1997 however was balanced out by uplift from the resurgent dome. Although the configuration of wells for the CD-IV project are different than the existing project and reinjection of the cooling brine could help to reduce the degree of subsidence it should be expected that some degree of subsidence will be measured in the project area around the production wells. It is further noted that the rate of subsidence due from geothermal extraction will likely exceed the rate of uplift in the resurgent dome. This is because naturally occurring uplift typically takes thousands of years or more and the rate of subsidence from geothermal extraction is in the order of years and decades. Although the earthquake swarm in the caldera that occurred in the 1980's contributed to a rapid rate of uplift it is unlikely to repeat anytime soon and it is not expected that another uplift event will balance out any future subsidence from extraction during the length of this project. Subsidence in these areas can affect the integrity over time of the pipelines and other underground and aboveground facilities. Although the degree of subsidence is anticipated to be relatively minor, when combined with ground shaking events from the injection process, it could lead to compromised equipment which could lead to a release, either slow or catastrophic, of hazardous materials into the shallow groundwater system and/or surface waters. The EIR/EIS did not adequately address the risk to the public and the environment from impacts from subsidence when combined with ground shaking events that could occur from this project.

I14-78 cont.

V) The EIR/EIS fails to thoroughly review the risks of induced seismicity from the project

It has been shown that the injection of fluids into an area that is tectonically active and that has active faults proximal to the injection area can increase the amount of earthquakes in that vicinity (Majer and Peterson, 2008). Section 4.8.4.1 of the EIR/EIS states that "Although earthquakes typically occur naturally, seismicity has at times been induced by human activity, including the development of geothermal fields, through both production and injection operations (Geothermal Energy Association, 2007). In these cases, the resulting seismicity has been low-magnitude events known as microearthquakes." Thus far, as indicated in Section of the EIR/EIS 4.8.4.1 it has only been smaller earthquakes which have been correlated with geothermal injection wells, however, it has been shown in previous studies by Nicholson and Wesson (1990) that when the volume of injection fluids into an area increases so too does that quantity and strength of the earthquakes. Components, including the proposed power plant, substation, several wells and transmission lines, lie within the Hilton Creek fault zone. In 1980 several M+6 earthquakes occurred along this fault. As mentioned above, although previous geothermal injection activities in the existing geothermal plants in California have been linked to earthquakes they have not yet been large enough cause damage. However, as stated above as injection levels increase so does the frequency and magnitude of the earthquakes. The probabilistic seismic hazard assessment (PHSA) indicates that at the CD-IV project site there is a 10% chance of exceeding peak ground acceleration (PGA) values of 0.40g-0.50g over the next 50 years, depending on site specific ground conditions. According to the Modified Mercalli Intensity Scale an earthquake

I14-79

within this range is a very strong earthquake with slight damage to newer reinforced buildings, considerable damage in ordinary substantial buildings, great damage in poorly built structures, heavy furniture overturned, the fall of chimneys, factory stacks, columns and monuments. The EIR/EIS does not adequately address the increased seismic risk from the proposed injection activities combined with the already existing injection activities. A full-scale open review is needed of the impacts of the combined injections onto the existing risk of fault rupture in this area. The current EIR/EIS fails to address these issues. **I14-79 cont.**

CONCLUSION

In conclusion, the EIR/EIS for the Casa Diablo IV Geothermal Development Project does not put forth and fair and full review of areas discussed above pertaining to geology, soil and water resources for this project. The EIR/EIS should include additional review and information on the referenced items above prior to approval so that the risks to the environment and to the community can be thoroughly understood and evaluated by the public and the decision-makers. **I14-80**

Very Truly Yours,

Heidi M Rhymes

Heidi Rhymes, PG

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Daniel Sutter, Don B. Fox, Brian J. Anderson, Donald L. Koch, Philipp Rudolf von Rohr and Jefferson W. Tester, 2011, *Sustainable Heat Farming of Geothermal Systems: A case study of heat extraction and thermal recovery in a model EGS Fractured Reservoir*, Atkinson Center for a Sustainable Future and the Cornell Energy Institute, Cornell University, Ithaca, NY.

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Sanyal, Subir, 2005, *Injection Related Problems Encountered in Geothermal Projects and their Mitigation: the United States Experience*, World Geothermal Congress, Florence, Italy.

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PROFESSIONAL EXPERIENCE

Senior Project Geologist **January 2004 – present**
IA Sciences, Petaluma, California
Currently manages environmental projects, environment project oversight, and third-party review. Includes review, analysis, interpretation and comment/advise on projects pertaining to hazardous waste sites and groundwater and soil impacted sites. Performs file reviews for contaminated sites and prepares summary reports. Researches and comments on environmental impacts from subsurface contamination including groundwater, soil and soil vapor, including review of subsurface contaminant transport, groundwater flow, soil stratigraphy and hydrogeologic data to determine risk and remediation goals. Project management includes report and plan preparation, proposal development, estimating, data collection, analysis interpretation, and reporting. Coordinates and interacts with regulatory agencies on compliance issues. Reviews and provides updates on regulatory/compliance standards and requirements. Performs peer reviews and environmental damage claim assessments for insurance carriers. Also performs indoor air quality investigations and reporting.

Senior Project Geologist **June 2002 to January 2004**
Miller Brooks Environmental, Oakland, California
Managed the implementation and direction of environmental investigation programs for multi-site, small to large, petroleum distribution and marketing companies. Worked and met with regulators and prepared local, state and federally required reports and documents. Managed compliance testing and discharge reporting requirements. Performed peer reviews, property development investigations, and damage claim evaluations for insurance companies. Performed function as company Health and Safety Officer and prepared health and safety plans and risk assessment reports for projects.

Senior Project Geologist **August 2001 to May 2002**
Dominion Environmental (currently IA Sciences), Petaluma, California
Managed environmental projects, reviewed technical data, prepared reports, proposals, planning documents, costs estimates and contract documents. Investigated associated environmental and public health risks and prepared summary reports and presentations. Provided consultation on hazardous materials storage and handling practices. Interacted with local, state and federal regulatory agencies on compliance issues. Performed health & safety oversight, planning, training and assisted with industrial hygiene investigations.

Project Geologist **September 1997 to August 2001**
Clearwater Group, Inc., Oakland, California
Supervised 10 – 15 managers, scientists, and technicians and served as operations manager of satellite office. Directed program implementation for multi-site clients. Prepared and implemented plans and permits including workplans, action plans, health and safety plans, NPDES and air quality permits. Conducted environmental research, support and reporting for environmental litigation cases, damage claim evaluations and property development. Served as representative for environmental and property development issues at hearings and meetings. Served as Corporate Health & Safety Officer and managed safety compliance issues, reporting and conducted appropriate training.

Project Geologist **January 1996 – July 1997**
Walden Associates Inc., Oyster Bay, New York
Responsible for environmental investigative work to assess the nature and extent of contaminant releases. Conducted and coordinated assessments and remedial projects. Prepared workplans, corrective action plans, reports and permitting documents. Served as Corporate Health and Safety Officer and conducted all trainings, reporting and compliance management.

Environmental Health and Safety Assistant and Waste Management Coordinator **January 1994 to January 1996**
Department of Environmental Health & Safety, State of New York, Stony Brook, New York
Worked under EH&S Manager and performed and assisted with safety program development, implementation and trainings. Responsible for compliance with all applicable federal, state and local hazardous waste regulations, discharge reporting and operation of the Hazardous Materials Management Facility. Worked with facilities maintenance on facility inspections, storage, transportation oversight and disposal of

hazardous waste. Collateral duties included confined space safety, industrial hygiene sampling, indoor air quality investigation, hazard communication program, chemical hygiene program implementation and compliance inspections.

ADDITIONAL PART-TIME EMPLOYMENT

Lieutenant/Chemical Safety Division Officer **September 1997 to June 2003**
US Coast Guard Reserve, Pacific Strike Team, Novato, California
Directly supervised 15 response technicians and scientists. Directed hazardous materials response operations in area of responsibility. Worked on environmental investigations for EPA Superfund sites. Conducted unit training on safety and monitoring. Served as Chemical Division Safety Officer.

Waste Management Intern **August 1993 –to December 1993**
Marine Science Research Center, Stony Brook, New York
Conducted groundwater sampling, data collection and interpretation for municipal solid waste landfill sites. Conducted research project on the environmental and public health effects of improper lead waste disposal. Conducted research project on the disposal routes and environmental consequences of medical waste disposal on local beaches.

Environmental Intern **June 1993 to August 1993**
Atlantic States Legal Foundation, Syracuse, New York
Conducted research project and report on waste discharges (TRIs) from steel mills to the Great Lakes basin in accordance with the Emergency Planning and Community Right to Know Act (EPCRA). ASLF is a not-for-profit corporation providing technical, legal, and organizing services to citizens, citizen groups, local governments, and others on environmental issues.

Environmental Health & Safety Assistant **January 1992 to December 1993**
Department of Environmental Health & Safety, State of New York, Stony Brook, New York
Worked under Environmental Health and Safety Manager and Industrial Hygiene Manager and performed environmental surveys and inspections. Responded to and remediated chemical spills. Assisted with Hazcom/Community Right-to-Know program.

Environmental Intern **January 1990 to December 1992**
New York Public Interest Research Group
Performed research, outreach and public education on waste-to-energy plants and the pollution associated with. Also performed research and public education in support of the 5-cent bottle return program for Suffolk County.

ACADEMIC BACKGROUND

- *Bachelor of Science* – Major in Environmental Geology (Minor in Marine Science), State University of New York at Stony Brook – December 1993
- *Master of Professional Science*– Environmental/Waste Management – State University of New York at Stony Brook – May 1997

REGISTRATIONS, CERTIFICATES, & PUBLICATIONS

Current State of California Professional Geologist (PG) #7050
Asbestos Building Inspector and Site Supervisor/Contractor
Lead Sampling Technician
Hazardous Materials Response – Operations level
Hazardous Materials Response – Technician level
Hazardous Materials Response – Supervisor level

USCG DOT Pollution Investigation Qualification
USCG DOT Hazardous Materials Response Qualification
Confined Space Entry & Rescue – I and II
Indoor Air Quality Investigation
NYS Emergency Medical Technician (EMT) (expired)
40-hour Hazwoper training and instructor

Publication: *Environmental & health effects of improper lead shield waste disposal* – Journal of Dental Medicine (April 1999)

References available upon request

ATTACHMENTS

Comment Letter I14

Earthquake Hazard Associated With Deep Well Injection– A Report to the U.S. Environmental Protection Agency

U.S. GEOLOGICAL SURVEY BULLETIN 1951

Prepared in cooperation with the Environmental Protection Agency

Comment Letter I14

Earthquake Hazard Associated With Deep Well Injection—A Report to the U.S. Environmental Protection Agency

By CRAIG NICHOLSON and ROBERT L. WESSON

Prepared in cooperation with the
Environmental Protection Agency

Under certain circumstances, the increased pore pressure resulting from fluid injection, whether for waste disposal, secondary recovery, geothermal energy, or solution mining, can trigger earthquakes. This report discusses known cases of injection-induced seismicity and how and why earthquakes may be triggered, as well as conditions under which the triggering is most likely to occur. Criteria are established to assist in regulating well operations so as to minimize the seismic hazard associated with deep well fluid injection

U.S. GEOLOGICAL SURVEY BULLETIN 1951

U.S. DEPARTMENT OF THE INTERIOR
MANUEL LUJAN, Jr., Secretary

U.S. GEOLOGICAL SURVEY
Dallas L. Peck, Director

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EARTHQUAKE MAGNITUDE SCALE APPROXIMATIONS

Local (M_L)	Body-wave (m_b)	Surface-wave (M_S)	Moment (M)
4.6	4.55	—	4.6
4.8	4.8	—	4.8
5.0	5.0	4.4	5.0
5.2	5.2	4.7	5.2
5.4	5.4	5.0	5.4
5.6	5.55	5.3	5.6
5.8	5.7	5.6	5.8
6.0	5.85	5.9	6.05
6.2	6.0	6.2	6.30
6.4	6.15	6.4	6.55
6.6	6.3	6.75	6.85
6.8	6.5	7.05	7.15
7.0	6.7	7.35	7.45
7.2	6.9	7.65	7.80
7.4	7.1	7.95	8.15

Earthquake Hazard Associated With Deep Well Injection—A Report to the U.S. Environmental Protection Agency

By Craig Nicholson[1] *and* Robert L. Wesson[2]

SUMMARY

Within the United States, injection of fluid into deep wells has triggered documented earthquakes in Colorado, Texas, New York, New Mexico, Nebraska, and Ohio and possibly in Oklahoma, Louisiana, and Mississippi. Investigations of these cases have led to some understanding of the probable physical mechanism of the triggering and of the criteria for predicting whether future earthquakes will be triggered, based on the local state of stress in the Earth's crust, the injection pressure, and the physical and the hydrological properties of the rocks into which the fluid is being injected.

Of the well-documented cases of earthquakes related to fluid injection, most are associated with water-flooding operations for the purpose of secondary recovery of hydrocarbons. This is because secondary recovery operations often entail large arrays of wells injecting fluids at high pressures into small confined reservoirs that have low permeabilities. In contrast, waste-disposal wells typically inject at lower pressures into large porous aquifers that have high permeabilities. This explains, in large part, why, of the many hazardous and nonhazardous waste-disposal wells in the United States, only two have ever been conclusively shown to be associated with triggering significant adjacent seismicity. These are wells located near Ashtabula, Ohio, and near Denver, Colo. In the case near Ashtabula, a series of small, shallow earthquakes was triggered close to the bottom of a 1.8-kilometer (km)-deep well; the largest of these was of magnitude (M) 3.6 and occurred in 1987. In the Denver case, the injection well responsible was located at the Rocky Mountain Arsenal, where fluid was being injected into relatively impermeable crystalline basement rock. This caused the largest known injection-induced earthquakes to date (three M 5–5.5 earthquakes), the largest of which caused an estimated $0.5 million in damages in 1967. Although these induced earthquakes were by no means devastating, they did occasion extensive attention and concern and led, at least in the Denver case, to the cessation of all related injection well operations.

In each of the well-documented examples, convincing arguments that the earthquakes were induced relied upon three principal characteristics of the earthquake activity. First, there was a very close geographic association between the zone of fluid injection and the locations of the earthquakes in the resulting sequence. Second, calculations based on the measured or the inferred state of stress in the Earth's crust and the measured injection pressure indicated that the theoretical threshold for frictional sliding along favorably oriented preexisting fractures likely was exceeded. And, third, a clear disparity was established between any previous natural seismicity and the subsequent earthquakes, with the induced seismicity often being characterized by large numbers of small earthquakes that persisted for as long as elevated pore pressures in the hypocentral region continued to exist.

Earthquakes are generated by slip on faults or fractures. A fault or fracture in close proximity to a high-pressure injection well thus becomes a potential location for induced earthquakes. The conditions for sliding on a fault are characterized by the Mohr-Coulomb failure criterion, which relates the shear stress required for fault slip to the inherent cohesion or shear strength and the coefficient of friction on the fault, the normal stress resolved across the fault, and the pore fluid pressure. This relation, which depends on the orientation of the faults or the fractures relative to that of the existing state of stress, as well as on the effect of any changes in pore pressure resulting from fluid injection, is normally characterized by using the Mohr circle description. In this simple model, as fluid pressure increases, the apparent strength of the fault decreases, thus shifting the Mohr effective stress circle closer towards the failure condition; as a result, the potential for induced earthquakes also increases.

Because the conditions for failure strongly depend on the state of stress in the Earth's crust, measuring the *in situ* stress conditions is important to assess accurately the potential for inducing earthquakes. Several approaches are possible, but the most reliable method is the hydraulic fracture technique in which the pressure required to create

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small fractures in the wellbore is measured precisely. This method is a variation of the standard hydrofracture technique that is used to increase the transmissivity of a reservoir. Although pressures are monitored during commercial hydrofracture operations, few, if any, of these pressure records would constitute an adequate or precise stress measurement. However, because sufficient measurements of stress are now available across much of the United States, a number of regional stress patterns have begun to emerge, and, thus, it is now possible to predict the general orientation and, to some extent, the magnitude of the principal stresses at a given site. Supplemental measurements would be required, however, to provide accurate information relevant to the determination of maximum allowable levels of injection pressure at each specific site of well operations.

The hydrologic properties of the reservoir also have a strong effect on the potential for inducing earthquakes by deep well injection. Transmissivity and storativity control the rate at which pore pressure will increase in the reservoir formation as a result of fluid injection. For a given volume of fluid flow, higher values of transmissivity and storativity allow lower injection pressures required to attain a desired injection rate and, consequently, a lower potential for triggering earthquake activity. Transmissivity and storativity can be estimated from tests made during well completion and can be verified later by actual pressure-time records acquired during well operation. Estimates of the changes in pore pressure as a result of fluid injection into a particular reservoir formation can be predicted by analysis of the pressure history at the wellbore and by using variations of the standard techniques from reservoir engineering or ground-water hydrology.

Unresolved issues relating to the hazard associated with earthquakes induced by deep well injection include a relatively poor understanding of the causes of natural earthquakes in the Central and the Eastern United States and difficulties in quantifying either the spatial or the temporal variations in tectonic stress or in assessing the potential for fault reactivation in general. There is also considerable uncertainty in estimating the maximum size of expected induced earthquakes or in quantifying the significance of small induced earthquakes (should they begin to occur near the bottom of an injection well) relative to the specific level of risk. An additional environmental concern, about which little is understood, is the potential for induced earthquakes to breach the confining layer of a waste-disposal reservoir, which would then permit the possible upward migration of contaminated fluids. This possibility emphasizes the need to monitor an area once adjacent seismicity is detected, to determine accurately the relative position of the earthquakes to the zone of fluid injection, and to assess the type and the extent of the faulting involved.

On the basis of the present understanding of the phenomena of injection-induced earthquakes, several factors are recommended for consideration in the development of regulations and procedures for controlling deep well injection operations. These recommendations are made from a seismological point of view alone and are not intended to supersede or replace alternative considerations made for other purposes. The recommended considerations include the following:

Site Selection

- Reservoirs that are characterized by high transmissivity and storativity and, therefore, are capable of receiving fluid at low injection pressures are less likely to be the site of induced earthquakes.
- An estimate of the tectonic stress based on regional or surface measurements made before drilling could serve as an early warning of potential earthquake problems and unanticipated low formation fracture or breakdown pressures.
- Because faults within the range of influence of an injection well are the potential loci for induced earthquakes, the absence of significant faults reduces the possibility of triggered seismicity. Geologic and geophysical surveys conducted to detect faults that may intersect the reservoir also would help in evaluating the integrity of the confining layer.
- The existence of regional seismicity in the vicinity of a proposed site should be taken as evidence of sufficient levels of tectonic stress and of the presence of potential slip surfaces (faults) necessary for natural and induced earthquakes.

Well Drilling and Completion

- Estimates of the storativity and the transmissivity of the reservoir based on standard measurements of permeability, porosity, and reservoir thickness made at the time of well completion would provide an important means of predicting the buildup of injection pressure required to maintain a given injection rate.
- If it can be accomplished without threatening the confining zone, then a stress measurement that uses the hydraulic fracture technique in or below the reservoir rock is the key environmental parameter for predicting the potential for induced earthquakes and the possibility of low-formation fracture pressures.
- Careful measurement of the initial formation pore pressure at the time of well completion and before injection provides important information on the proximity to failure conditions in the unaltered natural state.
- If anticipated injection pressures approach the levels expected to trigger earthquakes according to the Mohr-Coulomb failure criterion, assuming regional or generic values for the coefficient of friction and the cohesion of faults, then more precise local measurements of these values would reduce, if possible, the

uncertainty in the specific level of injection pressure at which earthquakes would be expected.

Well Operation and Monitoring

- If reliable measurements of the local stress field are available, then it is possible to estimate the maximum injection pressure that can be used without fear of fracturing the formation or inducing earthquakes by allowing slip on a preexisting fault. These estimates can be made by using the Mohr-Coulomb failure criterion.
- Actual pressure-time curves measured at the wellhead can be compared with predicted curves to assure that the reservoir is behaving as assumed. Any increase in apparent transmissivity should be scrutinized as possible evidence for the opening of fractures or the occurrence of faulting.
- If the maximum injection pressure at a site approaches the critical level anticipated to trigger the occurrence of earthquakes, then it would be prudent to monitor the injection operation by using at least one high-sensitivity seismograph. Monitoring should continue as long as significant levels of elevated fluid pressure are maintained in the reservoir.
- The occurrence of any earthquakes near the bottom of an injection well should be reviewed carefully to assess the possibility that potentially damaging earthquakes might be induced and the potential for fracturing or faulting through the containment zone. Installation of additional seismic monitoring stations would then be recommended to locate and analyze any subsequent earthquake activity.

INTRODUCTION

The injection of waste into deep isolated aquifers is being increasingly utilized for the disposal of certain types of hazardous fluid materials (Environmental Protection Agency, 1974, 1985). Other deep well injection operations are carried out routinely for the disposal of nonhazardous waste (for example, excess oil field brine), solution mining, purposes of geothermal energy extraction, the secondary recovery of hydrocarbons, and the underground storage of natural gas intended for later redistribution during peak winter months. Of these different types of well operations, secondary recovery is by far the most common use of deep well fluid injection (Mankin and Moffet, 1987). Although most deep well injection operations have no impact on earthquake activity, it has been shown conclusively that, under some conditions, the increase of fluid pressure in the reservoir associated with deep well injection can trigger or induce earthquakes. The first and best known instance, as well as the largest, of these induced earthquakes occurred during the mid-1960's in association with the waste injection well at the Rocky Mountain Arsenal near Denver, Colo. Since this discovery, additional examples of earthquakes induced by deep well injection have been documented (pl. 1; table 1). It is conceivable, if not likely, that other examples of such induced earthquakes may have gone unnoticed because they were small and no seismograph stations were nearby to record them.

Investigations of several of the earthquakes associated with deep well injection have led to some understanding of the probable physical mechanism for the triggering and of the criteria for predicting whether earthquakes will be triggered that depend on the local state of stress in the Earth's crust, the injection pressure, and the physical and the hydrologic properties of the rocks into which the fluid is being injected. The purpose of this report is to summarize the current state of understanding of this phenomenon, to describe the criteria for predicting whether earthquakes will be triggered by fluid injection, and to indicate from a seismological point of view factors to be considered in developing regulations and operating procedures to minimize the seismic hazard associated with deep well injection.

Although several research issues remain unresolved, considerable information is currently available that may be of use in the development of operating procedures for deep injection wells that will minimize the possibility of problems associated with induced earthquakes. Fortunately, favorable conditions for the siting of a deep injection well, namely the desirability of high permeability and porosity in the injection zone and a site situated away from known fault structures also tend to be conditions for which the occurrence of induced earthquakes is less likely. Thus, implementation of these recommendations probably would have minimal adverse impact on site selection or operational procedures for injection wells located at otherwise favorable sites.

This report also includes four appendixes. Appendix A contains case histories of earthquakes associated with well operations. Appendix B is a brief summary of reservoir-induced seismicity. Appendix C describes the components of the Modified Mercalli Intensity Scale. Appendix D is a glossary.

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Table 1. Acknowledged cases of seismicity associated with well operations

Well site or oil field location	Type	Depth (m)	Injection pressure (bars)	Maximum earthquake magnitude	Year injection began-ended	Year of earthquakes
Ashtabula, Ohio	Waste disposal	1,845	100	3.6	1986–	1987
Cogdell Canyon Reef, Tex.	Secondary recovery	2,071	199	4.6	1956–	1974–79
Dale, N.Y.	Solution mining	426	55	1.0	1971	1971
Rocky Mountain Arsenal, Denver, Colo.	Waste disposal	3,671	76	5.5	1962–66	1962–67
Fenton Hill, N. Mex.	Geothermal/stimulation	2,700	200	<1.0	1979	1979
Flashing Field, Tex.	Gas withdrawal	3,400	?	3.4	1958–	1973?–83
The Geysers, Calif.	Geothermal	3,000	?	4.0	1966–	1975–
Gobles Field, Ontario, Canada	Secondary recovery	884	?	2.8	1969–	1979–84
Imogene Field, Tex.	Gas withdrawal	2,400	?	3.9	1944–	1973?–83
Love County, Okla.	Secondary recovery/stimulation	3,622	277	2.8?	1965–,1979–	1977–79
Matsushiro, Japan	Research	1,800	50	2.8	1970	1970
Northern Panhandle, Tex.	Secondary recovery	2,022	21	3.4	1979–	1983–84
Calhio, Perry, Ohio	Waste disposal	1,810	114	2.7?	1975–	1983–87
Rangely, Colo.	Secondary recovery/research	1,900	83	3.1	1958–	1962–75
Rocky Mountain House, Alberta, Canada.	Gas withdrawal	4,000	?	4.0	1970–	1974–
Sleepy Hollow, Neb.	Secondary recovery	1,150	56	2.9	1966–	1977–84
Snipe Lake, Alberta, Canada	.....do.	?	?	5.1	1963–	1970
Cold Lake, Alberta, Canada	Secondary recovery/waste disposal	?	?	~2.0	?	1984–
Permian basin fields:				4.4		1964–
Dollarhide, Tex.-N. Mex.	Secondary recovery	2,590	138	~3.5	1959–	1964–
Dora Roberts, Tex.	....do.	3,661	431	~3.0	1961–	1964–
Kermit Field, Tex.	....do.	1,829	221	~4.0	1964–	1964–
Keystone I Field, Tex.	....do.	975	103	~3.5	1957–	1964–
Keystone II Field, Tex.	....do.	2,987	176	~3.5	1962–	1964–
Monahans, Tex.	....do.	2,530	207	~3.0	1965–	1964–
Ward-Estes Field, Tex.	....do.	914	117	~3.5	1961–	1964–
Ward-South Field, Tex.	....do.	741	138	~3.0	1960–	1964–
War-Wink South, Tex.	Gas withdrawal	1,853	?	~3.0	1969–	1964–

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OVERVIEW OF EARTHQUAKES INDUCED BY DEEP WELL INJECTION

Well-documented examples of seismic activity induced by fluid injection include earthquakes triggered by waste injection near Denver (Healy and others, 1968; Hsieh and Bredehoeft, 1981); secondary recovery of oil in Colorado (Raleigh and others, 1972), southern Nebraska (Rothe and Lui, 1983), West Texas (Davis, 1985), and western Alberta (Milne, 1970) and southwestern Ontario, Canada (Mereu and others, 1986); solution mining for salt in western New York (Fletcher and Sykes, 1977); and fluid stimulation to enhance geothermal energy extraction in New Mexico (Pearson, 1981). In two specific cases—near Rangely, Colo. (Raleigh and others, 1976), and in Matsushiro, Japan (Ohtake, 1974)—experiments to control directly the behavior of large numbers of small earthquakes by manipulation of fluid injection pressure were conducted successfully. Table 1 gives a brief listing of each of the cases in which seismicity was clearly associated with fluid injection or other types of adjacent well activities. A more complete summary is provided in Appendix A.

Other cases of induced seismicity, which were the result of either fluid injection or reservoir impoundment, were reviewed and discussed by Simpson (1986a). Unlike fluid injection, however, induced seismicity associated with dams and reservoirs also is affected by the actual physical weight of the water impounded. By contributing to the local stress regime, this effect of the water load can change the local hydrologic properties of the reservoir rock and thus magnify the resulting changes in pore fluid pressure associated with elevating the local water table (Roeloffs, 1988). A brief discussion of the phenomenon of reservoir-induced seismicity is presented in Appendix B.

Although it is true that earthquakes can be triggered without fluid injection (for example, see the sections on the Wilmington and the Flashing oil fields in Appendix A), most of the earthquakes induced by well activities are associated with water-flooding operations to enhance the secondary recovery of hydrocarbons (table 1). This is not surprising because the conditions for failure are much more favorable in injection operations of this type. Fluid injection for the purpose of secondary recovery typically involves injection at high fluid pressures into confined reservoirs of limited extent and low permeability. Often, the producing field is a structural trap, perhaps defined by fault-controlled boundaries. However, in waste-disposal operations, it is preferable to inject into large porous aquifers having high permeabilities that are away from known fault structures. Furthermore, waste-disposal operations typically involve only one to a few wells at any one location, whereas secondary recovery techniques often involve large arrays that comprise tens of wells over the entire extent of the producing field. These differences between the two types of injection operations make well activities for the purpose of secondary recovery much more conducive to triggering adjacent seismicity.

In each of the well-documented examples of earthquakes triggered by deep well injection, convincing arguments that the earthquakes were induced relied upon three principal characteristics of the earthquake activity. First, there was a very close geographic association between the zone of fluid injection and the locations of the earthquakes in the resulting sequence. Second, calculations based on the measured or the inferred state of stress in the Earth's crust and the measured injection pressure indicated that the theoretical threshold for frictional sliding along favorably oriented preexisting fractures, as indicated by the Mohr-Coulomb failure criterion, was likely exceeded. And, third, a clear disparity was established between any previous natural seismicity and the subsequent earthquakes, the induced seismicity often being characterized by large numbers of small earthquakes occurring within a relatively short time interval.

Many of the sites where earthquakes have occurred operate at injection pressures well above 100 bars ambient (table 1). The exceptions tend to be sites characterized by a close proximity to recognized surface or subsurface faults. In the Rangely and the Sleepy Hollow, Nebr., oil field cases, faults are located within the pressurized reservoir and were identified on the basis of subsurface structure contours. The Attica-Dale, N.Y., and the Matsushiro cases occurred close to prominent fault zones exposed at the surface (the Clarendon-Linden and the Matsushiro fault systems, respectively). In the most prominent case of induced seismicity as the result of waste-disposal operations, the Rocky Mountain Arsenal well near Denver, fluid was inadvertently injected directly into a major subsurface fault structure, which was identified later on the basis of the subsequent induced seismicity (Healy and others, 1968) and the properties of the reservoir into which fluid was being injected, as reflected in the pressure-time record (Hsieh and Bredehoeft, 1981).

The Rocky Mountain Arsenal case is considered to be the classic example of earthquakes induced by deep well injection. Before this episode, the seismic hazard associated with deep well injection had not been appreciated fully. At the Rocky Mountain Arsenal, injection into the 3,700-meter (m)-deep disposal well began in 1962 and was quickly followed by a series of small earthquakes, many of which were felt in the greater Denver area (fig. 1*A*). It was not until 1966, however, that a correlation was noticed between the frequency of earthquakes and the volume of fluid injected (fig. 2). Pumping ceased in late 1966 specifically because of the possible hazard associated with the induced earthquakes; afterward, earthquakes near the bottom of the well stopped. Over the next 2 years (yr), however, earthquakes continued to occur up to 6 km away from the well as the anomalous pressure front, which had been established around the well during injection, continued to migrate outward from the injection point. The largest earthquakes in the sequence (M 5.0–5.5) occurred in 1967 (fig. 1*B*), long after injection had stopped and well away from the point of fluid injection itself.

These results imply that the fluid pressure effects from injection operations can extend well beyond the expected range of actual fluid migration. Indications have shown, however, that the risk posed by triggered earthquakes can be mitigated by careful control of the activity responsible for the induced seismicity. As shown by a number of the cases detailed in Appendix A, seismicity eventually can be stopped either by ceasing the injection or by lowering pumping pressures. The occurrence of the largest earthquakes involved in the Rocky Mountain Arsenal case a year after pumping had ceased, however, indicates that the process, once started, may not be controlled completely or easily.

CONDITIONS FOR EARTHQUAKE GENERATION

The case histories of injection-induced seismicity documented in Appendix A demonstrate that, in sufficiently

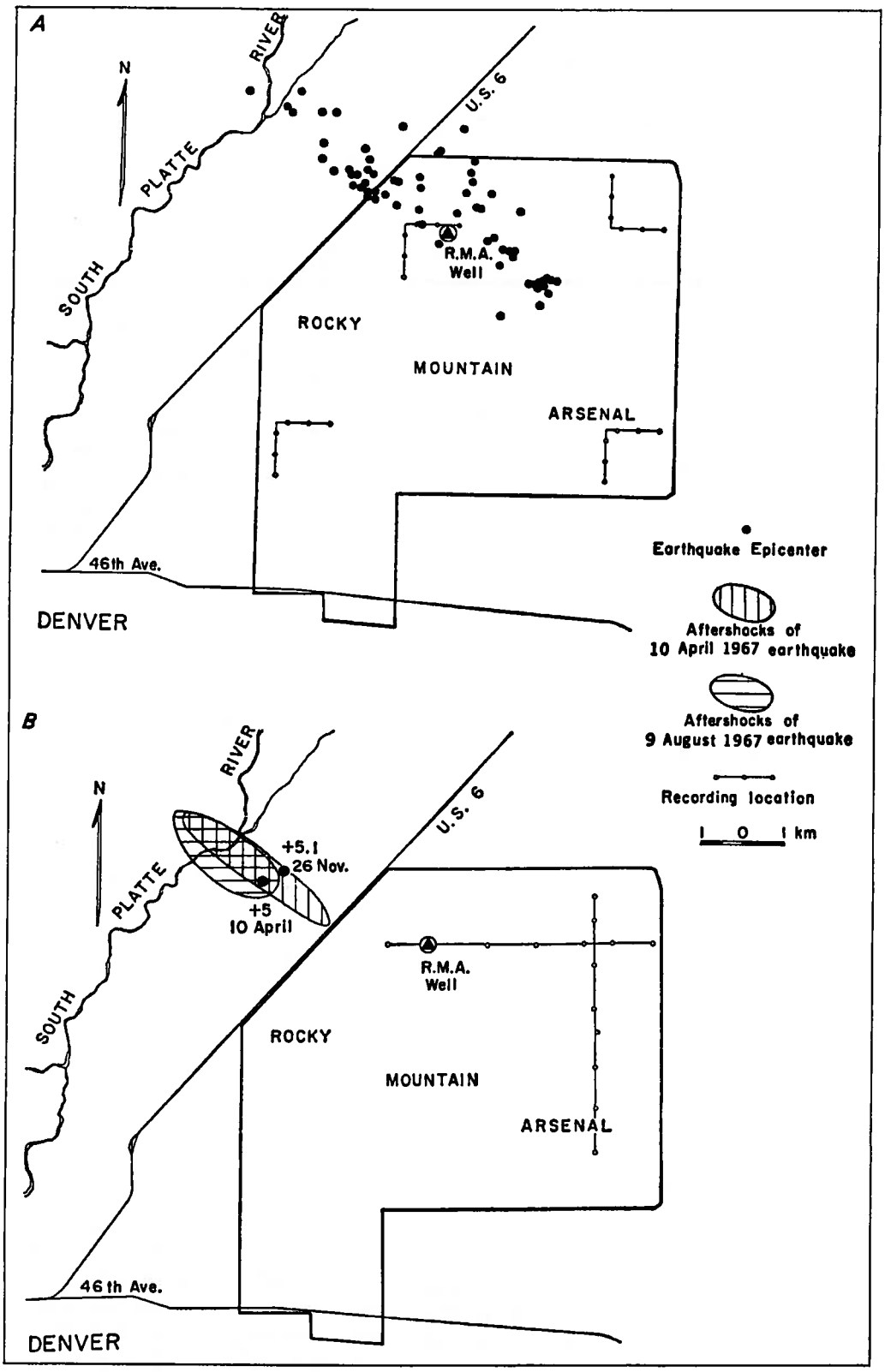


Figure 1. Earthquake activity near the Rocky Mountain Arsenal waste-disposal well, Colorado. *A*, Epicentral distribution of earthquakes during January and February 1966. *B*, Aftershock distributions of the large 1967 earthquakes. Reprinted from Healy and others (1968) and published with permission.

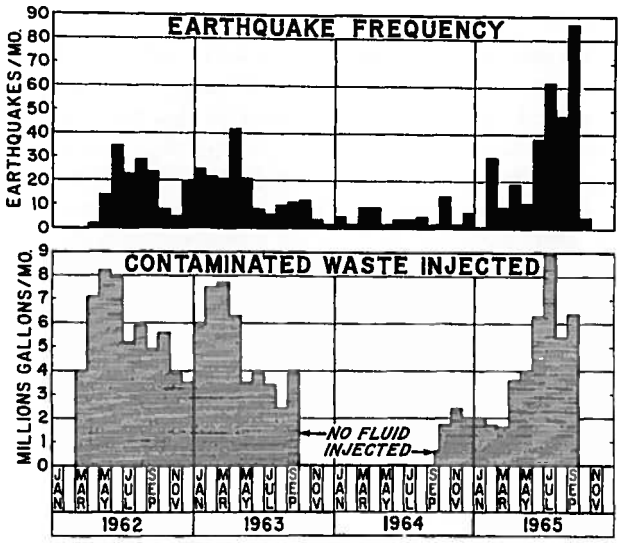


Figure 2. Correlation between earthquake frequency (top) and volume of contaminated waste injected (bottom) at the Rocky Mountain Arsenal well, Colorado. Reprinted from Healy and others (1968) and published with permission.

prestressed regions, elevating formation fluid pressure by several tens of bars can cause a previously quiescent area to become seismically active. However, not all high-pressure injection wells trigger earthquakes. The reasons why depend on the characteristics of the earthquake faulting process, the local hydrologic and geologic properties of the zone of injection, the *in situ* stress field, and the specific conditions for earthquake triggering, many of which have not been understood or appreciated until recently. A fundamental distinction must be recognized, however, between factors that *cause* earthquakes versus mechanisms that may *trigger* earthquakes. Earthquakes result from the sudden release of stored elastic strain energy by frictional sliding along preexisting faults. The underlying causes of earthquakes are, therefore, the forces that are responsible for the accumulation of elastic strain energy in the rock and that raise the existing state of stress to near critical levels. Consequently, the hazard associated with fluid injection is not that it can generate sufficient strain energy for release in earthquakes, but that it may act locally to reduce the effective frictional strength of faults and, thereby, to trigger earthquakes in areas where the state of stress and the accumulated elastic strain energy are already near critical levels as a result of natural geologic and tectonic processes.

Mohr-Coulomb Failure Criterion

Because the shear strength of intact rock is considerably greater than the frictional strength between rock surfaces, slip during an earthquake typically occurs along preexisting faults and will occur when the shear stress (τ) resolved across the fault exceeds the inherent shear strength (τ_0) and the frictional stress on the plane of slip. Quantitatively, this condition is termed the Mohr-Coulomb failure criterion and is expressed by the following linear relation:

$$\tau_{crit} = \tau_0 + \mu\sigma_n,$$

where τ_{crit} is the critical shear stress required to cause slip on a fault, μ is the coefficient of friction, and σ_n is the normal stress acting across the fault (Jaeger and Cook, 1979). For weak fault zones that have little cohesion, τ_0 is nearly zero, and slip will occur when τ is greater than or equal to an amount that is simply the product of μ and the stress normal to the plane of slip; that is, the frictional strength of the fault:

$$\tau_{crit} = \mu\sigma_n.$$

Figure 3 shows values of maximum shear stress (τ) as a function of effective normal stress (σ_n) for a variety of rock types (Byerlee, 1978). For most rock types, the data indicate that μ ranges between 0.6 and 1.0.

When fluid is present in the rocks, the effective σ_n is reduced by an amount equal to the pore pressure, and the shear stress (τ) required to cause sliding is reduced to the following:

$$\tau_{crit} = \mu\,(\sigma_n - p).$$

This reduction in the effective strength of crustal faults is the essential mechanism of induced seismicity; that is, for a constant state of tectonic stress, the effective strength of crustal faults can be reduced below the critical threshold by increasing the fluid pressure contained within the rocks, which leads to a sudden slip and the occurrence of an earthquake.

Description of the State of Stress By Using the Mohr Circle

A simple graphical method for describing the state of stress and how it is altered by the introduction of fluids under pressure is given by the Mohr circle diagram (fig. 4, right; Jaeger and Cook, 1979; Simpson, 1986a). The stresses acting on a given fault plane can be specified with respect to an orthogonal coordinate system and are referred to as the principal stress axes along which stresses are purely compressional. The stress components relative to these principal axes are called the principal stresses and are usually designated σ_1 (maximum), σ_2 (intermediate), and σ_3 (minimum). Shear (τ) and normal (σ_n) stresses along and across fractures of various orientations are linear combinations of the maximum and the minimum compressive stresses (σ_1 and σ_3, respectively) and are defined by the

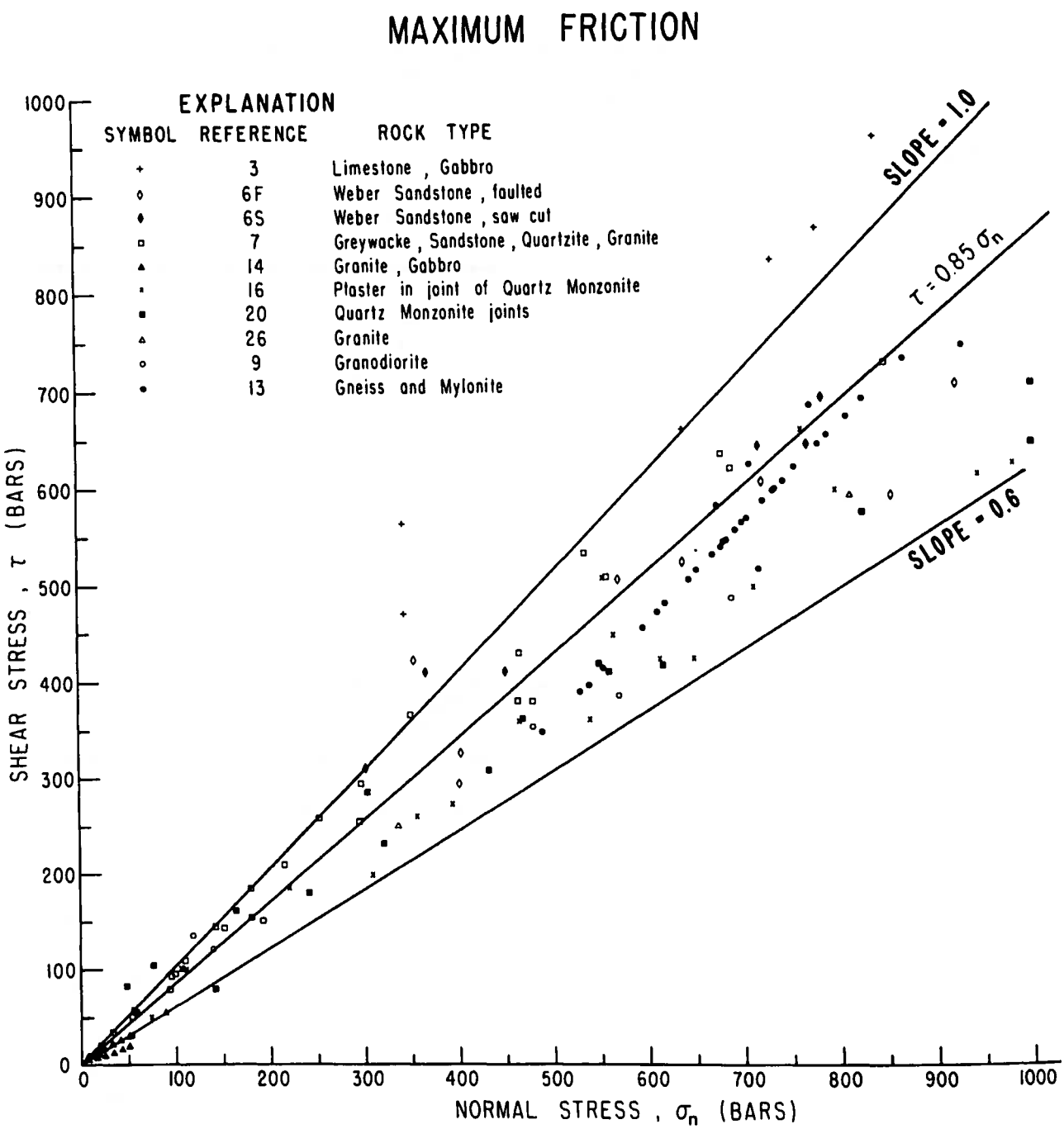


Figure 3. Maximum shear stress as a function of effective normal stress for a variety of rock types. The data suggest that the coefficient of friction ranges between 0.6 and 1.0. τ, shear stress; σ_n, normal stress; and μ, coefficient of friction. Reprinted from Zoback and Healy (1984) and published with permission.

locus of points around the Mohr circle, whose center is the average between σ_1 and σ_3 (fig. 4*B*, right). Thus, for a specific fault plane oriented at angle α with respect to the σ_3 direction (fig. 4*B*, left), τ and σ_n acting along and across that plane will be determined by a specific point on the Mohr circle (identified by angle 2α drawn from the middle, fig. 4*B*, right). Larger stress differences between the maximum and the minimum principal stresses (that is, the deviatoric stress) result in larger Mohr circles and, thus, larger available shear stresses for causing slip along favorably oriented fractures.

The Coulomb failure criterion is represented by a line that has a slope equal to μ and an intercept equal to τ_0 (fig. 4*A*). Relative effective values of σ_1 and σ_3 necessary for

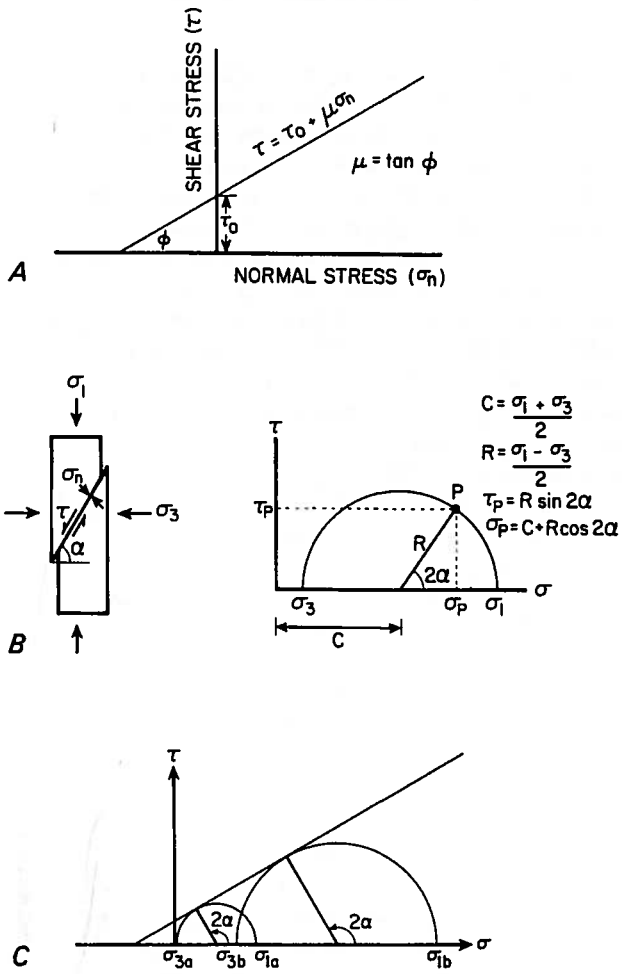


Figure 4. Relations between effective stresses and conditions for failure (slip) on a preexisting fault. *A*, Coulomb's law for failure in dry rock showing the relation between the shear stress (τ) required for failure and the normal stress (σ_n) acting across the plane of slip. Here τ_0 is the cohesion, μ is the coefficient of friction, and ϕ is the angle of internal friction. *B*, The Mohr circle diagram (right), which provides a graphical method by which the maximum (σ_1) and the minimum (σ_3) principal (compressive) stresses can be resolved into shear (τ) and normal (σ_n) components on a plane at angle α to the σ_3 direction (left). The resolved shear (τ_p) and the normal stress (σ_p) define a point (P) given by the radius (R) and center (C) of the Mohr circle. *C*, The Mohr-Coulomb failure criterion. Given any particular state of stress, failure will occur on a plane containing the intermediate stress (σ_2) and oriented at an angle α to σ_3 if the Mohr circle containing points σ_1 and σ_3 intersects the Columb failure curve defined in *A*. Reprinted from Simpson (1986a) and published with permission.

failure thus define circles tangent to this failure envelope (fig. 4*C*). In other words, fault planes whose orientations with respect to a given stress field (σ_1 and σ_3) define values along the Mohr circle that intersect the failure envelope for a given τ_0 and μ will be most likely (most favorably oriented) to slip (fig. 4*C*).

Figure 5 shows how an initial stress state (right Mohr circle) determined at the bottom of a well near Perry, Ohio, is modified by changes in pore pressure (Appendix A). As discussed in the previous section, in the presence of a fluid, compressive stresses are opposed by the hydrostatic fluid pressure. This reduces the effective stress levels by an amount equal to the formation pore pressure and moves the Mohr circle to the left (fig. 5, middle circle). In this example, the state of stress under hydrostatic conditions is close to but does not exceed the failure criterion for a fracture that has no cohesion. Increasing the pore pressure by an amount equal to a nominal injection pressure of 110 bars moves the Mohr circle even farther towards the failure envelope (fig. 5, left circle) and, in fact, for the example shown, indicates that a critical stress level is reached for fractures having τ_0 of as much as 40 bars and μ of 0.6. Fractures that have less cohesion or lower coefficients of friction also would be susceptible to failure.

Conditions for Induced Seismicity

By using the Mohr-Coulomb failure criterion, it is now possible to specify the conditions under which seismicity is most likely to be triggered by fluid injection. First, the existing regional stress field needs to be characterized by high deviatoric stress; that is, the difference between σ_1 and σ_3 is large, which results in large Mohr circles (compare circles in fig. 4*C*). This does not require that the state of stress itself be large, only that large stress differences exist for different fault orientations. In fact, many area identified as close to incipient failure are characterized by relatively low states of stress (σ_{1a} and σ_{3a} in fig. 4*C*). This

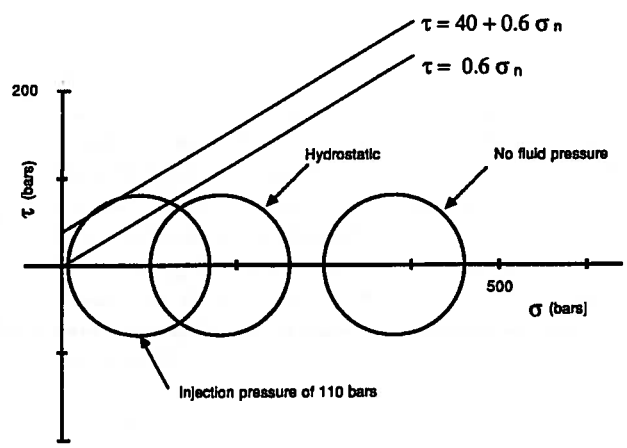


Figure 5. Estimates of shear stress and principal stresses in relation to possible Coulomb failure curves at a nominal depth of 1.8 km near the bottom of an injection well near Perry, Ohio (table 1). τ, shear stress; σ, principal stress; and σ_n, normal stress.

is because low stress states may correspond with low normal stresses acting across potential slip surfaces. Low normal stress implies low frictional strength; thus, faults are weak and easily induced to slip. In the Rocky Mountain Arsenal case, the induced earthquakes occurred in a region of normal faulting that is characterized by a relatively low state of stress and, as a consequence, by a relatively low effective normal stress (but a high shear stress) acting across the fault that slipped (Zoback and Healy, 1984).

Second, preexisting favorably oriented faults or fractures must be available for slip. In general, the shallow part of the Earth's crust is characterized by numerous fractures of different sizes and orientations. However, many of these fractures are small and are capable of generating only small earthquakes of little consequence, and many may not have the proper orientation relative to the existing regional tectonic stress field such that the conditions for failure are met. Thus, for fluid injection to trigger substantial numbers of significant earthquakes, a fault or faults of substantial size must be present that are properly oriented relative to the existing state of stress, characterized by relatively low effective shear strength, and sufficiently close in proximity to well operations to experience a net pore pressure increase. As discussed in in the section "Hydraulic Factors in Earthquake Triggering," the effects of fluid injection dissipate rather quickly as distance from the well increases. This implies that, for typical values of hydrologic properties commonly associated with aquifers of large spatial extent targeted as reservoirs for waste disposal by fluid injection, the pore pressure effect beyond about 10 km is minimal.

Third, injection pressures at which well operations are conducted are relatively high; for example, the Cogdell Canyon Reef oil field in West Texas (table 1), where the largest earthquake known to be associated with secondary recovery operations in the United States was triggered (Davis, 1985), operates at fluid injection pressures of nearly 200 bars above ambient. Other extensive well operations that are in the same tectonic province and, in fact, operate within the same pay zone (the Canyon Reef Formation) are not inducing adjacent seismicity, but these wells typically operate at injection pressures of 100 bars or less. Similarly, the Calhio waste-disposal wells in northeastern Ohio (table 1) may have triggered several small earthquakes in close proximity (<5 km) to the injection site (Nicholson and others, 1988), yet a number of other injection wells that utilize the same basal sandstone layer (the Mount Simon Formation) for the disposal of hazardous and nonhazardous wastes have not done the same. These other wells, however, typically operate at about half the pressure utilized by Calhio. Interestingly, a waste-disposal well located near Ashtabula, Ohio, that became operational in July 1986 and that utilized the same reservoir formation and similar injection pressures to those used by the Calhio wells (Appendix A) triggered a M 3.6 earthquake and a large number of aftershocks in July 1987 (Armbruster and others, 1987).

The hydrologic properties of a reservoir are responsible for how rapidly fluid is accepted and, thus, control the injection pressure required to maintain a constant fluid injection rate (volume of fluid flow into the well). These properties also control how rapidly the pore pressure increase in the reservoir dissipates with distance from the point of fluid injection. Aquifers of large spatial extent, which require low injection pressures for high injection rates, also dissipate the pressure effect most rapidly. This insures that, unless fluid is injected directly into a fault zone (as in the Rocky Mountain Arsenal case), the net pore pressure change from fluid injection will not extend for any appreciable distance from the well. Thus, the distance between a favorably oriented fault or fracture capable of slip and an operating injection well also will become a critical factor in determining the potential for induced seismicity.

Assessing the proximity of favorably oriented preexisting fractures to a potential waste-disposal site in the Central and the Eastern United States is difficult because many of the fault structures responsible for earthquakes in the past and, presumably, the most likely ones responsible for earthquakes in the future are not easily identified. Unlike large historical earthquakes in the Western United States, those that have occurred in the East have yet to produce any primary surface manifestation. This makes identification of active faults or potentially active faults difficult. Reducing the risk of siting an injection well near a major fault may require extensive subsurface geologic mapping to assess the proximity of potential fault structures. Substantial progress has been made, however, in the ability to assess the local state of stress and, thus, to ascertain the degree to which any potential faults or fractures in the vicinity of the well may be close to failure (Evans, 1988).

STATE OF STRESS IN THE EARTH'S CRUST IN THE UNITED STATES

Estimating the state of stress throughout the continental United States has become a very active area of research over the past several years. Its determination is extremely important to a further understanding of regional patterns of crustal deformation and to any accurate assessment of the local seismic hazard. The amount of energy available to be released in an earthquake is determined by the amount of elastic strain energy stored in the rocks of the Earth's crust. The amount of strain energy available for release depends, in turn, on the state of stress. It is the state of stress that determines how close to failure a preexisting fault may be and, as shown in the section "Hydraulic Factors in Earthquake Triggering," how much fluid pressure is required to trigger fault slip or to hydrofracture intact rock. Because of

its importance, the variation in time and space of the magnitude and the direction of the stress field has become the subject of recent intense study. In many cases, the techniques developed to determine the state of stress actually measure secondary effects, such as strain. The greatest difficulty, however, is measuring the necessary parameters at depths where earthquakes actually occur; otherwise, questionable extrapolations must be used from measurements made at shallow depths. In the case of earthquakes induced by fluid injection, the seismicity is likely to be shallow and in close proximity to the well itself. Thus, the advantage in assessing the potential for an existing well to trigger earthquakes is that its presence provides reasonable access to the hypocentral regions where any potential induced events are most likely to occur.

Determining Magnitudes and Orientations of the Local State of Stress

Measurements of the state of stress can be accomplished through a variety of techniques. In general, it is somewhat easier to determine the orientation of the principal stresses than it is to determine their magnitude. Nevertheless, orientations alone are important because the current stress regime may be substantially different from that which existed when major faults in the area were originally produced. This is especially true in the Eastern United States, where most faults are old, seismicity is relatively low, and the identification of active fault structures is more difficult. The orientation of the principal stresses determined from actual *in situ* measurements (fig. 6) can thus aid in identifying those faults that have orientations conducive to slip in the existing tectonic stress field. Orientations and, to some extent, relative magnitudes of the principal stresses can be determined from earthquake focal mechanisms (Michael, 1987), borehole elongations (Gough and Bell, 1981; Plumb and Hickman, 1985), core-induced drilling fractures (Evans, 1979; Plumb and Cox, 1987), and, in some cases, the orientation of young geologic features, such as dikes, volcanic vent alignments, or recent fault offsets (Zoback and Zoback, 1989). Reliable determination of the absolute magnitude of the principal stresses typically requires measurements made by using the hydraulic fracture technique.

Stress Orientation Indicators

Earthquake Focal Mechanism Solutions

Earthquake focal mechanisms are some of the most commonly utilized indicators of principal stress directions (Michael, 1987). Focal mechanism solutions define two alternative planes of slip, as well as two stress axes—one of compression and one of tension (see fig. A1). A discussion of the possible orientations that these particular stress axes may have relative to the principal stress directions is given by McKenzie (1969).

The principal contribution of focal mechanism solutions is that they readily identify the specific type of faulting and the orientation of actual planes of slip (faults) in the local area. By inference, the relative magnitude of the state of stress can then be derived, if one of the three principal stresses (σ_1, σ_2, or σ_3) is assumed to correspond with the vertical stress (S_v) induced by the weight of the overburden. Thus, in areas dominated by normal faulting, S_v corresponds with σ_1, implying that the magnitude of the other two orthogonal stresses (S_H and S_v, which correspond to the maximum and the minimum horizontal compressive streses, respectively) are less than the overburden pressure. In regions of strike-slip faulting, S_v is intermediate, and, in regions of thrust faulting, S_v is less than either S_H or S_h (Anderson, 1951). If the orientation of the principal stresses is known from other data in the same stress province, then focal mechanisms can be used to predict the orientation of available planes of slip and the degree to which such planes are close to the plane of maximum shear.

Wellbore Breakouts

Wellbore breakouts, also known as borehole elongations, are a phenomenon of wellbore deformation induced by inhomogeneous stresses in the crust (fig. 6*C*). When a well is drilled into a medium, the presence of the cavity creates stress concentrations around the borehole wall (Hubbert and Willis, 1957). These stress concentrations are greatest in the section of the wall parallel to the direction of the minimum horizontal compressive stress, S_h. Bell and Gough (1979) interpreted the elongation of the borehole to be the result of spalling of weak material off the wellbore wall caused by localized compressive shear failure in the region where the compressive stress concentration is largest. Subsequent data (Plumb and Hickman, 1985; Plumb and Cox, 1987) has confirmed that wellbore breakouts are indeed the result of stress-induced shear failure under compression and that the orientations of the borehole elongations consistently reflect the orientation of S_h (Zoback and others, 1985). Measurement of the shape of the borehole wall with depth by using standard logging techniques (dipmeter or televiewer) can assess the consistency of the orientations of S_H and S_h as a function of depth, as well as their spatial variation between wells (fig. 6*A*).

Core-Induced Fractures

A recently identified stress orientation indicator, similar in some respects to wellbore breakouts, is the presence of core-induced drilling fractures observed in retrieved bottom-hole cores. These phenomena, also called petal centerline fractures, typically consist of near-vertical or steeply dipping planar fractures observed in the oriented rock cores (fig. 6*C*) and are believed to represent extensional fractures formed in advance of a downcutting drill bit

(Kulander and others, 1977; GangaRao and others, 1979). However, unlike wellbore breakouts, which are compressional features (and, therefore, form parallel to S_h), the orientation of these fractures is thought to parallel the maximum horizontal compressive stress, S_H. Evans (1979) examined oriented cores from 13 natural gas wells in Pennsylvania, Ohio, West Virginia, Kentucky, and Virginia and determined core-induced fracture orientations for hundreds of meters of core in most of the wells. Plumb and Cox (1987) also compiled regional data sets of core-induced fracture orientations (fig. 6*B*). The inferred S_H directions derived from these measurements are generally consistent within wells, between nearby wells, and with adjacent hydraulic fracturing results, borehole elongations, and focal mechanism solutions (fig. 6).

Fault Offsets and Other Young Geologic Features

In the presence of an inhomogeneous stress field, young geologic features, such as dikes or volcanic vent alignments, are most likely to propagate in a direction parallel to S_H. This assumes, however, the absence of any preexisting fabric or other structural features, such as faults, that may preferentially control dike or vent-alignment formation. Fault offset data can be used like focal mechanism solutions to help constrain the orientation and the relative magnitudes of the existing stress field (Angelier, 1979; Michael, 1984), the added advantage being that the actual fault plane is known. The stress orientations derived, however, are valid only for the time period during which fault slip occurred and so are not necessarily valid for the

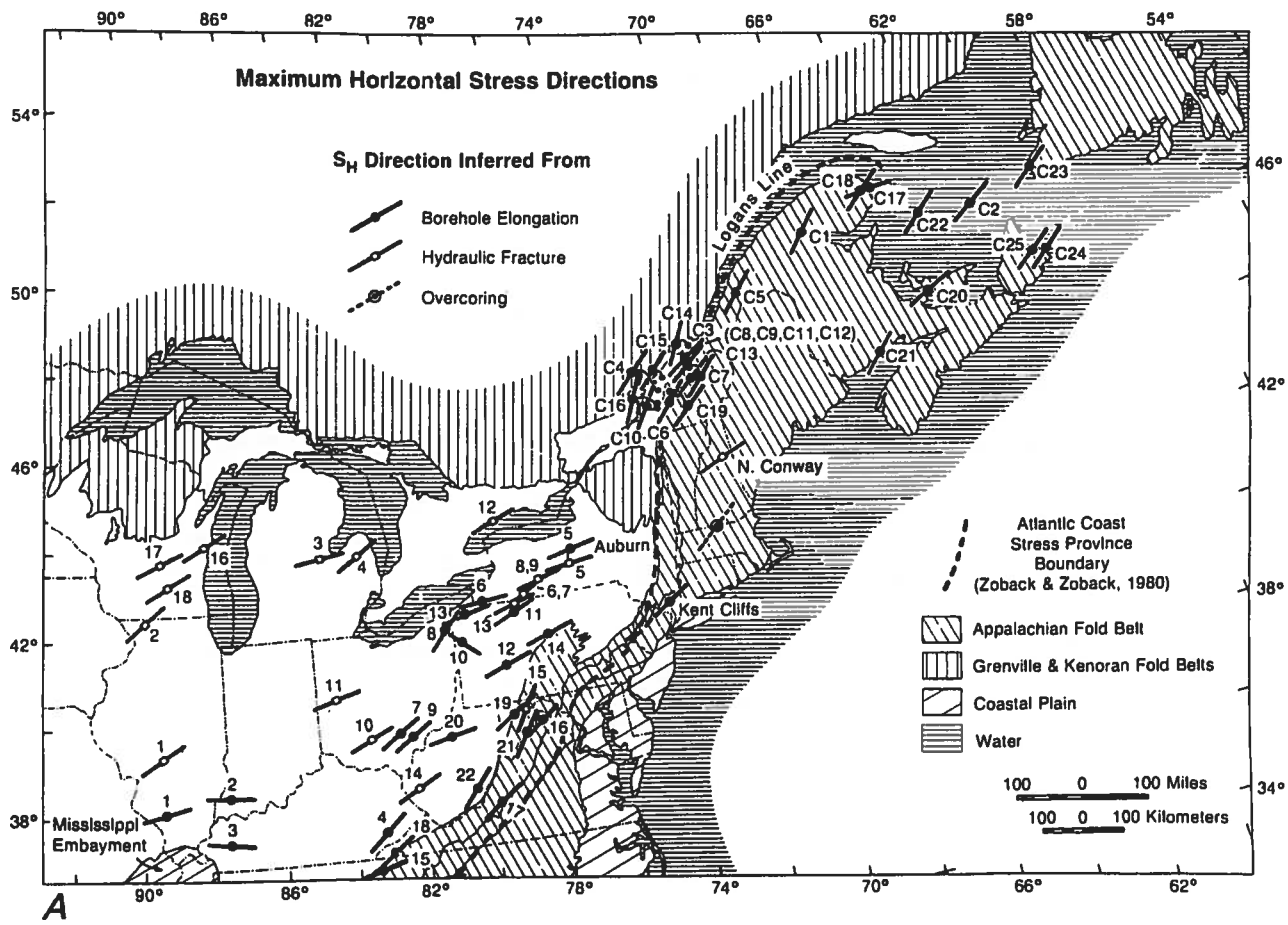
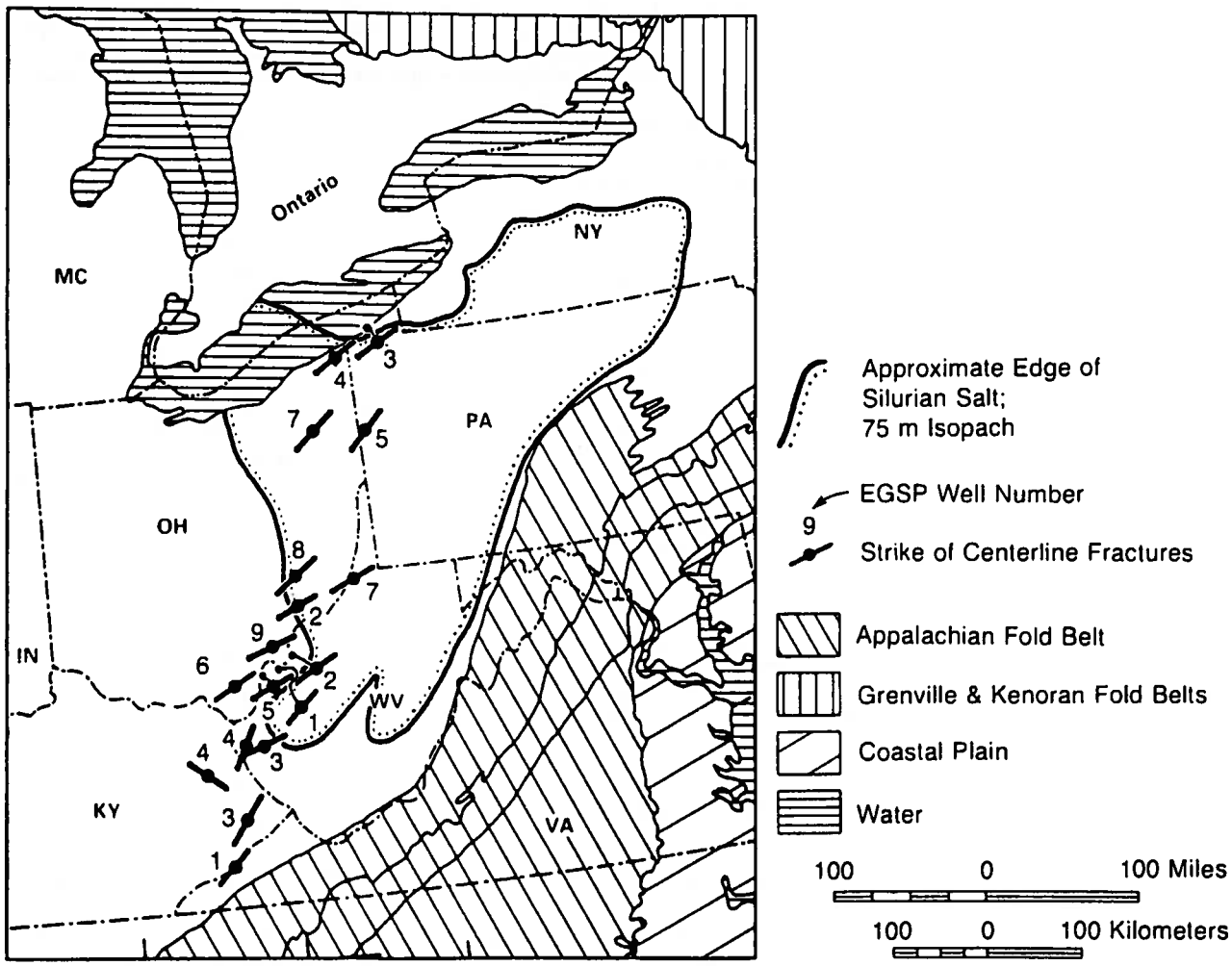


Figure 6. Maximum horizontal stress directions, strikes of core-induced fractures, and the orientation of various stress indicators. *A*, Maximum horizontal stress directions based on borehole measurements—borehole elongation data (dots); hydraulic fracture data (squares); and overcoring measurements (circled dots). *B*, The strikes of centerline fractures observed in Eastern Gas Shales Project (EGSP) cores. East-northeast-trending centerline fractures found throughout the Appalachian Basin correlate with contemporary stress directions shown in *A*. *C*, The relation between orientations of various stress indicators and principal stress directions observed in wells from the Appalachian Basin. Reprinted from Plumb and Cox (1987) and published with permission.

Coring-Induced Fractures



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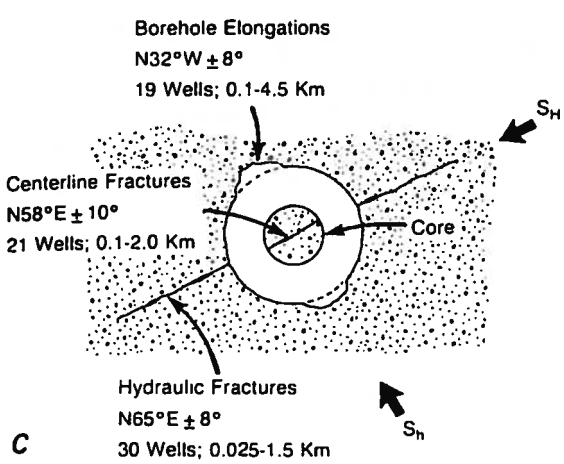

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Figure 6. Continued.

current tectonic stress field, particularly if the age of faulting is old.

Hydraulic Fracture Stress Measurements in Wells and Types of Pressure-Time Records

The most reliable measurements of the magnitude and the orientation of *in situ* stresses are made by the hydraulic fracture technique (Noorishad and Witherspoon, 1984). The principle involved with this technique is similar to that for core-induced fractures in that failure results from tension rather than from compression. In the hydraulic fracture technique, one principal stress is assumed to be parallel to the borehole and equal in magnitude to the overburden pressure; that is, S_v. If at any point the fluid pressure in the

borehole exceeds the strength of the intact rock and the stress concentration around the wellbore, then a hydraulic fracture is produced (fig. 6*C*). Because the points at which the borehole wall is weakest correspond to a vertical plane perpendicular to S_h, the hydraulic fracture will most likely propagate in that plane. The magnitude of S_h, therefore, can be determined from the pressure acting on the hydraulic fracture immediately after pumping into the well is stopped and the well is shut in. This is called the instantaneous shut-in pressure (ISIP). The magnitude of S_H can then be determined, providing that the assumption of elastic stress concentration around a circular borehole is valid. In some cases, however, the material around the wellbore clearly cannot support the concentration of stresses and fails in compression, resulting in borehole elongation (Bell and Gough, 1983), as discussed above. When this happens, the assumption of elastic behavior near the wellbore is clearly not valid, and S_H cannot be determined in the intervals exhibiting wellbore breakouts.

Basically, the method of hydraulic fracture stress measurement is to pack off an unfractured section of the wellbore and then to increase the fluid pressure in that section until a fracture occurs in the borehole wall. Because the section is isolated (that is, packed off), the pressure is monitored carefully, and, because only a small volume of fluid is used, a small controlled fracture is produced rather than a massive hydraulic fracture, as in the case of well stimulation to enhance circulation (Pearson, 1981). The fluid pressure required to cause the fracture is called the fracture pressure or the breakdown pressure (P_b). After a fracture is produced, fluid pressure in the packed-off section is then cycled repeatedly to determine the pressure required to reopen the fracture (P_{fo}) by pumping small volumes at a constant flow rate and by permitting "flow-backs" to occur following each injection cycle to allow for the drainage of excess fluid pressure. In general, the pressure and flow records produced under these controlled conditions will reflect both of the procedures used during hydraulic fracturing and the *in situ* stress field. Thus, careful analysis of the pressure-time histories recorded during hydrofracturing can be used to estimate the magnitude of the principal stress components. Stress orientation is then determined by using a borehole televiewer or impression packer to ascertain the orientation of the hydraulic fracture created. Figure 7 shows an example of a typical hydraulic fracture pressure-time record from a well drilled to a depth of 185 m in crystalline rock near the San Andreas Fault in central California. In the case of a waste-disposal well, this measurement ideally would be made in the anticipated zone of injection or, if possible, in the basement rock below the waste-disposal aquifer, so as not to interfere with the integrity of the confining layer.

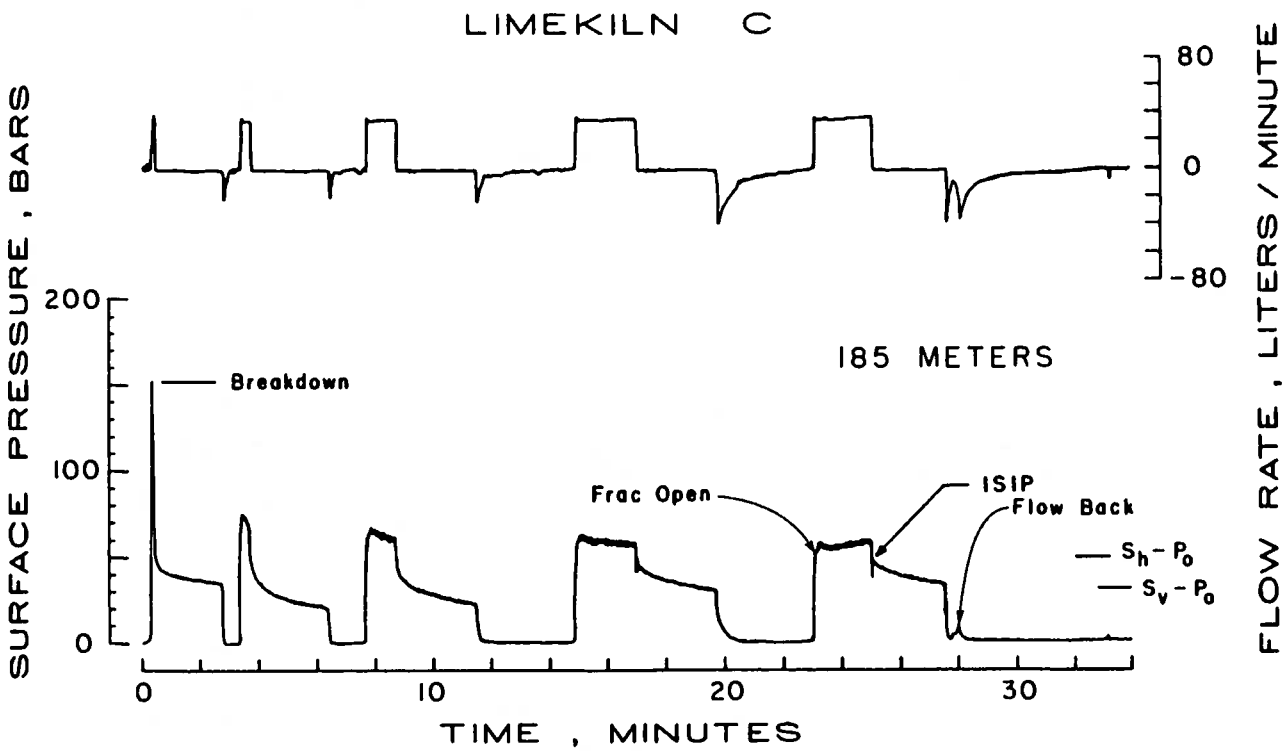


Figure 7. Surface pressure and flow versus time records during a hydraulic fracture stress measurement made at a depth of 185 m in the Limekiln C well, which was drilled 4 km from the San Andreas Fault in central California. The breakdown, fracture opening, and instantaneous shut-in surface pressures (ISIP) are indicated. S_h, minimum horizontal stress; S_v, vertical stress; and P_o, initial pore pressure. Reprinted from Hickman and Zoback (1983) and published with permission.

It should be noted that when the term "fracture pressure" is used in commercial stimulation operations, it rarely corresponds with the value of the "breakdown pressure" referred to in hydraulic fracturing stress measurements. This is because, in commercial stimulation operations, the section of the borehole wall to be fractured often contains preexisting fractures of random orientation that possess various cohesive strengths of unknown quantity. Because commercial stimulation, therefore, typically involves reopening preexisting cracks rather than generating a new fracture of known orientation, "fracture pressure" from commercial hydrofracture operations often represents an unspecified value between the breakdown pressure (P_b) and the fracture-opening pressure (P_{fo}) discussed in the context of hydraulic stress measurement techniques.

From the results of Hubbert and Willis (1957), Haimson and Fairhurst (1967) derived the following equation:

$$P_b = 3S_h - S_H - p + T_0,$$

which relates P_b to S_h and S_H, the initial formation pore pressure (p), and the formation tensile strength (T_0). As mentioned before, S_h can be determined from the ISIP. Determination of the magnitude of S_H requires knowledge of T_0. A good *in situ* measure of T_0 can be inferred from the difference between P_b and P_{fo} (fig. 8*A*). In practice, several successive cycles of fluid injection may be required to measure this quantity accurately (fig. 8*B*). It was then recognized that, if the initial formation p and the ISIP were known, then S_H could be determined directly from P_{fo}:

$$P_{fo} = 3S_h - S_H - p$$

(Bredehoeft and others, 1976). Figure 7 shows how each of the three values (P_b, P_{fo}, and the ISIP) are reflected in the pressure-time history of an actual hydraulic fracture record.

On the basis of the equations above for P_b and P_{fo}, at least three types of pressure-time histories can be identified, depending on the relative values of P_b, P_{fo}, and S_h. Figure 9 shows examples of these three types of pressure records and how each can be distinguished.

Comparison of Fracture Pressure and the Mohr-Coulomb Failure Criterion

The increase in formation pore pressure by fluid injection in a well can induce either a new hydraulic fracture or slip on a preexisting fault. In both cases, the critical pressure necessary for failure is dependent on the *in situ* stress field. Pressure limitations of maximum allowable injection pressures established for various waste-disposal operations typically are set below the estimated value of P_b to prevent an uncontrolled fracture of the confining layer

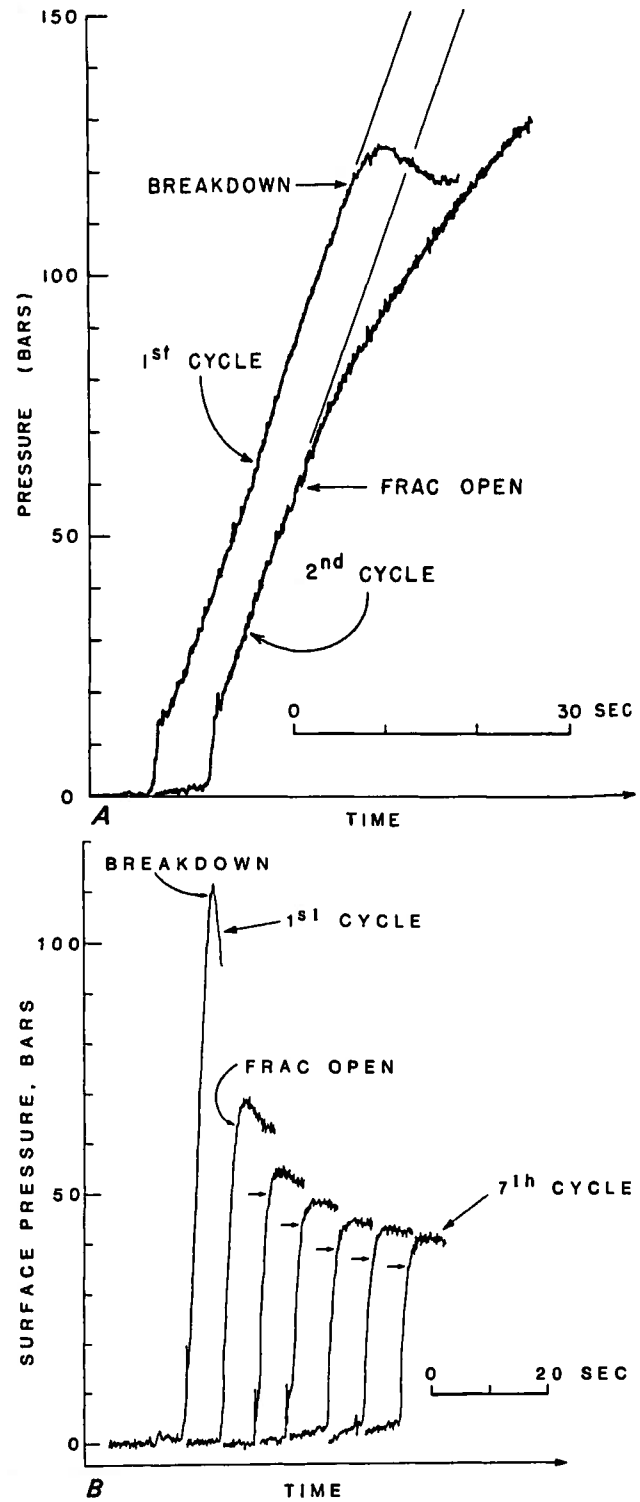


Figure 8. Injection pressure versus time during initial hydraulic fracturing and subsequent cycles of pumping. *A*, Differences between the initial cycle in which a fracture occurs (breakdown) and the subsequent cycles that reopen (fracture-opening pressure) and possibly extend the previously formed crack. *B*, Multiple pumping cycles showing the decrease in fracture-opening pressure with each cycle. Reprinted from Hickman and Zoback (1983) and published with permission.

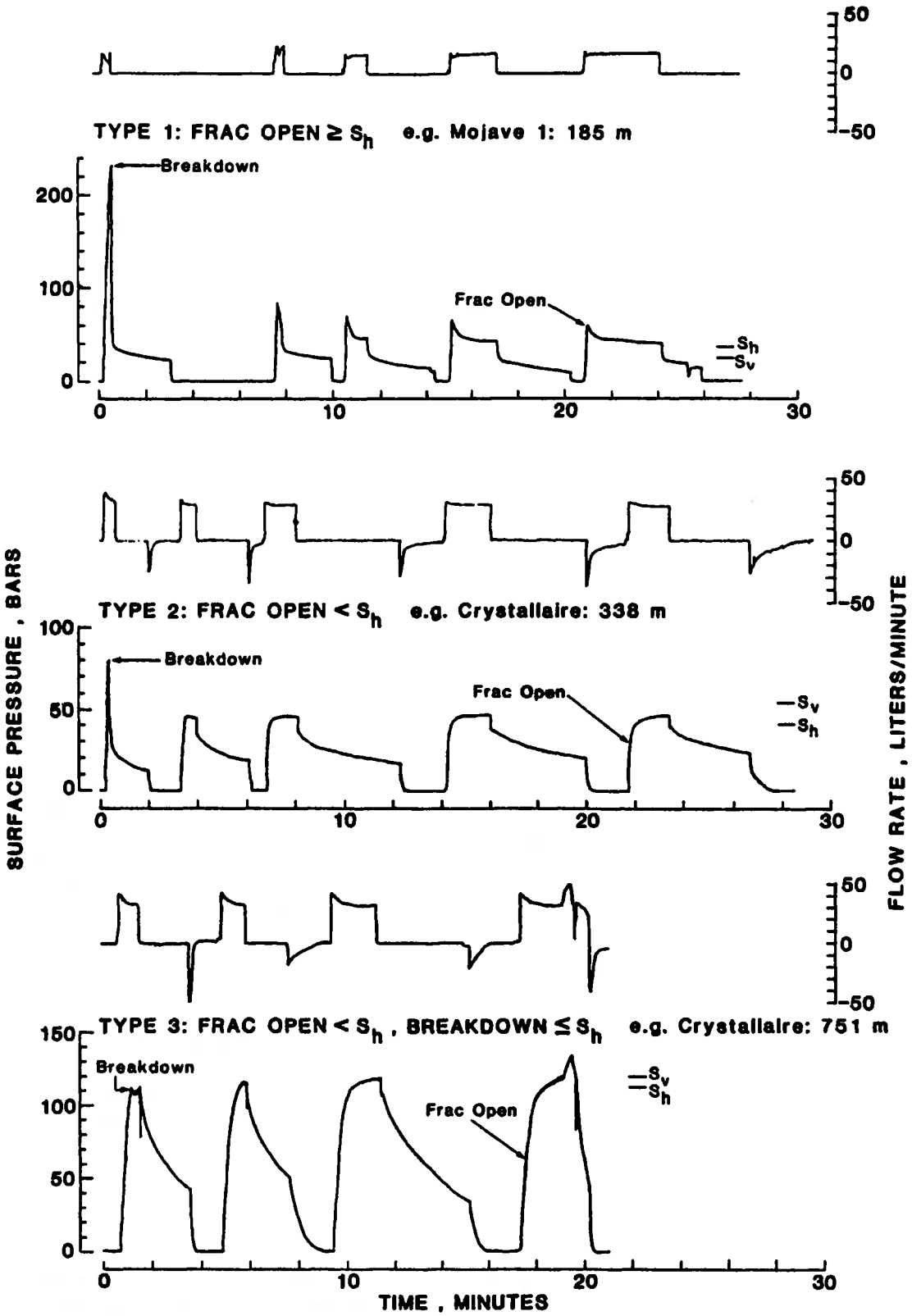


Figure 9. Three different types of hydraulic fracture pressure-time histories taken from two wells drilled near the San Andreas Fault in southern California. The examples are defined by the differences in the magnitudes of the breakdown and fracture opening pressures relative to the minimum horizontal principal stress. The calculated magnitude of the vertical stress is shown for comparison. S_h, minimum horizontal stress; and S_v, vertical stress. Reprinted from Hickman and Zoback (1983) and published with permission.

above the aquifer used for waste disposal and the potential contamination of potable water supplies. Although the concept of P_b is well recognized in the drilling and well-operations industry, its dependence on the regional tectonic stress field, as well as on the tensile strength of the rock, often is not appreciated fully. Thus, before reasonable levels of injection pressure are set, accurate knowledge of the existing state of stress is extremely important.

In terms of the relative magnitudes of fluid pressure needed to induce slip on a preexisting fault versus the fluid pressure necessary to cause a hydraulic fracture, the pressure needed to cause slip is typically much lower; for example, suppose the state of stress can be characterized by a regime in which the vertical stress (S_v) is close to S_H and the stress ratio α of S_h to S_H is 0.65. The breakdown pressure (P_b) required to hydrofracture intact rock is then given by the following equation:

$$P_b = S_v\,(3\alpha - 1) - p + T_0.$$

At a nominal depth of 2 km and for a rock density of 2.6 grams per cubic centimeter, S_v is about 510 bars. If T_0 is taken to be 40 bars and p is near hydrostatic (p = 200 bars), then P_b = 325 bars, or 125 bars above ambient. Fracture-opening pressure (P_{fo}) would be 285 bars, or 85 bars above ambient. However, the critical fluid pressure (P_{crit}) necessary to induce sliding on a favorably oriented preexisting fracture that has no cohesion is equal to the following:

$$P_{crit} = (K\,\sigma_3 - \sigma_1)/(K - 1),$$

where $K = [(\mu^2 + 1)^{1/2} + \mu]^2$ (Jaeger and Cook, 1979). For μ = 0.6 and the stress regime given above, this relation reduces to the following:

$$P_{crit} = S_v\,(3\alpha - 1)/2\ ,$$

which, for the values of α and S_v given above, yields P_{crit} = 242 bars, or only 42 bars above ambient. If the fault exhibits cohesion, then the critical fluid pressure required to induce slip is proportionately greater. Nevertheless, under the conditions assumed above, an increase in fluid pressure of 42 bars above ambient would be sufficient to induce slip on planes having no cohesion that contain σ_2 and are oriented about 30° relative to σ_1; 85 bars above ambient would be sufficient to open preexisting fractures (increase transmissivity) oriented parallel to σ_1; and 125 bars would be sufficient to fracture the intact rock of the borehole wall hydraulically.

Thus, setting maximum injection levels at pressures below that required to fracture the intact borehole wall will *not* guarantee the prevention of induced seismicity if favorably oriented preexisting faults are present near the well. Conducting a controlled hydraulic fracture stress measurement, however, will determine the safe level of fluid injection pressure to prevent an uncontrolled hydrofracture and the proximity to failure of any adjacent potential slip surface.

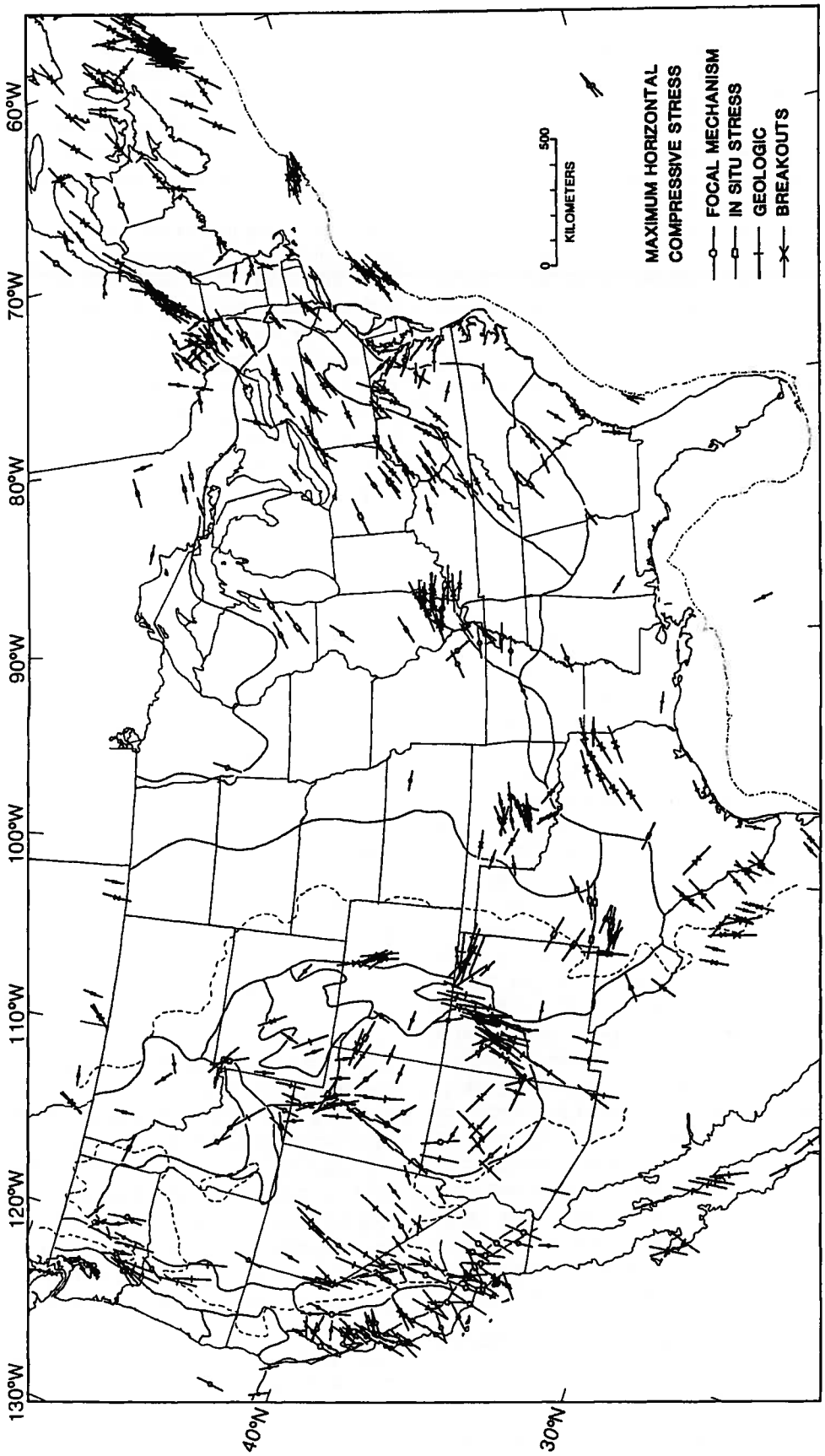
Summary of Stress Measurements to Date

Compilations of various stress measurements have been made by several investigators (Sbar and Sykes, 1973; Lidener and Halpern, 1978; Zoback and Zoback, 1980, 1989). These summaries suggest that the continental United States can be divided into distinct stress provinces, within which the stress field is fairly uniform in magnitude and in direction. Figures 6 and 10 show some of the most recent compilations of stress orientations within the conterminous United States (Plumb and Cox, 1987; Zoback and Zoback, 1989). Both sets of compilations identify the type of stress indicator used at each site. A more generalized stress map showing average principal stress orientations, the stress regime, and delineating the stress provinces is shown in figure 11. In some cases, the boundary between various provinces is sharp, whereas, in others, it is broad and transitional.

Much of the Central and the Eastern United States, where a large number of waste-disposal wells are concentrated, is characterized by a compressive stress regime (fig. 11). Reverse and strike-slip faulting would be most likely to occur in this part of the country, as the vertical stress (S_v) is less than one or both of the horizontal stresses. Because the maximum principal compressive stress (σ_1) is horizontal and typically oriented northeast to east, planes striking 30° to 45° relative to S_H would be oriented most favorably for slip. For large parts of the Central United States, the magnitudes of the principal stresses indicate that only relatively small increases in pore pressure along such favorably oriented fractures are required to induce slip (Evans, 1988).

HYDROLOGIC FACTORS IN EARTHQUAKE TRIGGERING

In all the well-documented cases of injection-induced seismicity, the increase of pore pressure resulting from the fluid injection is the key perturbation to the natural environment responsible for triggering the earthquakes. A well-developed body of theory and computational techniques exists for the estimation of the temporal and the spatial distribution of the pressure field generated by an injection operation. Relatively straightforward analytic techniques are available for most simple geometries, such as radial flow in a confined horizontal aquifer. Numerical modeling techniques are also available for more complicated geometries. The most complete analyses of the hydrologic factors involved in earthquake triggering were conducted in association with the Rocky Mountain Arsenal and the Rangely earthquake sequences (Raleigh and others,


130°W
120°W
110°W
100°W
90°W
80°W
70°W
60°W
40°N
30°N
0
500
KILOMETERS
MAXIMUM HORIZONTAL
COMPRESSIVE STRESS
FOCAL MECHANISM
IN SITU STRESS
GEOLOGIC
BREAKOUTS

1976; Hsieh and Bredehoeft, 1982). In the Rocky Mountain Arsenal case, the pressure field was dominated by a fault or fracture zone of finite width that had high permeability relative to the country rock. Although the reservoir geometry was less complex at Rangely, the pressure field also seemed to be affected by the presence of a zone of high permeability that coincided with a mapped subsurface fault (see fig. A2A). For most cases of Class I injection wells (that is, those wells used for the disposal of hazardous waste), sites are chosen to avoid faults where possible, and, in such cases, estimating the development of the pressure field established around the well by fluid injection can rely on using relatively simple methods. However, if, after the completion of the well, evidence comes to light suggesting that a more complex model of reservoir geometry is appropriate, then it would be necessary to reassess the net effect of fluid injection by utilizing more precise and sophisticated techniques for analysis.

Most of the common methods available for calculation of the pressure field from an injection well are adaptations of standard techniques used in ground-water modeling (Davis and DeWiest, 1966; Freeze and Cherry, 1979; Fetter, 1980). However, as mentioned above, changes in the standard techniques are required in the presence of faults, fractures, or other possible pathways for anisotropic fluid flow. In addition, if fluid is being injected into a rock of extremely low permeability, typical of the crystalline basement where most earthquakes occur, then other factors of importance may also come into play. Methods for calculating ground-water flow in such low-permeability environments are discussed by Neuzil (1986).

The critical reservoir characteristics for predicting the pressure field around an injection well are the transmissivity and the storativity of the rocks. The lower the transmissivity is, the more confined the "pressure bulb" around the bottom of the well is and the more likely that high pore fluid pressures will be established, thus increasing the concern for earthquake triggering. Inasmuch as earthquakes occur on faults and these same faults can act as zones of high permeability (high transmissivity), determining the presence of faults or fractures is important for predicting the occurrence of induced seismicity.

In many cases where potentially active faults occur at some distance from the injection well, accurate fluid pressure changes are difficult to anticipate because detailed information about the hydrologic properties of the reservoir away from the injection well are lacking; for instance, supposing waste is injected into a basal sedimentary unit overlying crystalline basement, although much may be known about the zone of injection, little may be known about the hydrologic characteristics of the deeper basement rock, where the potential for earthquakes—owing to the presence of faults and fractures—may be significant. As shown below, some estimate of the average characteristics of the reservoir in the vicinity of a well can be inferred from measurements made during well completion and detailed monitoring of the pressure-time history.

◀ **Figure 10.** Maximum horizontal compressive stress orientations throughout the conterminous United States. Solid lines, physiographic provinces typically exhibiting nearly uniform stress fields. Reprinted from Zoback and Zoback (1989) and published with permission.

Reservoir Properties

For a given reservoir geometry, the fluid pressure field generated by injection is governed by transmissivity and storativity, which are functions of porosity (n), the permeability, and the elastic constants of the aquifer. These parameters can be determined from laboratory tests on well cores, piezometer tests, or pumping tests. Pumping tests have the desirable characteristic that they average over a large *in situ* volume of the aquifer and, therefore, represent the most realistic estimates. The storativity (S), which gives the amount of fluid released per unit column of aquifer for a unit decline in head, can be calculated from the following expression:

$$S = \rho g h\,(\alpha_v + n\beta),$$

where ρ is fluid density, g is the acceleration of gravity, h is the aquifer thickness, α_v is the vertical compressibility of the aquifer, and β is the fluid compressibility. Transmissivity (T) is defined as follows:

$$T = Kb,$$

where K is the saturated hydraulic conductivity, and b is the thickness of the aquifer (Freeze and Cherry, 1979). Hydraulic conductivity (K) is simply as follows:

$$K = k\rho g/\eta,$$

where k is the specific or intrinsic permeability, and η is the dynamic viscosity of the fluid. The storativity and the transmissivity of the reservoir can be estimated from pumping tests by using curve-matching techniques that apply either the Theis log-log plot or the Jacob semi-log plot methods (Freeze and Cherry, 1979).

Fluid Pressure Changes Resulting From Injection

For purposes of illustration, two types of reservoir models are presented—an infinite isotropic reservoir and an infinite strip reservoir that has infinite length but finite width and thickness; that is, rectangular cross section. These models are simply for the purpose of studying how fluid pressure may propagate horizontally away from an

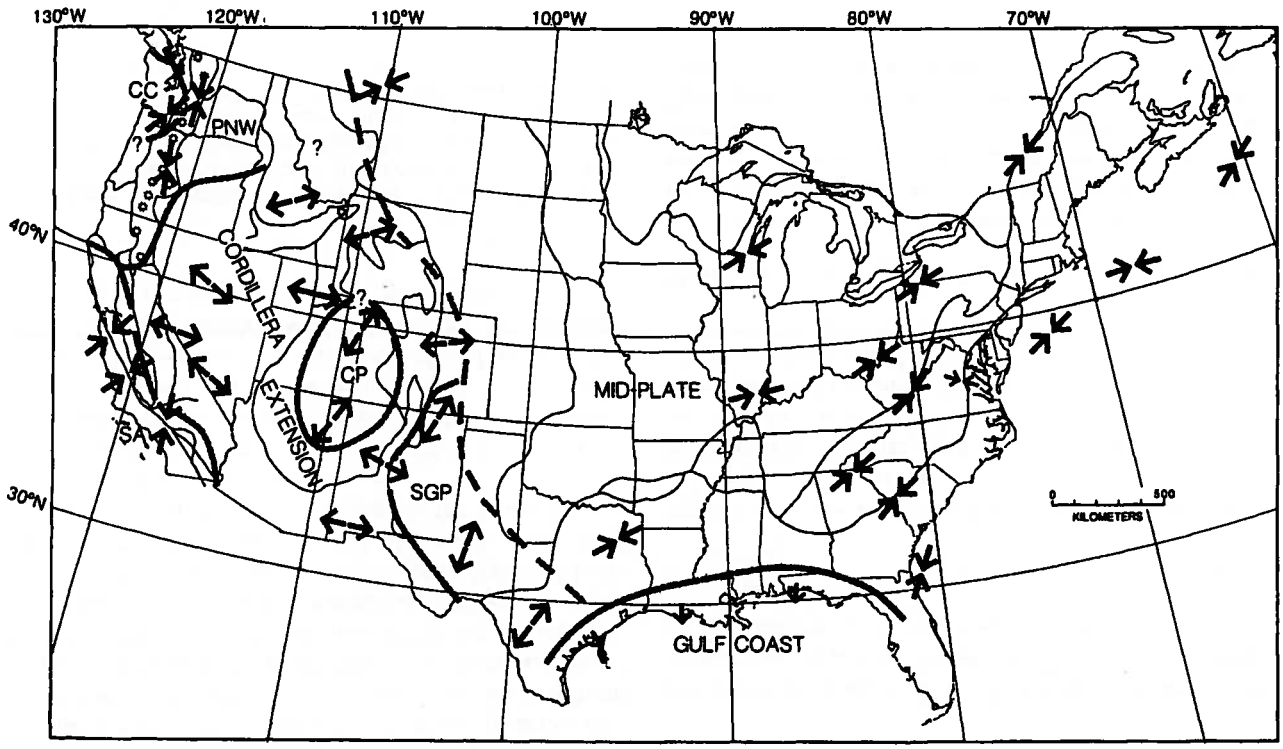


Figure 11. Generalized stress provinces of the conterminous United States. Outward-pointing arrows, areas characterized by extensional deformation (that is, normal faulting); inward-pointing arrows, regions dominated by compressional tectonism (that is, reverse and strike-slip faulting); dashed lines, horizontal stress provinces—CC, Cascade convergent; PNW, Pacific Northwest; SA, San Andreas; CP, Colorado Plateau; and SGP, Southern Great Plains. Reprinted from Zoback and Zoback (1989) and published with permission.

injection well. They do not address the question of how fluid pressure effects might migrate downward from the injection horizon towards potential earthquake-producing structures in the basement.

Infinite Reservoir Model (Radial Flow)

The simplest model for estimating the development of a pressure field around an injection well is radial flow in a single infinite isotropic aquifer of constant thickness. The fluid pressure $p(r,t)$ at distance (r) and time (t) as a result of a constant flow rate (Q) into a reservoir that extends uniformly in all directions is given by the following equation:

$$p(r,t)=\frac{\rho g Q}{4\pi T}\int_{u}^{\infty}\frac{e^{-\xi}}{\xi}\,d\xi\,,$$

in which $u = r^2S/4Tt$ (Freeze and Cherry, 1979). Figures 12 and 13 show example calculations for the pressure field around an injection well in Ohio. The values of storativity [5.4×10^{-5} square meters per second (m^2/s)] and transmissivity (4.5×10^{-6} m^2/s) in the radial flow model are rather low compared to those for optimal waste-disposal operations; thus, the pressure at the wellbore required to achieve the desired rate of fluid injection is rather high. Figure 12 shows the pressure change versus time curve at the wellbore for a well that has a radius of 12 cm and assuming a constant injection rate of 6.7×10^6 liters per month (L/mo). Figure 12 also shows how a change in shape of the reservoir can effect the pressure-time history at the wellbore. Thus, whether pressure is rising because of fluid injection or falling because injection has stopped (in this case, after a nominal injection period of 15 yr), the pressure history is characteristic of the reservoir geometry.

In the radial flow model, the pore pressure (p) rises relatively rapidly during the first few years and then continues to rise at an ever-decreasing rate. Once injection has stopped, the decline in pressure at the wellhead is most rapid in the radial flow model. The attenuation of the pressure field with distance away from the well is shown in figure 13. With increasing time, the pressure bulb around the well continues to grow. After 10 yr of injection, the pressure increase at a distance of 5 km from the well is about 15 percent of the value at the wellbore.

Infinite Strip Reservoir Model

If fluid flow is confined to a narrow reservoir of finite width, then the fluid pressure at a given distance from the

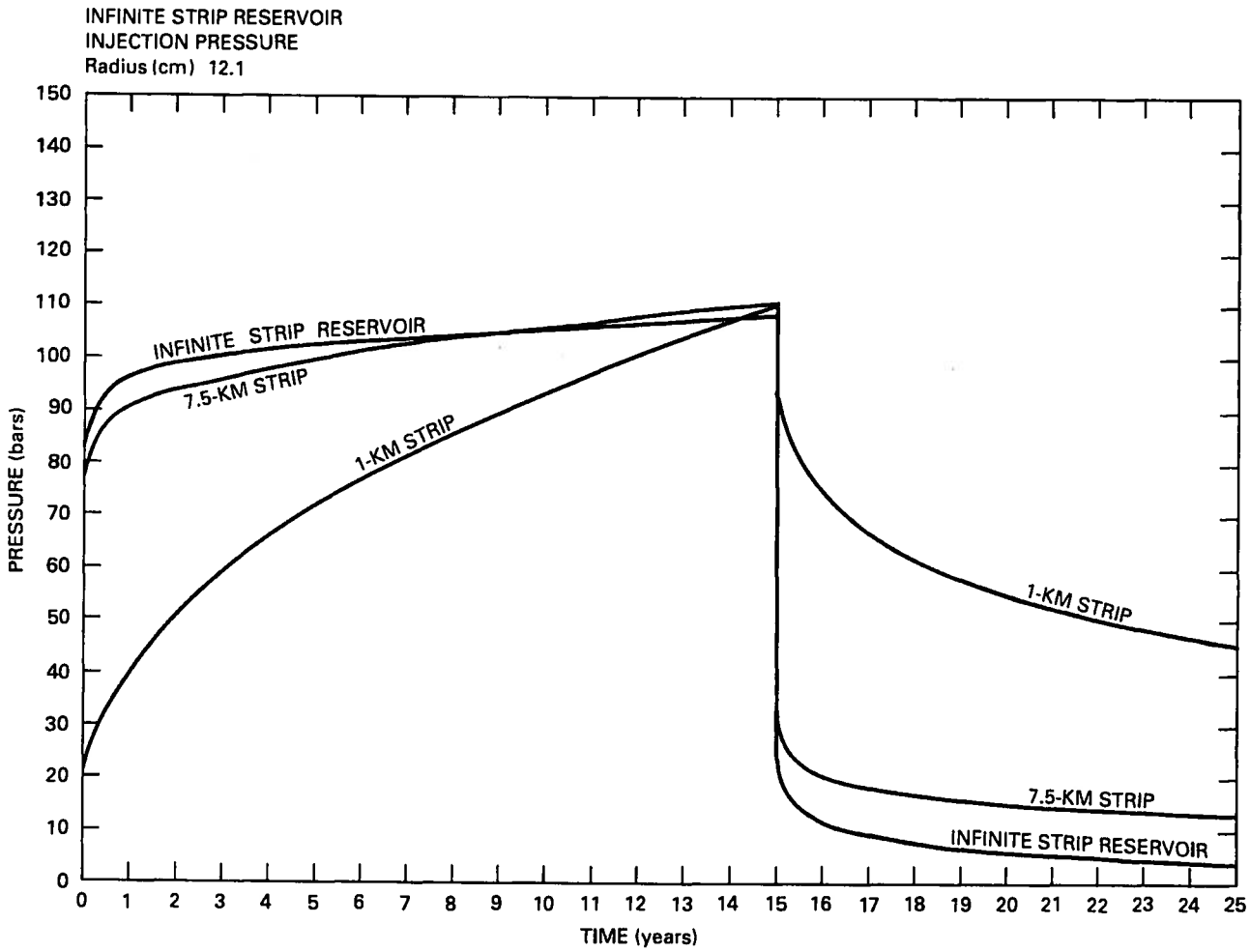


Figure 12. Injection pressure versus time as calculated from the equations in the text for radial flow (infinite width) and finite width (1.0 and 7.5 km) reservoir models. An injection rate of 6.7 million L/mo is used and is assumed to cease after 15 yr. Transmissivities are varied between models to produce approximately 110 bars of wellhead pressure after 15 yr (from Wesson and Nicholson, 1986).

well will be higher than that of the radial flow case. This type of model was used by Hsieh and Bredehoeft (1981) to calculate the pressure distribution around the Rocky Mountain Arsenal well implicated in the 1967 Denver earthquake sequence. Even if no specific evidence suggests that such a similar linear zone of high permeability is characteristic of a particular reservoir geometry, such calculations still may be useful to illustrate how large a pressure buildup is possible at any given distance and to show how the pressure history at the wellbore is diagnostic of the shape of the reservoir into which fluid is being injected.

For injection into the center of a strip of finite width (w) and infinite extent in the x direction, a constant injection rate (Q) produces a pressure given by the following:

$$p(x,y,t)=\frac{\rho g Q}{4\pi T}\sum_{m=-\infty}^{\infty}\int_{u_m}^{\infty}\frac{e^{-\xi}}{\xi}\,d\xi\,,$$

where y is the distance from the center of the strip, and $u_m = [x^2 + (y + mw)^2]S/4Tt$. Figure 12 shows how the pressure at the wellbore will increase with time for reservoirs of infinite length and various widths. Figures 14 and 15 show the attenuation of the pressure field with distance away from the well for the same two models. Two strip models are considered—a width of 1 km and a transmissivity of 2.0×10^{-5} m^2/s and a width of 7.5 km and a transmissivity of 4.5×10^{-6} m^2/s. The transmissivities are selected to make the pressure-time curves comparable to those exhibited by the radial flow case discussed in the previous section. Two points are clear. First, for a constant fluid injection rate, the pressure required at the wellbore initially rises more gradually for either of the two infinite strip reservoir models than for the case of radial flow but continues to rise at a more rapid rate at later time intervals. Second, the narrower the postulated reservoir is, the higher the formation fluid pressure that will be achieved with time

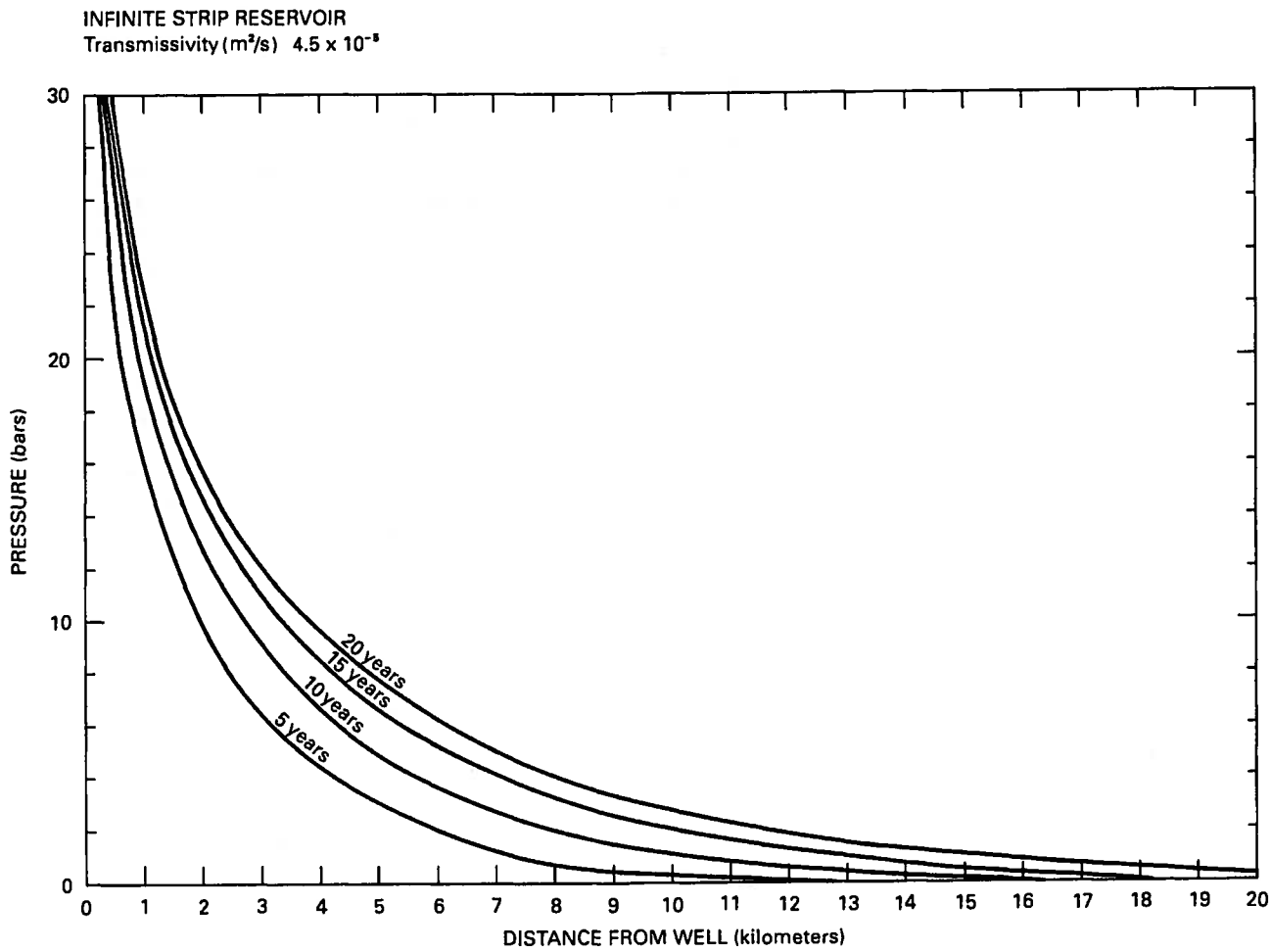


Figure 13. Calculated increased pore pressure versus distance as a result of injection into a confined reservoir of infinite extent (radial flow) and transmissivity of 4.5×10^{-5} m^2/s (from Wesson and Nicholson, 1986). Time intervals are 5, 10, 15, and 20 yr.

at large distances from the wellbore. Moreover, once injection has ceased, the decline in pressure at the wellhead is more gradual for either of the two infinite strip models than for radial flow. Because reservoir geometry has such a significant effect on the pressure-time curves, it is evident that analysis of the history of injection pressure at the wellhead can be used to help discriminate the shape of the reservoir into which fluid is being injected.

UNRESOLVED ISSUES

Although much is known about how earthquakes are induced by deep well injection, full understanding of the earthquake process is far from complete. Many issues remain unresolved and, as such, produce large uncertainties in the confidence with which adequate and appropriate regulations can be formulated. The following problems are considered to be some of the principal unresolved questions that bear directly on the issue of accurate seismic risk assessment.

The Problem of Seismicity in the Central and the Eastern United States

From a seismic hazard point of view, the contiguous United States can be divided along a boundary roughly corresponding to the eastern front of the Rocky Mountains. Most of the earthquakes in the area to the west (pl. 1) are associated with active, well-defined geologic processes. In contrast, the cause of many of the earthquakes in the Central and the Eastern United States is still poorly understood. In the West, the association of earthquakes, particularly large ones ($M \geq 6.5$), with geologic faults is well established. In many cases, these faults are visible at the surface, and, by using geologic techniques, it is possible to demonstrate that displacement has occurred along these faults during the geologically recent past. However, with the exception of

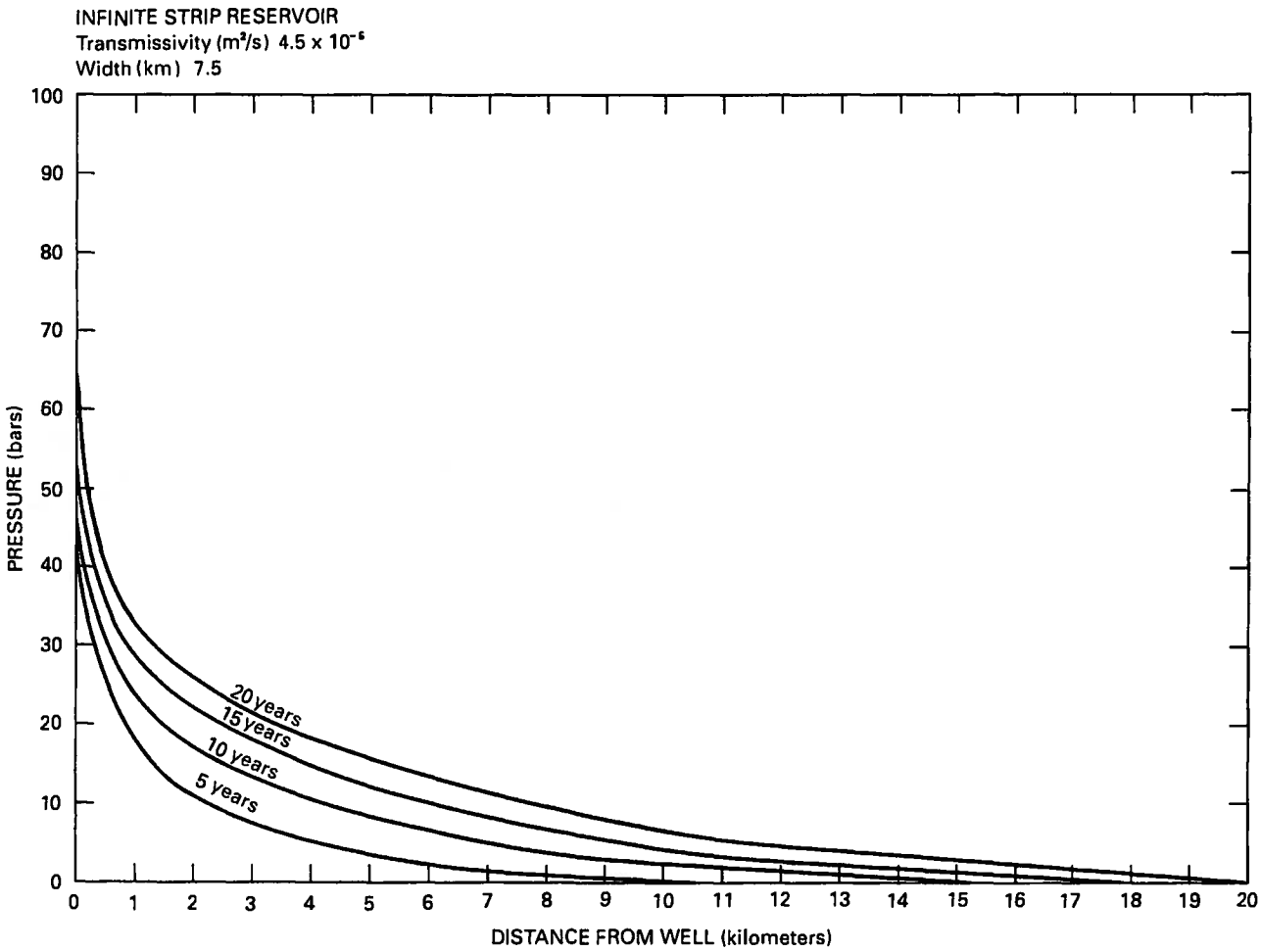


Figure 14. Increased pressure versus distance along the axis of an infinite strip reservoir 7.5 km wide and transmissivity as in figure 13 (from Wesson and Nicholson, 1986). Time intervals are 5, 10, 15, and 20 yr.

evidence for subsurface faulting in the vicinity of the 1811–12 New Madrid, Mo., earthquakes, the relation between faults and earthquakes in the Central and the Eastern United States has been much more elusive. This issue has been clouded even further by the discovery of the Meers Fault in the Wichita Mountains of Oklahoma, along which large, relatively recent movement has occurred (Gilbert, 1985), yet no current or historical seismicity has been associated with it (Lawson, 1985). The Charleston, S.C., earthquake of 1886 provides perhaps the best example of some of the difficulties involved. Despite the continuing occurrence of small earthquakes in the Charleston area, as well as extensive regional and local geologic and geophysical investigations, no commonly agreed upon fault or faults judged to be responsible for the large historic earthquake has yet to be discovered. Consequently, the primary basis for estimating future locations of earthquakes in the Central and the Eastern United States remains the catalog of historic earthquake epicenters.

Magnitudes of Induced Earthquakes

Although it seems extremely unlikely that deep well injection alone could induce a truly large earthquake in the Central or the Eastern United States, no satisfactory method is currently available for estimating the maximum size of earthquake that might be produced. Indeed, no method exists for estimating the increased probability for triggering earthquakes of any magnitude as the result of raising the pore fluid pressure through deep well injection.

Observations indicate that the magnitude of an earthquake increases roughly as the logarithm of the length of fault along which displacement occurs (fig. 16). Slip is also proportional to fault length. Thus, a magnitude 8 earthquake typically involves faulting along hundreds of kilometers of fault and several meters of slip, whereas a magnitude 3 earthquake might involve faulting over a surface that has a dimension of several tens of meters and slip of only a few centimeters. The magnitudes of the largest earthquakes

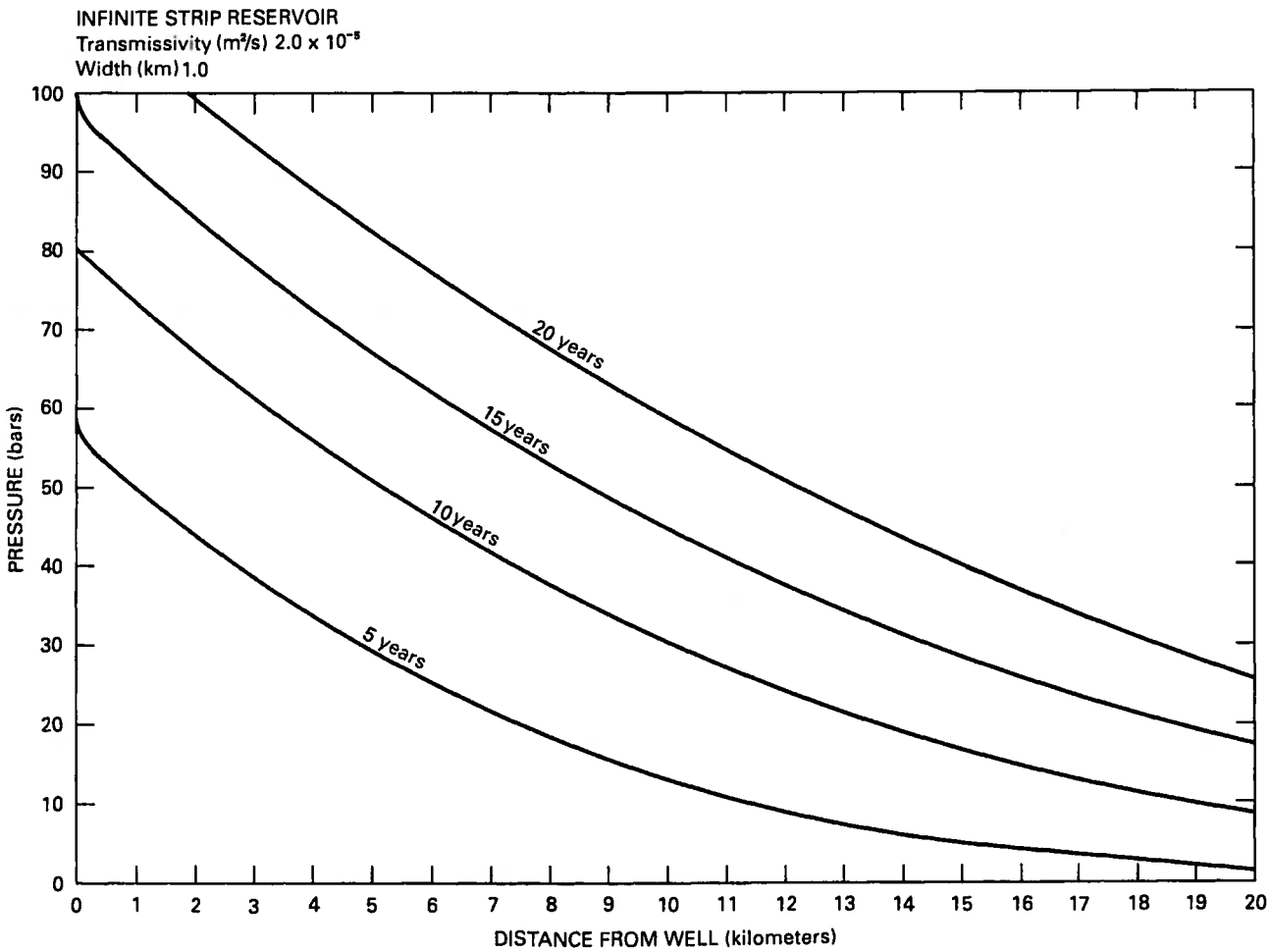


Figure 15. Increased pressure versus distance along the axis of an infinite strip reservoir 1 km wide and transmissivity of 2.0×10^{-5} m^2/s (from Wesson and Nicholson, 1986). Time intervals are 5, 10, 15, and 20 yr.

associated with deep well injection were between 5 and 5.5 (table 1, Rocky Mountain Arsenal in 1967 and Snipe Lake, western Alberta, in 1970). Although none of the induced earthquakes recorded so far would be considered devastating, the potential for damage from such earthquakes could be larger than for those in more tectonically active regions because many of the induced events are shallow and occur in areas of low expected seismic hazard and in regions of low attenuation of seismic waves; for example, the Attica earthquake of 1929 discussed in Appendix A. Earthquakes in the Central and the Eastern United States typically cause damage over much larger areas as compared to earthquakes of the same size in the Western United States. This is primarily the result of the lower attenuation of seismic waves in the East versus the West, but other factors also may be involved.

One of the factors that may affect earthquake damage potential and that seems to distinguish earthquakes in the Central and the Eastern United States from those in the West is a tendency for eastern earthquakes to be associated with relatively small rupture areas for a given magnitude earthquake. If true, then this would imply that eastern earthquakes exhibit more slip per unit fault area than do western earthquakes and would imply that eastern earthquakes reflect higher stress drops. This would be coincident with the thinking that the crust of the Earth beneath the Central and the Eastern United States is older, colder, and, therefore, stronger than that beneath the Western United States. This is also consistent with the idea that large earthquakes east of the Rocky Mountains typically have much longer repeat times than those to the west, allowing faults to heal and regain much of their frictional strength lost during dynamic slip in past earthquakes (fig. 16; Kanamori and Allen, 1986). This apparent difference is important because, if correct, smaller faults in the vicinity of a well located in the Eastern United States could produce larger earthquakes than might be anticipated on the basis of relations derived from more seismically active areas in the West (Thatcher and Hanks, 1973).

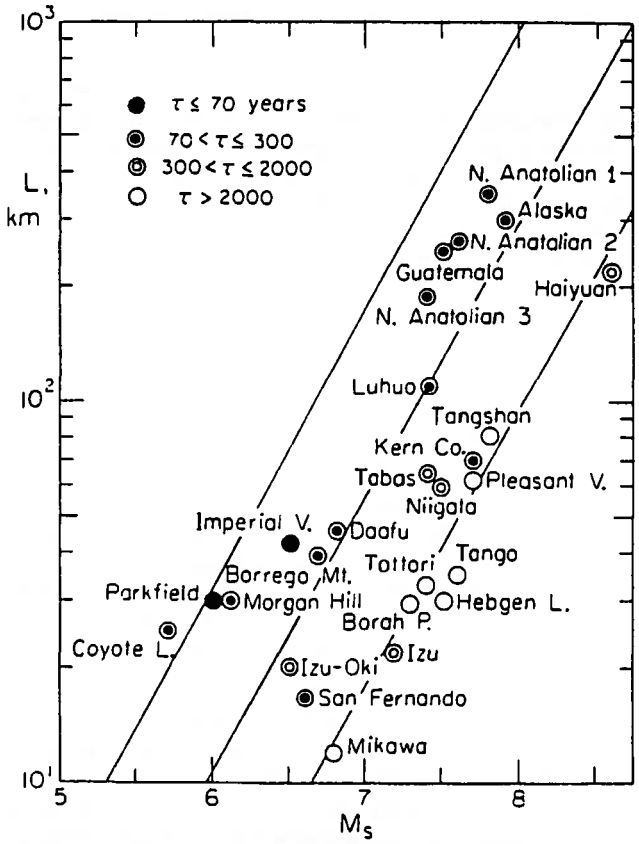


Figure 16. Relation between surface-wave magnitude and fault length. Shown for reference are theoretical lines of constant stress drop (1, 10, and 100 bars, left to right, respectively). Earthquakes that have longer repeat times generally exhibit shorter rupture lengths (L) for the same size earthquake; compare the 1983 M_S 7.3 Borah Peak, Idaho, earthquake with the 1976 M_S 7.5 Guatemala earthquake. M_S, surface-wave magnitude; L, fault length; and τ, repeat times. Reprinted from Kanamori and Allen (1986) and published with permission.

Potential for Reactivation of Old Faults

It is sometimes suggested that earthquakes in the Central and the Eastern United States occur on reactivated, geologically old faults. Currently, the phenomenon of reactivation is poorly understood (Sibson, 1985). Because of the large uncertainties in the inherent shear strength and the time-dependent nature of friction with slip on faults, no criteria exist for predicting whether an old fault might be reactivated, except to determine how close in orientation an existing fault may be relative to preferred planes of slip in the current regional tectonic stress field, as predicted by the Mohr-Coulomb failure criterion.

Importance of Small Induced Earthquakes

It is possible that a deep well injection operation may induce small earthquakes in the immediate vicinity of the bottom of the well, as has been the case in several of the secondary oil recovery and solution mining cases described in Appendix A. If these earthquakes are below the threshold for damage or, perhaps, even below the threshold for noninstrumental detection, then it is not unreasonable to ask whether these earthquakes constitute a risk. Two questions arise—Do these small earthquakes indicate the potential for larger, potentially damaging earthquakes? and do these small earthquakes indicate the possibility of breaching the confining horizon?

In answer to the first question, the occurrence of even small earthquakes indicates that, at least locally, the conditions for seismic slip are satisfied. In the Western United States, the association of small, natural earthquakes with a geologically recognizable fault is taken as sufficient evidence that the entire fault is active and, consequently, that a potentially larger earthquake, controlled by the dimension of the fault, is possible. Unfortunately, our lack of knowledge concerning the size and the distribution of buried faults in the Central and the Eastern United States prevents a similar line of reasoning. Thus, without detail subsurface information, it is not possible to estimate the maximum size of earthquake that could be induced once seismicity is detected near an active injection well.

The second question is more directly pertinent to the containment of hazardous wastes. The occurrence of small earthquakes near the bottom of a deep injection well may indicate faulting or fracturing processes that conceivably could lead to a breach in the overlying confining zone and, therefore, conceivably could permit hazardous materials to migrate upward toward potential drinking water supplies. An important consideration is, therefore, whether the induced seismicity is occurring within the sedimentary section or within the deeper basement rock, and, if so, how close to the confining layer is the zone of seismic activity. Such questions could only be addressed if additional seismic monitoring equipment is installed to locate accurately any subsequent earthquake hypocenters and to resolve the type and extent of faulting involved. However, until such answers are forthcoming, it would seem prudent to regard the occurrence of small earthquakes near the bottom of a deep injection well with concern.

Spatial and Temporal Variability of Tectonic Stress

Although the actual pressure of fluid injection is certainly a critical factor in determining the potential for inducing earthquakes through deep well injection, another key environmental parameter is the state of the preexisting tectonic stress field. If stress conditions on nearby faults have already reached critical levels near failure, then only a small change in pore pressure as a result of fluid injection may prove sufficient to trigger adjacent seismicity. Measurements available to date suggest that the orientations and, possibly, the magnitudes of the principal horizontal stresses are relatively constant, or at least slowly varying,

over wide regions of the country. This suggests that once a particular injection operation has triggered earthquakes, other injection wells in the same tectonic stress province may be equally likely to induce similar seismic activity.

Insufficient measurements exist, however, to indicate how rapidly in time and space the stress field may actually vary. In the Central and the Eastern United States, there is at present little indication that the tectonic stress field changes rapidly with time. In the Western United States, geodetic measurements suggest that small, but significant, stress changes can occur over time scales of months to years (Raleigh and others, 1982). In particular, the occurrence of a major earthquake nearby could dramatically affect the local stress field on a time scale of seconds. Assessing the spatial variation in stress is almost as troublesome; for example, some areas in the Central and the Eastern United States tend to have small earthquakes more frequently than others. Whether this is related to the spatial variation in the tectonic stress field or, alternatively, to the spatial distribution and orientation of potential planes of slip is unknown.

CONSIDERATIONS FOR FORMULATING REGULATIONS AND OPERATIONAL PROCEDURES

In terms of the earthquake hazard associated with deep well injection, the three critical parameters that need to be evaluated are the magnitude of the preexisting tectonic stress, the injection pressure, and the proximity and the characteristics of any faults or fractures that may be affected by pore pressure increases caused by fluid injection operations. The preexisting tectonic stress can be measured at the time of well completion or can be extrapolated from measurements made in adjacent wells within the same geologic province. The injection pressure will be controlled by the desired injection rate and by the hydrologic properties of the receiving reservoir. Although the presence of large faults may be obvious at the surface, the presence of smaller faults within the proposed reservoir formation may be extremely difficult to detect. Thus, the two earthquake-related factors that are most amenable to regulation or control are the site selection (and by inference, the characteristics of the reservoir chosen for injection) and the maximum injection pressure.

The following recommendations are made from the point of view of addressing the potential seismic hazard associated with injection-induced earthquakes. These recommendations are not intended to replace or reduce existing procedures or restrictions established on the basis of environmental concerns or other considerations and, therefore, do not constitute by any means a complete list of all the factors needed to be considered in discussing potential hazards associated with the disposal of hazardous waste by deep well injection.

Site Selection

Reservoir That Has High Transmissivity and Storativity

The potential operator of a waste-injection well desires a reservoir that has high transmissivity and storativity because, for a given volume of fluid to be injected, the higher the transmissivity and the storativity are, the lower the required injection pressure will be. High transmissivity and storativity also are very desirable from the point of view of reducing earthquake hazard because the lower the injection pressure is, the less likely the prospect of inducing or triggering earthquakes becomes.

Stress Estimate

An estimate of the state of stress in the area of the projected reservoir is important at an early stage in the selection of a potential site of deep well injection because, to a large extent, the state of stress controls the formation fracture pressure and the pressure threshold for triggering slip on preexisting faults (the Mohr-Coulomb failure criterion). An estimate of high deviatoric stress in the reservoir region should serve as a warning that the formation fracture pressure (P_b) and the Mohr-Coulomb failure pressure will be low.

The most reliable estimates of the state of stress in the reservoir will be those based upon measurements made in the reservoir rock itself. However, it is likely that a reasonable estimate can be made before drilling from the interpolation of regional stress measurements, particularly from hydrofracturing measurements made in the same reservoir rock at nearby wells. Surface or shallow well measurements also may be of value, although the extrapolation of such measurements to significant depths may be unreliable.

Absence of Faults

The possibility for triggering induced earthquake activity appears to be significantly enhanced if any part of the reservoir affected by the planned injection is cut by a significant fault or fracture. Obviously, the presence of a fault that might present a flow path through the confining zone is also of concern in evaluating the integrity of the reservoir. Moreover, because the effect of the fluid injection pressure typically extends farther from the wellbore than the distance to which any of the injected fluid actually migrates, faults or fractures that are beyond the anticipated migration distance should be considered carefully.

Clearly, it is easier to prove the existence of a fault than to prove the absence of one. Before drilling, the existence of a fault may be inferred from surface geologic mapping, subsurface geologic studies in nearby wells, or geophysical studies, such as gravity, magnetic, or seismic reflection surveys. It should be remembered, however, that should drilling or operation of the well reveal a previously

unknown fault or fracture, then an analysis and reevaluation of the fluid injection operations may be required.

Regional Seismicity

Inasmuch as the occurrence of earthquakes, even relatively small ones, indicates the existence of faults or fractures and the presence of stresses sufficiently high to cause seismic fault slip, a proposal to locate a deep injection well in an area of significant seismicity should be regarded with caution, particularly if there is any indication that some of the earthquakes occur near the depth of the reservoir. Potential well sites located along strike of regional basement structures that exhibit contemporary seismicity or of extrapolated linear trends in earthquake epicenters should also be avoided, if possible.

Well Drilling and Completion

Transmissivity and Storativity

Estimates of the transmissivity and the storativity of the reservoir are critical to the estimate of the maximum injection pressures required over time to accommodate the desired volume and rate of fluid injection. Insofar as possible, estimates of these quantities should be made by *in situ* measurements at the time of well completion and should be supplemented by laboratory measurements as required. Necessary measurements made at the time of well completion include the effective permeability, the average thickness of potential injection zones, and other related measurements, such as the porosity and the elastic constants of the reservoir formation.

Before beginning injection operations, it would be highly desirable for the potential operator to present a calculation of the predicted injection pressure that would be required to accommodate the desired rate of fluid flow and its expected increase over time. This calculation should be based on the inferred values of transmissivity and storativity measured in the borehole and would provide a standard against which any unusual or unanticipated changes in pressure history observed at the well could be evaluated.

Stress Measurement in Reservoir Rock

From the point of view of assessing the potential for inducing earthquakes through deep well injection, the most useful single measurement is a high-quality stress measurement made in the reservoir rock within the injection well itself. Currently, the most reliable and accurate method of making such a measurement is by using the hydraulic fracture technique. In general, the measurements made in association with standard commercial hydraulic fracture operations for well stimulation are not precise enough for this purpose. To make an adequate stress measurement, it is necessary to select an unfractured length of hole by using an impression packer or borehole televiewer; to use a carefully controlled low volume of fluid, which generally requires the use of a specially designed hydrofracture tool (called a double straddle-packer unit); and to monitor the operation by using sensitive fluid pressure equipment. It is also highly desirable to repeat the measurement at several places along the unfractured drill hole to obtain an estimate of the measurement uncertainty.

Given the importance of maintaining the integrity of the confining zone, there may be concern that even the small fractures created by the hydraulic fracture stress measurement technique or the subsequent propagation of those fractures could threaten the integrity of the confining zone. Certainly, if the well is to be stimulated by commercial hydraulic fracturing, then no incremental risk is associated with the fractures generated during the stress measurements. If the well is not to be stimulated, but a stress measurement is still desired, then it should be possible to keep the fractures generated very close to the borehole and nearly limited to the section of the borehole that has been packed off—if the stress measurements are done carefully and at low injection volume. Estimates of the size of the fracture generated by most controlled hydraulic stress measurements, based on borehole televiewer or impression packer results, typically are on the order of 10 m or less (K.F. Evans, Lamont-Doherty Geological Observatory, oral commun., 1987). Such fractures would not represent a significant threat to the integrity of a confining layer that is often chosen (and mandated in the case of hazardous-waste-disposal operations) to have a thickness 10 to 100 times larger. The primary benefit in making these measurements is that the operator and the regulator will have a direct measurement of the formation breakdown and the fracture reopening pressures, as well as a reliable estimate of the zero-cohesion Mohr-Coulomb failure pressure. With these measurements in hand, the operator and the regulator will be in a position to establish relatively safe maximum pressure levels for injection operations, which will minimize the possibility of creating uncontrolled new fractures or of extending or causing seismic failure on preexisting faults.

If it is judged to be undesirable to carry out hydraulic fracturing measurements in the reservoir itself out of concern for the integrity of the confining zone, then it may be possible to obtain meaningful and relevant measurements at depths in the borehole above or below the confining zone. Ideally, such measurements should be carried out at sufficient depth to avoid near-surface effects and possible zones of stress decoupling caused by low-strength sedimentary layers or structures, such as salt beds (fig. 6*B*), between the measurement depth and the reservoir. Strictly from the point of view of the relevance of the stress measurements, the deeper the better.

Pore Pressure Measurement

Because fluid pressures modify the local effective stress fields (and, by supposition, the frictional strength of faults), an important measurement required to understand the state of stress in the reservoir before the beginning of injection is the initial pore pressure (p) in the reservoir formation. This measurement also provides a baseline against which to evaluate, quantify, and monitor the expected increase in formation fluid pressure as a result of the subsequent injection operations.

Faulting Parameters

If there is any indication that the injection pressures will approach the zero-cohesion Mohr-Coulomb failure pressure, then it would be prudent to measure the coefficient of friction (μ) of the reservoir rock and the adjacent basement rock, as well as to estimate, if possible, the cohesion of any adjacent faults or fractures present (or potentially present) in the reservoir or surrounding country rock. These measurements would help provide better, more reliable estimates of the critical stress levels needed for fault slip, as determined by the Mohr-Coulomb failure criterion.

Well Operation and Monitoring

Determination of Maximum Allowable Injection Pressure

From the point of view of earthquake hazard, the key decision facing the operator and the regulator is the establishment of the maximum allowable injection pressure. Without considering the potential for slip on preexisting faults, an absolute upper limit of permissible injection pressure presumably would be the formation fracture (or breakdown) pressure (P_b). It should be emphasized, however, that the standard estimates of a "safe" maximum injection pressure, which are based on some fixed percentage of the so-called normal vertical gradient of formation fracture pressure of about 0.75 to 1.0 pound per square inch per foot may not be conservative at all. This is because the formation fracture pressure critically depends on the local state of stress and, in particular, on the deviatoric stress. The higher this stress is, the lower the formation fracture pressure will be, regardless of the expected values derived from the measured vertical overburden gradient. Strict "rules-of-thumb" that do not take into account the spatial variation in the state of stress will not specify adequately the "safe" upper limit of the formation fracture pressure.

In terms of potential earthquake triggering, however, the lowest possible critical injection pressure is the zero-cohesion Mohr-Coulomb failure pressure. This is the pressure at which frictional sliding would occur on favorably oriented preexisting faults or fractures with no cohesion. If the projected injection pressures are below this threshold, then no earthquake problems should be anticipated. In contrast, if the desired injection pressures are above this threshold, then it is necessary to consider whether any significant faults or fractures exist in close proximity to the point of fluid injection, what their orientation may be, and the magnitude of their possible cohesion. If, as a result of fluid injection, conditions on adjacent faults are allowed to reach the Mohr-Coulomb failure limit, taking into account the appropriate cohesion (τ_0), then earthquake activity should be anticipated.

Comparison of Actual and Predicted Pressure-Time Records

The pattern of fluid injection pressure measured at the wellhead over time and, indeed, the fall of pressure over time during any interruption in injection activities give important information about the average hydrologic characteristics of the reservoir. Comparison of the actual pressure versus time records with those predicted from the measured or the estimated reservoir characteristics (transmissivity, storativity, shape, physical extent) would provide an assessment of whether the initial assumptions, such as radial flow in a confined homogeneous aquifer, were correct or required modification. Obviously, any increase in the apparent transmissivity of the reservoir should be scrutinized as a possible indication that fluid has reached a fracture system. Unexpectedly rapid increases in injection pressure needed to maintain flow rates at constant volume over time may indicate a tighter reservoir formation than anticipated and, thus, a possible need to reduce the desired rate of fluid injection.

Seismic Monitoring

If any question exists about the possibility of inducing earthquakes, particularly if the projected injection pressure is above the zero-cohesion Mohr-Coulomb failure pressure, then it would be prudent to carry out a seismic monitoring program to detect the occurrence of any adjacent earthquake activity. This also would be advisable if the well is situated in an area that has a previously well-defined history of seismic activity or if the well site is in close proximity (less than 20 km) to a known major fault structure. Preferably, this monitoring program should begin as far in advance of the anticipated injection operations as possible to establish a background level of seismicity against which any potentially injection-induced earthquakes might be compared. To be meaningful, instrumentation should be sensitive enough to detect earthquakes in the magnitude 0 to 1 range located near the bottom of the well. Figure 17 is a seismogram of one such microearthquake detected within 3 km of the Calhio, Ohio, injection wells discussed in Appendix A. To obtain this degree of sensitivity in the presence of the high levels of seismic noise often associated with industrial activity in the vicinity of the well itself, it may be necessary to locate the monitoring equipment somewhat off-site or in

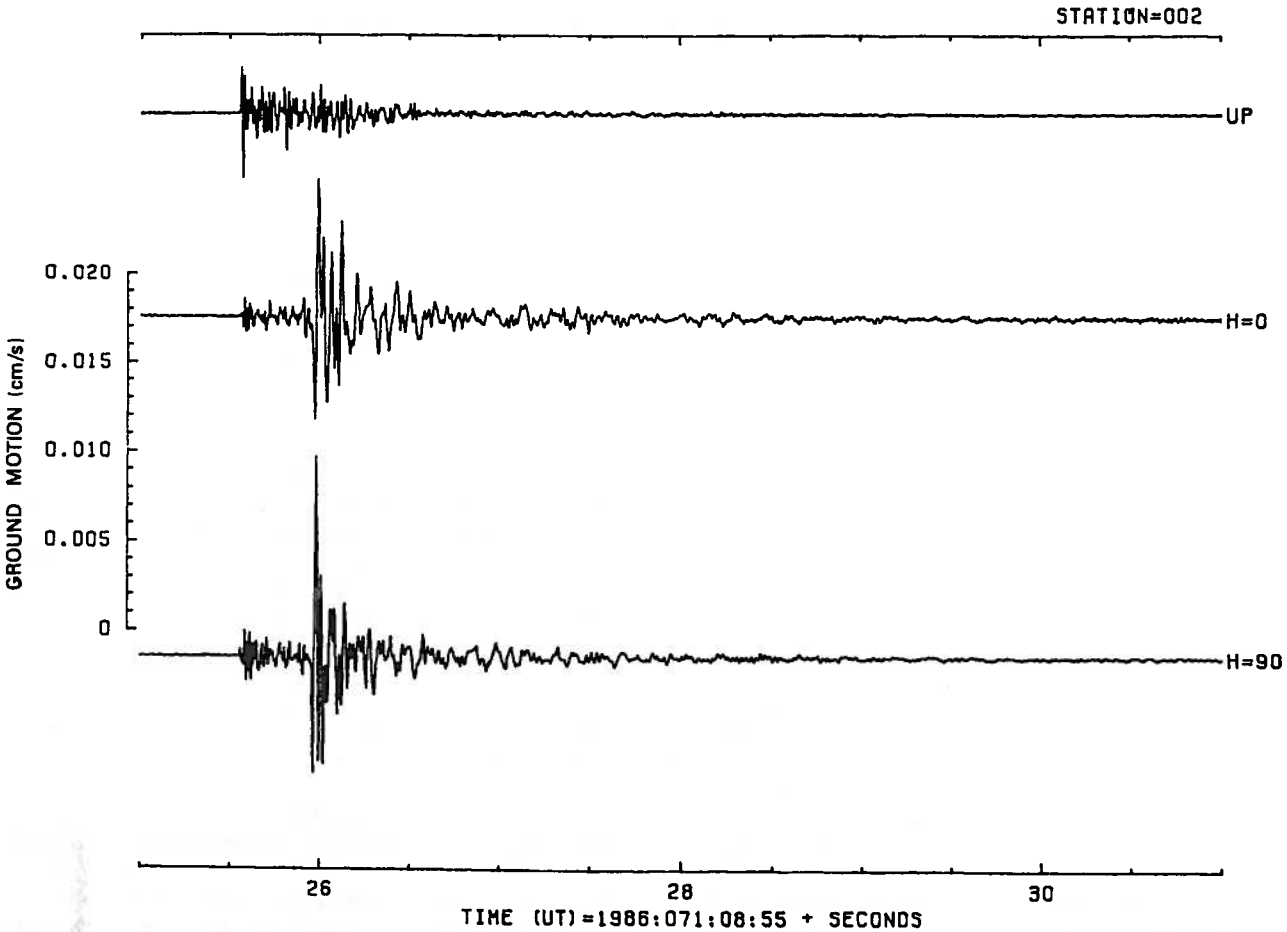


Figure 17. Seismogram of an earthquake that has a magnitude of about 0.5 and that is located at a depth of about 2 km and within less than 3 km of the bottom of an injection well in northeastern Ohio (from Wesson and Nicholson, 1986).

an adjacent borehole. Significant reductions in noise level can be obtained by placing the seismic instrumentation in boreholes at depths as small as a few tens of meters.

Monitoring should continue for as long as it takes to verify that elevated injection pressures are unlikely to trigger significant earthquake activity. This may require several years of observation because of the length of time involved to attain maximum (that is, critical) injection pressure at a constant injection rate and to allow for the diffusion of significant pore fluid effects away from the well. The time interval between initiation of injection and the largest earthquakes at the Rocky Mountain Arsenal site was 5 yr; for the Snipe Lake case (Appendix A), the time lag was 7 yr. Similar time intervals between injection and the largest earthquakes in the triggered sequence have been observed in other cases; however, the time between the initiation of injection and the onset of microearthquake activity is often short; for example, the Rocky Mountain Arsenal, the Attica-Dale, and the Ashtabula cases discussed in Appendix A.

Although one seismic station may be adequate for detecting earthquakes (and, in favorable cases, for estimating the distance of the earthquake to the station), a minimum of three stations would be necessary to determine the locations and focal depths of any earthquakes should they be detected in the vicinity of the well. Thus, once any induced seismicity is detected, it would then be appropriate to supplement an initial monitoring station with additional stations to provide reliable and accurate earthquake locations and focal depths.

Consideration of Small Earthquakes Near the Bottom of a Well

The occurrence of any earthquakes, even as small as magnitude 0, near the bottom of a well should be viewed with concern. Confirmation that earthquakes are indeed triggered by injection operations can often be obtained by comparing the frequency of earthquakes with the cycling of the injection pressure (fig. 2). It should be noted, however, that the pressure changes at the wellbore are damped out

with distance from the well. Therefore, induced or triggered earthquakes at some distance from the borehole should not be expected to correlate as well with the cycling of injection pressure as earthquakes in the immediate vicinity of the bottom of the well. If earthquakes thought to be related to injection operations are detected, then the following questions are appropriate: Is it possible that induced earthquakes might cause damage or injury in the surrounding area? and is it possible that the earthquakes indicate fault displacement that might threaten the integrity of the confining zone? If the answer to either of these questions is "yes," then consideration should be given to reducing the injection pressure. It should be remembered, however, that once the pore pressure in the reservoir or in adjacent rocks is raised above the critical pressure capable of triggering seismic faulting, lowering the pressure at the wellbore may not lead immediately to the cessation of earthquake activity. Seismicity would not be expected to stop until the pressure in the affected region has decayed below the critical value.

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APPENDIXES A–D

APPENDIX A—CASE HISTORIES OF EARTHQUAKES ASSOCIATED WITH WELL OPERATIONS

Rocky Mountain Arsenal, Colorado

The first well-documented case of injection-induced seismicity occurred at the Rocky Mountain Arsenal near Denver in 1966–67. The injection of 17 to 21 million L/mo of hazardous waste into a 3,671-m-deep disposal well was quickly followed by many felt earthquakes (fig. A1*A*) in a region where the last felt earthquake occurred in 1882 (Healy and others, 1968). Comparisons between the onset of seismicity and well operations and between earthquake frequency and average injection rate showed a convincing correlation (fig. 2; Evans, 1966a). Although injection ceased in February 1966, earthquakes triggered by the increased fluid pressure established around the wells continued for several years (fig. A1*C*). In 1967, three large earthquakes—each with a magnitude of greater than 5—occurred, causing minor structural damage in and around the greater Denver area.

In terms of their relative spatial distribution, a study of event locations indicated that the induced earthquakes began initially near the bottom of the injection well, then migrated out along a northwesterly trend for a distance of about 6 to 7 km (fig. A1*A*). After the earthquake sequence had been in progress for 5 yr (1½ yr after injection had stopped), earthquakes primarily occurred, not near the base of the well, but within the previously defined linear zone at a distance of 4 to 6 km from the well and at depths of 4 to 7 km. The largest earthquakes in the sequence (M 5–5.5) occurred in April, August, and November 1967 (fig. A1*B*), after which activity began to decline.

A total of 620 million liters (L) of fluid were injected at average rates of 478 L/min before well operations ceased. Maximum top-hole pressure (THP) reached 72 bars, which corresponded to an estimated bottom-hole pressure (BHP) of 415 bars (Evans, 1966a). Hsieh and Bredehoeft (1981) demonstrated that the records of pressure falloff at the disposal well were consistent with injection into a long narrow reservoir, a conclusion supported by the elongate shape of the seismogenic zone. No hydraulic stress measurements were ever made near the Rocky Mountain Arsenal. From the pressure at which the volume rate of fluid injection increased rapidly, Healy and others (1968) inferred a least compressive stress of 362 bars at the bottom of the disposal well and estimated a maximum compressive stress to be at least the overburden pressure of 830 bars. This assumption proved valid when it was demonstrated that the three largest earthquakes exhibited predominantly normal faulting along nodal planes that were parallel to the trend of earthquake epicenters (fig. A1*B*; Herrmann and others, 1981). Formation pore pressure before injection was estimated to be 269 bars. From these calculations and by using the Mohr-Coulomb failure criterion, a fluid pressure increase of 32 bars was determined to be sufficient to trigger seismic activity along favorably oriented preexisting fractures (Hsieh and Bredehoeft, 1981; Zoback and Healy, 1984). The observation that the earthquake locations were confined to those parts of the reservoir where the pressure buildup from fluid injection exceeded the critical threshold, as predicted by the Mohr-Coulomb failure criterion, strongly supports the conclusion that the earthquake activity was related to injection well operations and was consistent with fluid pressures within the reservoir initiating failure along favorably oriented fractures that had cohesive strengths of as much as 82 to 100 bars. The continuation of seismicity over time and the outward migration of earthquakes from the well were explained by the outward propagation of the critical levels of fluid pressure, even after the injection had stopped.

Rangely, Colorado

Water flooding for the secondary recovery of oil near Rangely began in 1958. Wells drilled to the producing horizon extended to depths of about 2 km. As of June 1970, 9,700 million L of water had been injected at a THP of about 83 bars; this represented a net increase of 2,300 million L after accounting for petroleum withdrawal (Gibbs and others, 1973). Following the installation of seismic monitoring equipment in 1962, earthquakes were found to be occurring within the oil field. In 1969, a dense network of stations was installed to determine accurate earthquake hypocenters and fault plane orientations. Seismic activity was found to be concentrated in a narrow zone, about 4 km long and 1.5 km wide, which crossed the boundary of the field to the southeast (fig. A2*A*; Raleigh and others, 1972). Hypocenters tended to cluster in two groups—one located at depths of 2 to 2.5 km near the wells and within the injection zone, and the other at depths of 3 to 5 km about 1 to 2 km from the wells. The maximum magnitude of the earthquakes generated was 3.1.

Hydraulic fracture data obtained at the bottom of one of the wells (fig. A2, top) indicated values for the maximum compressive stress (σ_1) of 552 bars, the intermediate principal stress (σ_2) oriented vertically and equal to 427 bars, and the least compressive stress (σ_3) of 314 bars. By using the Mohr-Coulomb failure criterion, Raleigh and others (1972) combined these hydraulic stress measurements with the locations and the fault orientations of the earthquakes, as well as laboratory-determined properties of the rock at depth to calculate that a pore pressure of about 260 bars (or 90 bars above the original formation fluid pressure of 170 bars) would have been sufficient to induce slip. This value was consistent with the formation fluid pressure of 275 bars measured in the oil field at the time that

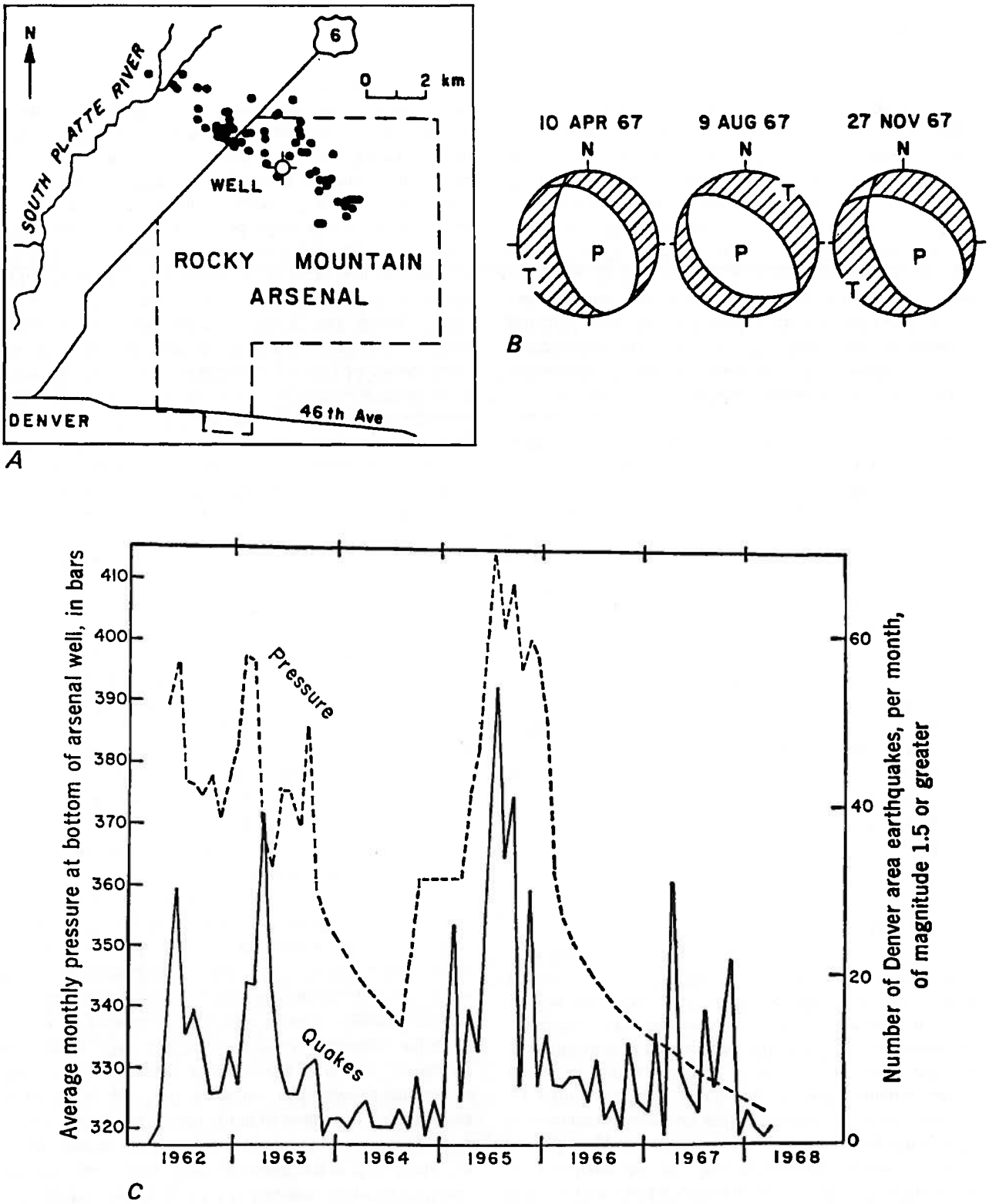
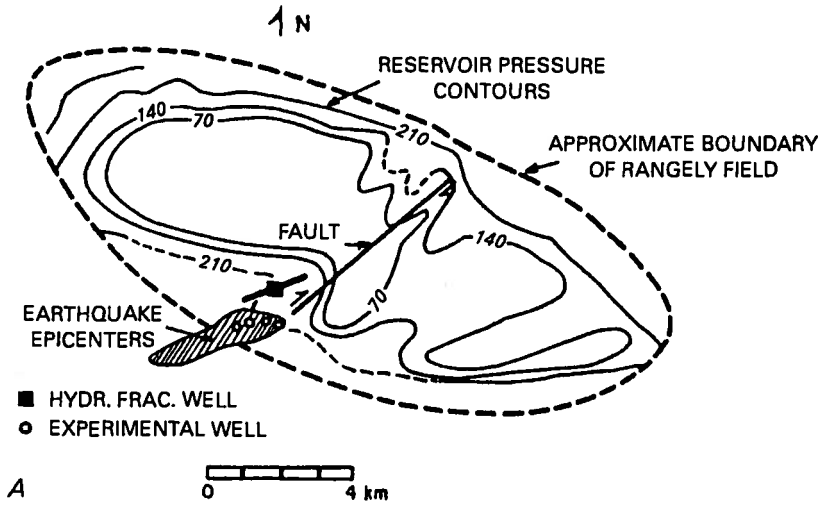


Figure A1. Earthquakes associated with the Rocky Mountain Arsenal well near Denver, Colo. *A*, Locations of earthquakes. Solid circle, location. *B*, Surface-wave focal mechanism solutions of the three largest Denver earthquakes. *C*, Numbers of earthquakes per month and average monthly injection pressure at the bottom of the well. *A*, reprinted from Healy and others (1968) and published with permission. *B* and *C*, reprinted from Zoback and Healy (1984) and published with permission.



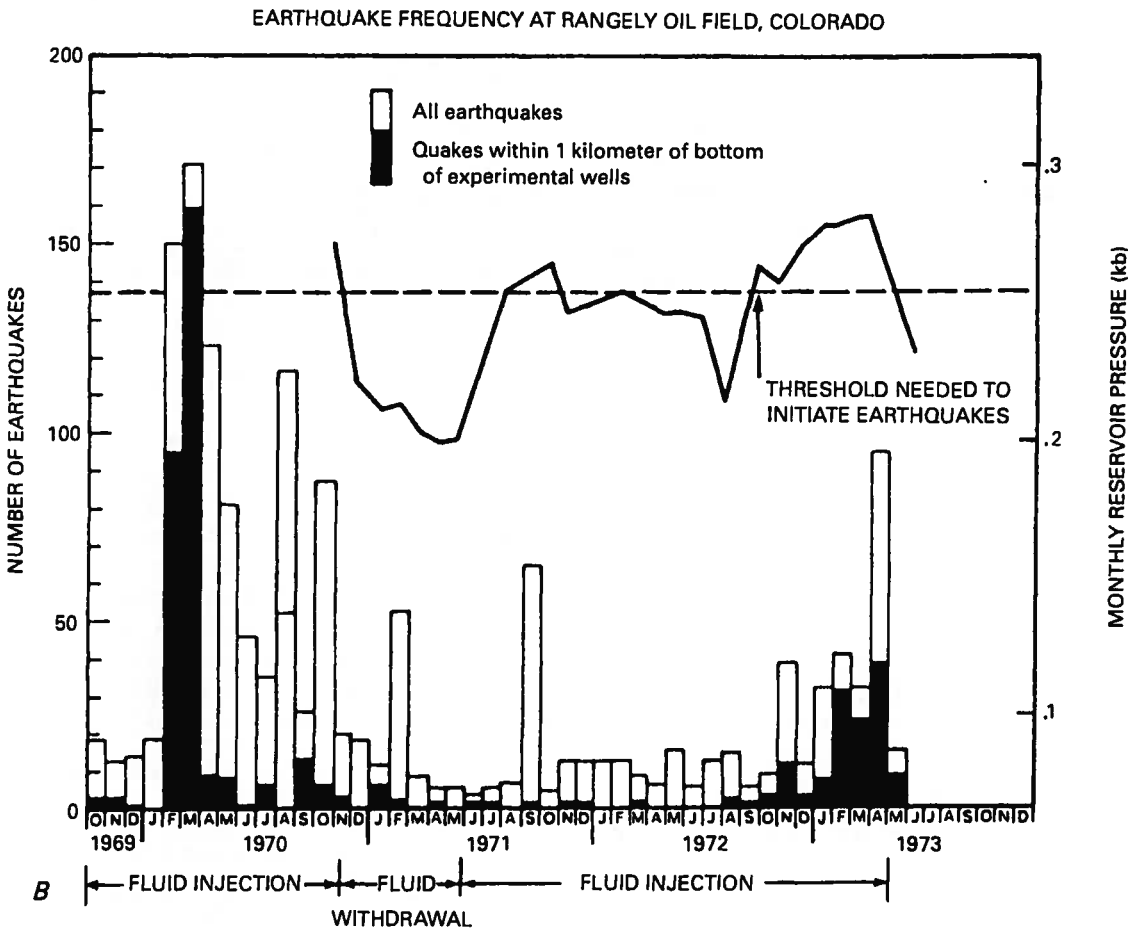


Figure A2. Seismicity and fluid injection, Rangely oil field, Colorado. *A*, Field geometry. Heavy dashed lines, approximate field boundary; light solid lines (dashed where inferred), reservoir pressure contours; hachured region, seismicity; solid square, location of the well used for hydrofracture stress measurements; and short line crossing the solid square, direction of the maximum horizontal compressive stress (S_H). *B*, Seismicity correlated with monthly reservoir pressure (heavy solid line). Reprinted from Raleigh and others (1976) and published with permission.

the induced seismicity began and corresponded to the critical pore pressure below and above which earthquake activity could be turned off and on when the injection pressure was varied intentionally in a later controlled experiment (fig. A2*B*; Raleigh and others, 1976). This experiment in earthquake control established the validity of the Mohr-Coulomb failure model in predicting the critical threshold of stress and pore pressure necessary for earthquake occurrence. Each time the fluid pressure in the part of the field where earthquakes had appeared previously exceeded the predicted threshold, more earthquakes began to occur (fig. A2*B*). Earthquake activity declined whenever the fluid pressure fell below the threshold.

Attica-Dale, New York

Solution mining for salt in the Attica-Dale area (fig. A3) triggered a marked increase in microearthquake activity in 1971. As many as 80 earthquakes per day were concentrated within 1 km of a 426-m-deep injection well (fig. A4; Fletcher and Sykes, 1977) in an area where the previous record of activity was less than 1 event per month. All these earthquakes were small and had estimated magnitudes of between -1.0 and 1.0. THP at the injection well typically operated between 52 and 55 bars, or only a few bars less than that calculated to induce sliding on preexisting fractures that have no cohesion, based on the Mohr-Coulomb failure criterion and analysis of hydrofracture stress measurements conducted about 100 km from the activity. Seismicity continued in the Dale brine field for as long as elevated pore pressure was maintained (fig. A5). The low level of background activity before high-pressure injection began, the dramatic increase in activity following injection, and the rapid cessation of activity following a decrease in injection pressure below about 50 bars (fig. A6) strongly suggest that this seismicity was induced by injection activities.

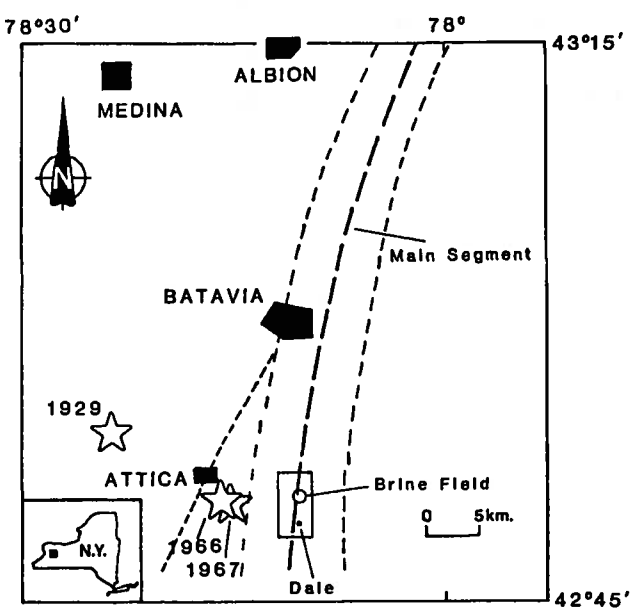


Figure A3. Location of the Dale brine field, western New York. Circle, field; heavy dashed line, Clarendon-Linden Fault; lighter dashed line, lesser secondary faults; stars, epicenters of large historical earthquakes near Attica in 1929, 1966, and 1967; and box, approximate area shown in figure A4 (from Nottis, 1986).

Texas Oil Fields

Permian Basin, West Texas and Southeastern New Mexico

Cases of induced seismicity associated with fluid injection operations for the secondary recovery of oil and gas have been suggested for several areas in Texas (pl. 1). One of the earliest reports alludes to an increase in seismicity associated with petroleum production and water-flooding operations in the Permian basin of West Texas near Kermit (Shurbet, 1969). A marked increase in earthquakes above magnitude 3 was observed to correlate with a dramatic increase in the number of injection wells operating at pressures greater than 70 bars. This increase in seismicity was of particular interest because of its proximity to a radioactive-waste-disposal site in southeastern New Mexico (fig. A7*A*; Rogers and Malkiel, 1979). About 20 earthquakes (the largest of which was about M 4.4) were recorded between November 1964 and December 1976. Twelve stations were subsequently installed to monitor this seismicity and to determine whether, in fact, the earthquakes were directly related to oil field activities. Between December 12, 1975, and June 26, 1977, 406 earthquakes were detected, most of which were at depths of less than 5.0 km and nearly all in areas that had active water-flooding operations (fig. A7*B*). Continued monitoring through September 1979 by the local network identified several pronounced clusters of seismic activity. The largest and most active area coincides with the War-Wink South oil and gas field located in the Delaware Basin region of Ward County, West Texas (Keller and others, 1981; Keller and others, 1987). Much of this seismicity is shallow and exhibits predominantly normal faulting (Keller and others, 1987), which is consistent with subsidence as a result of gas withdrawal. Other areas of activity include earthquakes in 1976 and 1977 associated with the Dollarhide oil field that extends into southeastern New Mexico, as well as more-recent seismicity located on the Central Basin Platform in the vicinity of the Keystone oil field (Orr, 1984; Orr and Keller, 1985). Nine of the local water-flooding projects that typically operated at injection pressures of greater than 100 bars are listed in table A1 (Texas Railroad Commission, 1971, 1985). These wells range in depth from 800 to 3,700 m. Measurements of *in situ* stress determined from hydrofracturing indicated a maximum regional compressive stress

Table A1. Characteristics of well operations and reservoir properties associated with possible induced seismicity

[Depth, bottom of well; thickness, of reservoir; k, permeability; THP, top hole pressure; BHP, bottom hole pressure; p_0, initial formation pore pressure; S_h, minimum horizontal compressive stress; S_H, maximum horizontal compressive stress; S_v, vertical stress; Max mag, maximum magnitude; ***, not applicable (injection not performed)]

Well site or oil field location	Depth (m)	Thickness (m)	k (mD)	Porosity (percent)	THP (bars)	BHP (bars)	p_0 (bars)	S_h (bars)	S_H (bars)	S_v (bars)	Max mag	Year of earthquakes
Ashtabula, Ohio	1,845	46	0.6	10	100	284	191	320	>460	460	3.6	1987
Catoosa, Okla.											4.7?	1956, 1960
Cogdell Canyon Reef, Tex.	2,071	43	18–30	7	199	406	215			476	4.6	1974–79
Dale, N.Y.	426	16			55	98		76	>109	109	1.0	1929?, 1966?, 1971
Rocky Mountain Arsenal, Denver, Colo.	3,671		0.03	2	76	415	269	362	<830	830	5.5	1962–67
East Texas, Tex.	1,113	3	200	23	103	214	70			256	4.3	1957, 1985
Fenton Hill, N. Mex.	2,700		.01		200	493	265	405	<635	635	<1.0	1979
Flashing Field, Tex.	3,400	50	13	15	***	71	352			768	3.4	1973–83
The Geysers, Calif.	3,000		<.05	3			<35	245	785	785	4.0	1975–
Gobles Field, Ontario, Canada	884	9			***		45			225	2.8	1979–84
Hunt Field, Miss.											3.6	1976–78
Imogene Field, Tex.	2,400	33	14	17	***	146	246			542	3.9	1973–84
Lake Charles, La.	1,411	49			93	234			<325	325	3.8	1983–
Love County, Okla.	3,622	427			277	632		538	~833	833	2.8?	1977?–, 1979
Matsushiro, Japan	1,800				50	230				460	2.8	1970
Northern Panhandle, Tex.	2,022	21	50	15	21	223	145			465	3.4	1983–84
Calhio, Perry, Ohio	1,810	88	6	8	114	294	200	320	>460	460	2.7?	1983–87
Rangely, Colo.	1,900	350	1	12	83	275	170	314	552	427	3.1	1962–75
Rocky Mountain House, Alberta, Canada.	4,000				***			>1,020	>1,020	1,020	4.0	1974–80
Sleepy Hollow, Nebr.	1,150	100	26		56	171	115		<265	265	2.9	1977–84
Snipe Lake, Alberta, Canada											5.1	1970
Permian basin fields:											4.4	1964–79
Dollarhide, Tex.-N. Mex.	2,590	59	17	14	138	397	179			596	~3.5	1964–79
Dora Roberts, Tex.	3,661	38	1	7	431	797	324			842	~3.0	1964–79
Kermit Field, Tex.	1,829	5	1	15	221	404	198			421	~4.0	1964–79
Keystone I Field, Tex.	975	11	21	20	103	200	90			224	~3.5	1964–79
Keystone II Field, Tex.	2,987	101	7	3	176	475	204			687	~3.5	1964–79
Monahans, Tex.	2,530	12	6	4	207	460	131			582	~3.0	1964–79
Ward-Estes Field, Tex.	914	11	35	16	117	208	103			210	~3.5	1964–79
Ward-South Field, Tex.	741	5	30	21	138	212	76			170	~3.0	1964–79
War-Wink South, Tex.	1,853	2.5	17	18	***					426	~3.0	1964–79

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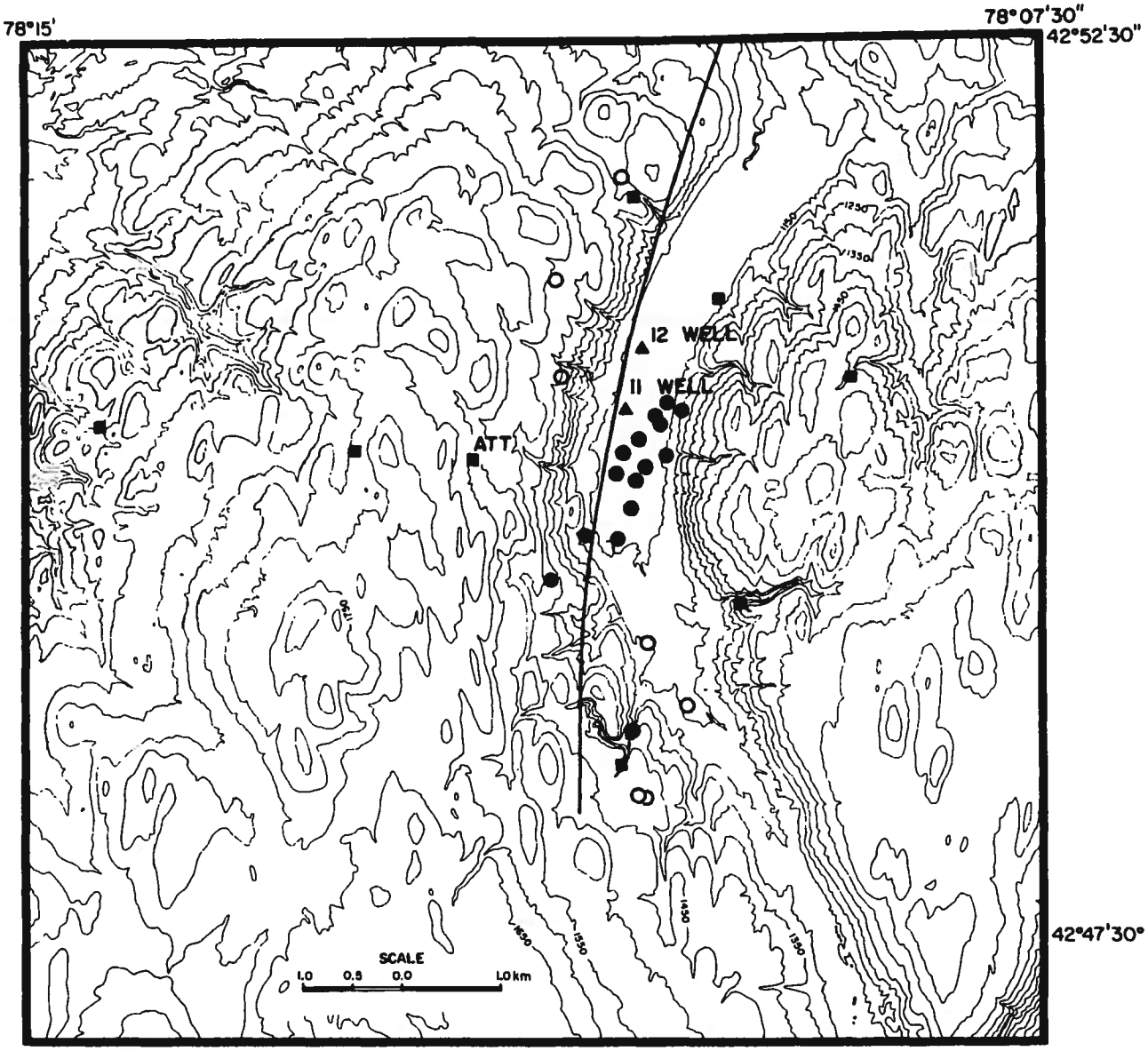


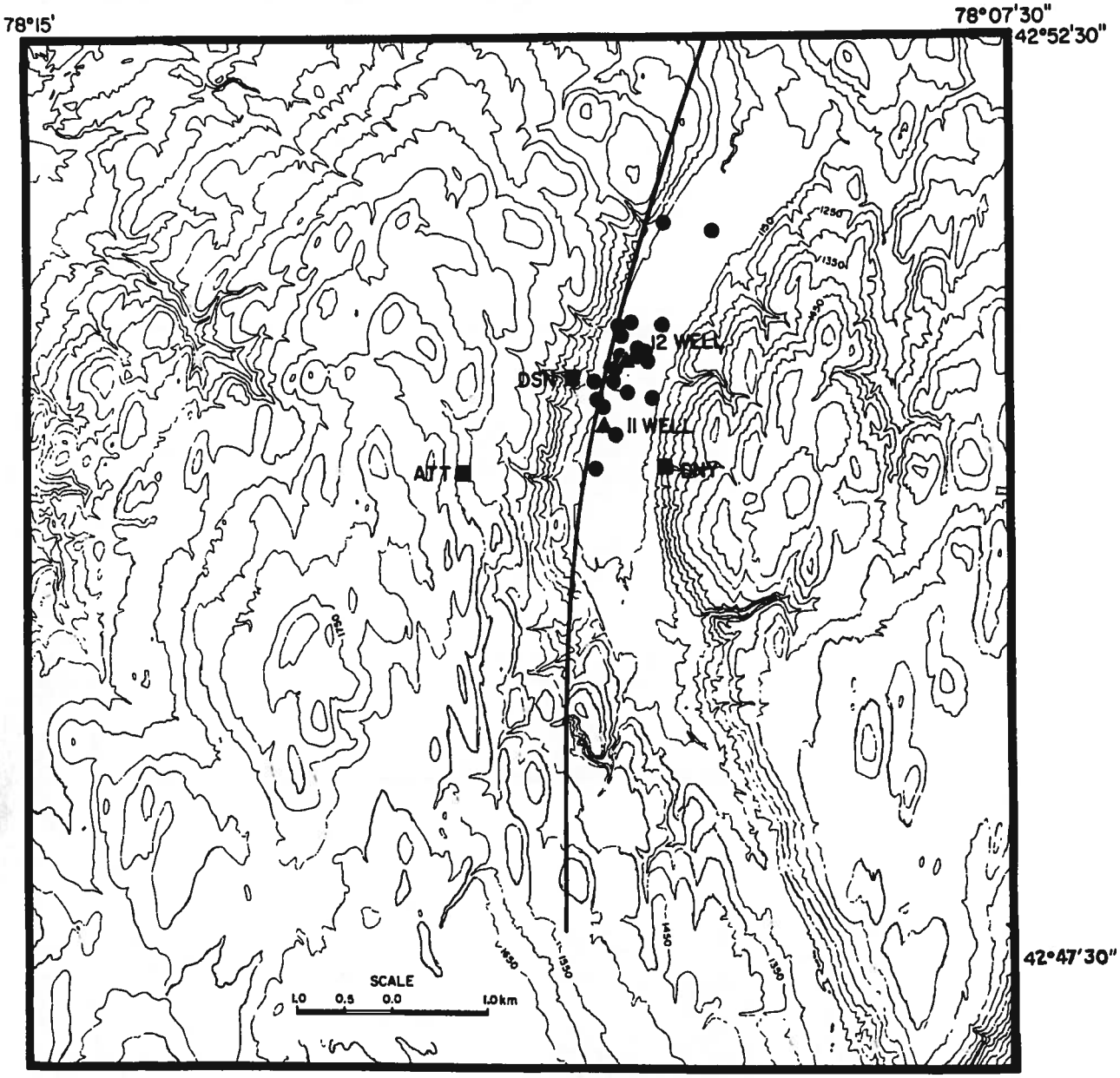
A

Figure A4. Epicenters of well located earthquakes near the Dale brine field, New York. Solid circles, well located earthquakes; squares, monitoring stations; triangles, injection wells; open circles, epicenters that have poor resolution; and solid line, Clarendon-Linden Fault. *A*, October 1971. *B*, November 1971. Reprinted from Fletcher and Sykes (1977) and published with permission.

of 150 bars and a minimum compressive stress of 85 bars at depths of about 485 m.

Cogdell Canyon Reef Oil Field, West Texas

The largest earthquake to occur in known association with an oil field injection operation within the United States was a magnitude 4.6 to 4.7 event near Snyder in June 1978. This earthquake, which was part of a sequence of events that apparently had been active since 1974 (Davis, 1985), was located in the Cogdell Canyon Reef oil field of West Texas (fig. A8). Initial formation pressure at the time of discovery (1949) amounted to 215 bars BHP. By 1956, pressure in the field had dropped to 79 bars BHP, which necessitated a water-flooding and pressure-maintenance program. A dramatic increase in the numbers of injection wells, volumes of fluid pumped, and effective pressures took place in the early 1970's, shortly after which the first felt earthquake was experienced (Harding, 1981a). Surface injection pressures ranged as low as 45 to 95 bars, but



B

Figure A4. Continued.

typically operated between 186 to 217 bars THP. By using the Mohr-Coulomb failure criterion, these higher values of injection pressure were determined to be sufficient to induce slip on favorably oriented fractures (Davis, 1985). Because injection pressure in the field remained fairly constant, there is little correlation between the injection pressure and the episodic nature of the earthquake activity. There is some correlation, however, between volumes of fluid injected and the rate of local earthquake occurrence (fig. A9). The data were interpreted to suggest that large (felt) earthquakes were preceded by a reduction in field permeability (which corresponded to a drop in volume of water accepted by the reservoir at constant pressure) followed by an increase in permeability after each of the major earthquake sequences (Harding, 1981a).

Because of the proximity of the earthquakes to oil field operations, a small local network of stations was operated from February 1979 through August 1981 (fig. A8; Harding, 1981a). As of 1985, a total of about 30 earthquakes had been spatially associated with the Cogdell

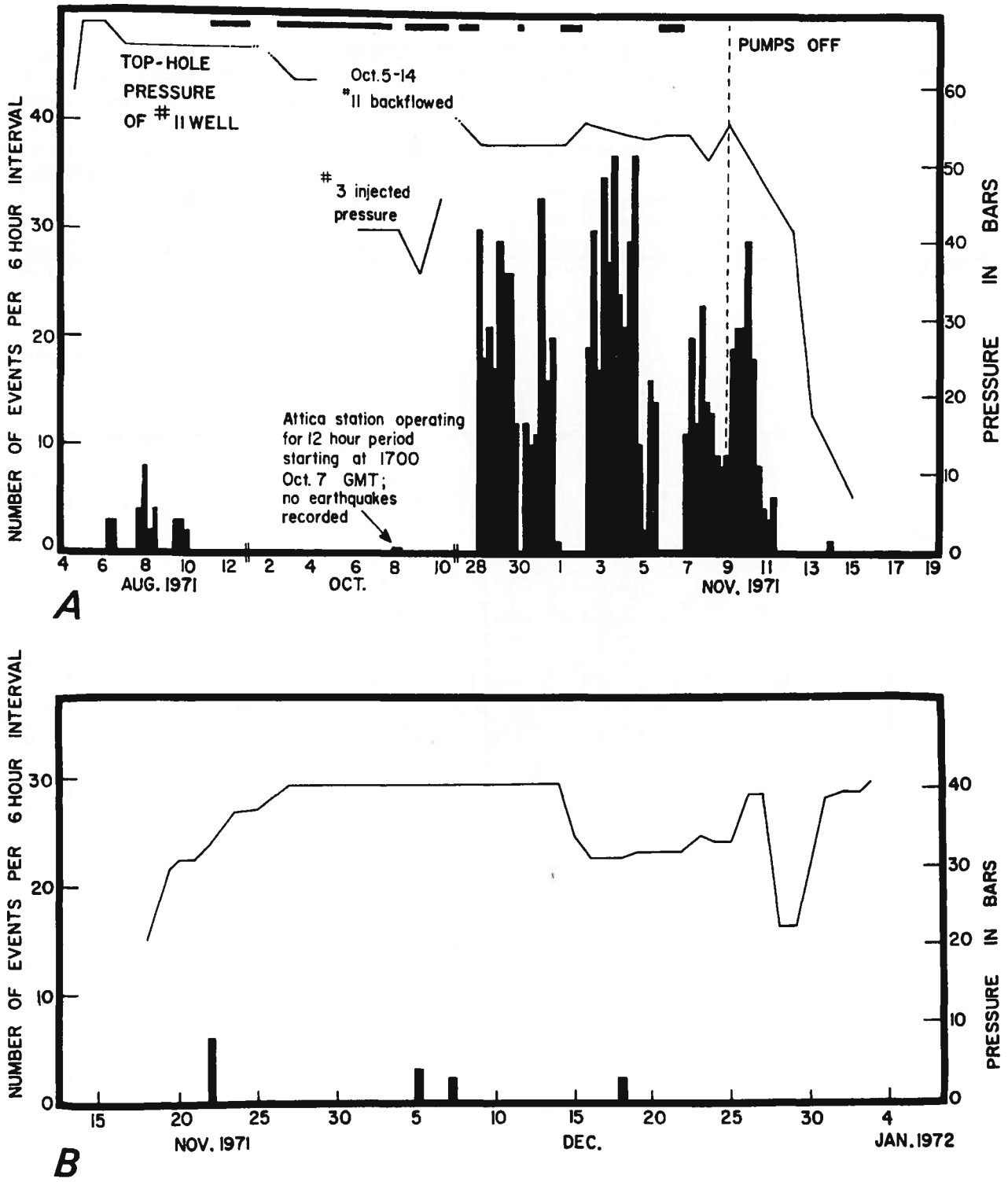


Figure A5. Number of earthquakes and pumping pressures (light solid lines) with time in the Dale brine field, New York. *A*, From August 4 to November 19, 1971, when top-hole injection pressures in well 11 typically exceeded 50 bars. Note the abrupt cessation of activity after pumping was shut down on November 9. *B*, Similar to *A* but from November 15, 1971, to January 4, 1972, when the maximum injection pressure did not exceed about 40 bars. Reprinted from Fletcher and Sykes (1977) and published with permission.

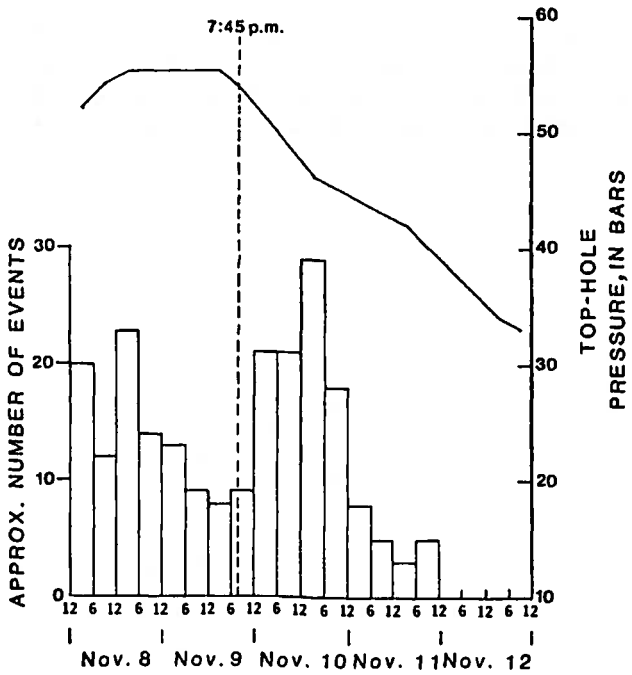


Figure A6. Enhanced section of figure A5 for well 11 of the Dale brine field, New York, showing the rapid decrease in seismicity after pumping ceased at 7:45 p.m. on November 9, 1971, and well pressure (solid line) subsequently declined below about 50 bars (from Nottis, 1986).

Canyon Reef oil field (fig. A8); most of the events occurred between April 1977 and August 1979. Many of the wells that penetrate to the Canyon Reef Formation operate at depths of between 2,070 and 2,265 m. These well depths coincide with the shallow focal depths (on the order of 3 km or less) of the earthquakes located within the oil field (Harding, 1981b) and are nearly the same as the focal depth (3 km) determined for the June 1978 event (Voss and Herrmann, 1980).

Atascosa County, South Texas

Seismic activity also has been identified with the *withdrawal* of oil and gas from two fields in south Texas (pl. 1; Pennington and others, 1986). Production from the Imogene oil and gas field began in 1944; the depth of the producing horizon is 2.4 km. Initial fluid pressure in the field was approximately 246 bars and was reduced to 146 bars by 1973. In the Flashing gas field, production began in 1958 at a depth of 3.4 km. Initial pore pressure in the producing formation was 352 bars but was reduced to only 71 bars (or 20 percent of the original value) by 1983. The rapid withdrawal of fluid and gas apparently resulted in subsidence and differential compaction of the producing horizon in both fields, which is similar to the situation in the War-Wink gas field. Seismic activity began in 1973; the largest earthquake (M 3.9) occurred in the Imogene field in March 1984. In both cases, the sizes and the number of earthquakes increased over time, which is consistent with a model for the evolution of the hydrologic characteristics of the field whereby the strength of the rock increases as fluid pressure decreases. The earthquakes are believed to be generated as formation pore pressure is reduced to the point that further fluid extraction and subsequent subsidence results in strain accumulation in the newly strengthened rock. If the strains are large enough, then the amount of energy accumulated in the rock is apparently sufficient to cause earthquakes as large as magnitude 3 to 4 (Pennington and others, 1986).

The Geysers, California

In a case similar to Atascosa County, Tex., a large number of small earthquakes ($M_L \leq 4$) have been triggered by the reduction in steam pressure caused by energy production in The Geysers geothermal area near Clear Lake in northwestern California (fig. A10; Oppenheimer, 1986). The Geysers is the site of a vapor-dominated steam field where, by the early 1980's, 150 wells had been drilled to depths of between 0.8 and 3.0 km. Earthquake activity has increased in The Geysers area by nearly a factor of two over seismicity levels before production; about 10 microearthquakes that have magnitudes of greater than 0.5 typically occur each day. Evidence that the increased seismicity was induced relied upon the spatial and the temporal distribution of the microearthquakes in the vicinity of the producing steam wells. During the period from 1975 to 1981, earthquakes were found to occur in previously aseismic areas within months following the initiation of steam extraction from newly developed regions of the reservoir. Seismic activity also correlated with energy production or rate of steam extraction (fig. A11). Earthquake hypocenters were found to extend from 0 to 6.5 km in depth, but earthquakes that had focal depths of less than 3.5 km were typically located within a few hundred meters laterally from the sites of active steam wells (Eberhart-Phillips and Oppenheimer, 1984). Although some of the extracted steam is condensed and reinjected, the reduction in effective normal stress caused by increased pore pressure is not considered to be the likely mechanism to explain the induced seismicity. Steam pressure in the field actually has declined by about 1 bar/yr since 1966 as a result of cooling, and the number of earthquakes did not correlate with volumes of steam condensate injected into the wells. The two possible mechanisms thought to be responsible for the increased seismicity are the increased shear stresses that are a result of volumetric thermal contraction caused by reservoir cooling (Denlinger and others, 1981) and by reservoir subsidence arising from large fluid mass withdrawal (Majer and McEvilly,

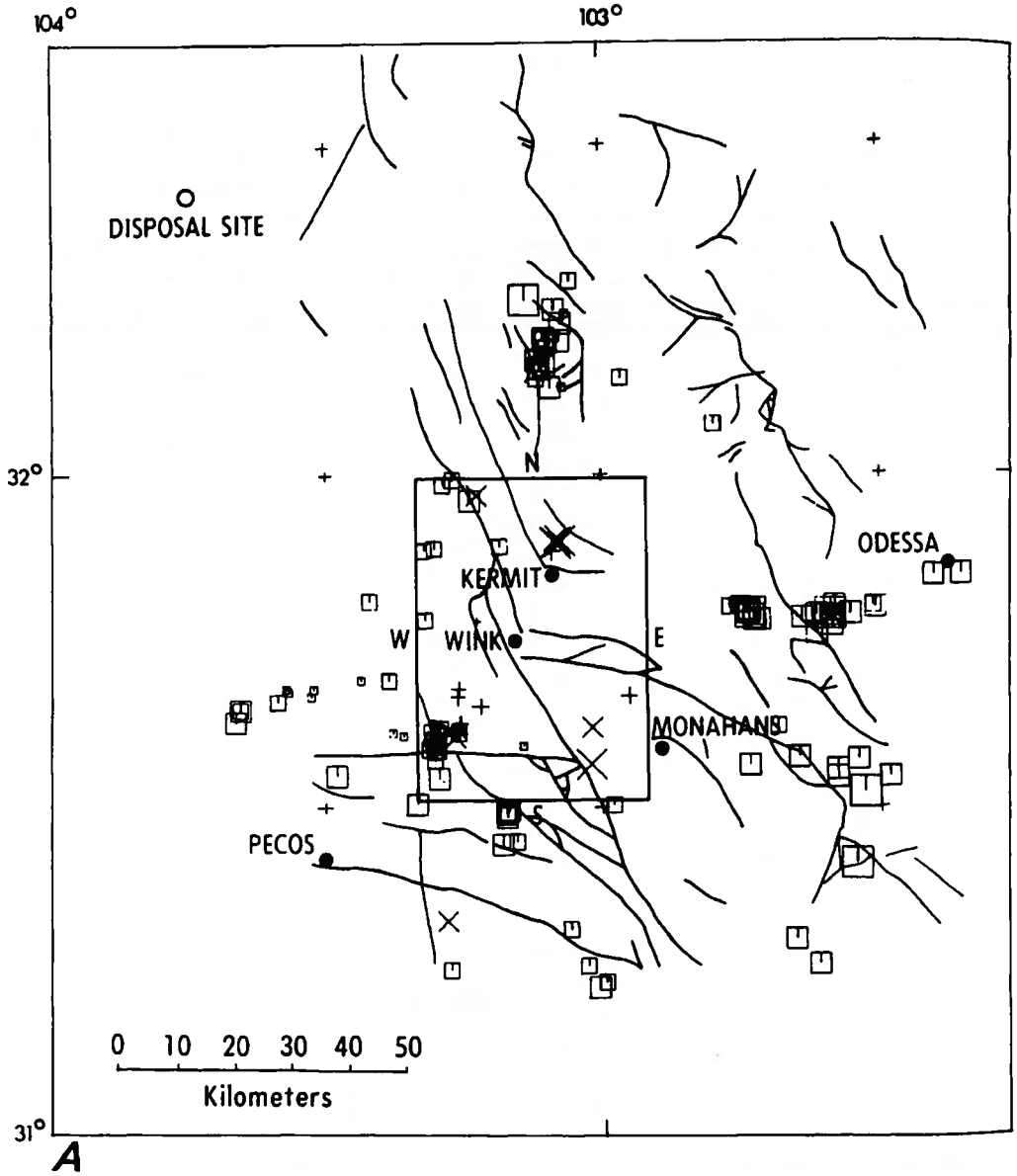


Figure A7. Earthquakes located in the Central Basin Platform of the Permian Basin, West Texas, from January 1976 to July 1977. *A*, Earthquake epicenters and known pre-Permian basement faults shown with solid lines; radioactive-waste-disposal site in New Mexico is shown by the open circle. *B*, Epicenters and outlines of oil fields; labeled fields are sites of active water-flooding operations during the same time period. *A* and *B*, Size of symbol indicates magnitude—X, 3.0 to 4.0; x, 2.0 to 3.0; +,1.0 to 2.0; +, ≤1.0; square sizes indicate less reliable earthquake epicenters in the same magnitude ranges. Reprinted from Rogers and Malkiel (1979) and published with permission.

1979) or, alternatively, the conversion of continuous aseismic slip into seismic slip (that is, earthquakes) by an increase in the coefficient of friction following the deposition of exsolved solids (probably silica) onto slipping fracture surfaces (Allis, 1982).

Fenton Hill, New Mexico

Several hundred microearthquakes were generated during a massive hydraulic fracturing experiment conducted at Fenton Hill (pl. 1) in March 1979 (Pearson, 1981). The

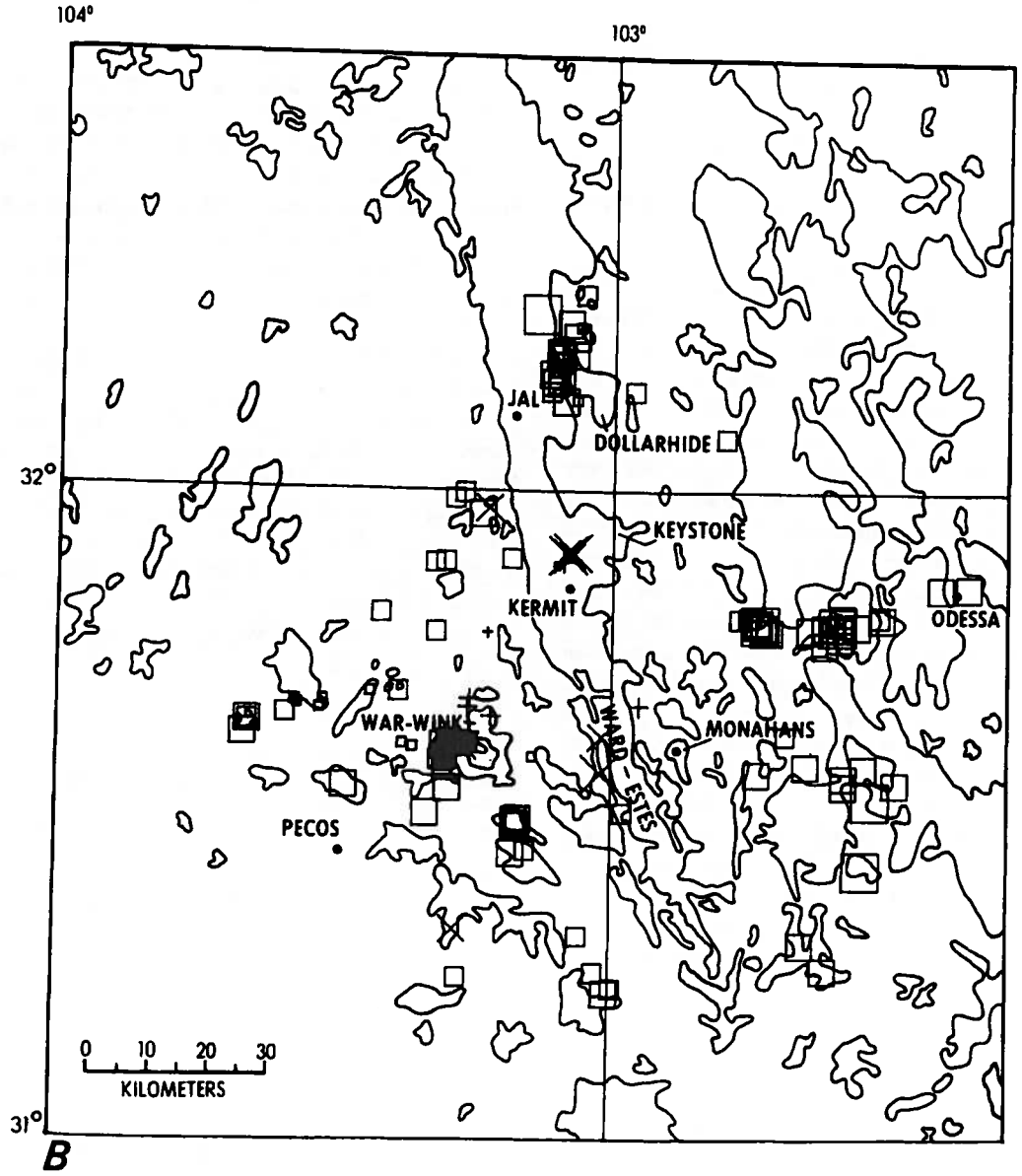


Figure A7. Continued.

purpose of the experiment was to stimulate a fracture in a deep (2,930-m) injection well that would propagate so as to intersect an adjacent production well to be used in a hot-dry rock geothermal energy project. Hydraulic stimulation involved nearly 460,000 L of water injected over a 5½-hr period. Maximum THP was held constant at 200 bars. During the experiment, activity averaged 3 to 4 microearthquakes per minute. Formation pore pressure before injection was measured at about 265 bars. Maximum and minimum effective horizontal stresses were found to be 370 and 140 bars, respectively. By using the Mohr-Coulomb failure criterion, Pearson (1981) determined that only 30 bars of increased pore pressure was sufficient to initiate slip on favorably oriented preexisting joints. Most of the small earthquakes appeared to be localized to within 30 m of the expanding hydraulic fracture. Unfortunately, the stimulated fracture failed to intersect the desired production well. In a subsequent attempt, 7.6 million L of water was injected at a depth of 3,400 m at a rate of 1,600 L/min, which triggered an additional 850 microearthquakes in the vicinity of the well (House and McFarland, 1985).

Sleepy Hollow Oil Field, Nebraska

After the installation of sensitive monitoring equipment in Nebraska in 1977, a concentration of seismic

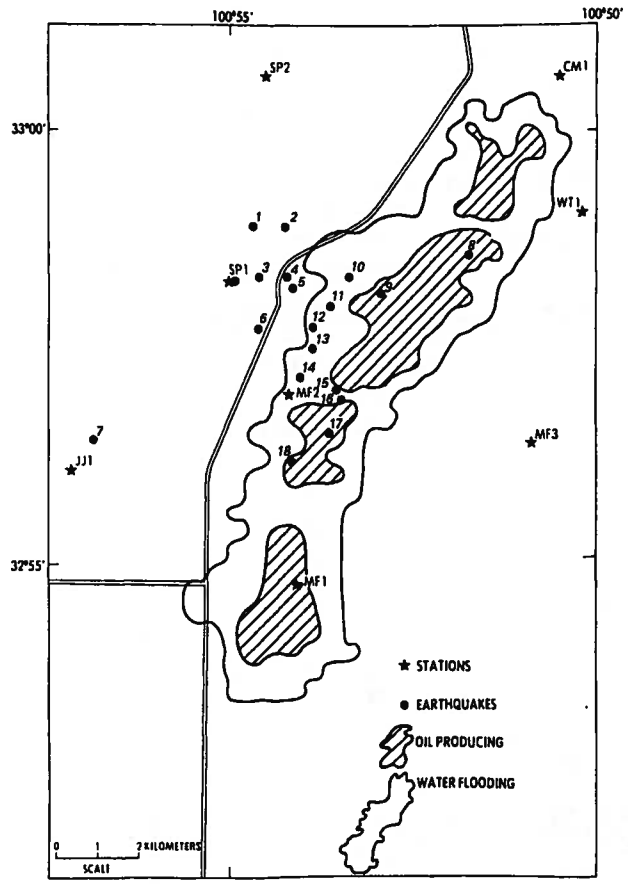


Figure A8. Epicenters of well located earthquakes in the Cogdell Canyon Reef oil field near Snyder, Tex. Also shown are the locations of network stations and the extent of water flooding and oil production (from Harding, 1981a).

activity was identified near the Kansas-Nebraska border (pl. 1). From March 1979 to March 1980, subsequent investigations using portable instruments (fig. A12*A*) detected 31 earthquakes in close proximity to the most productive oil field in the State—the Sleepy Hollow (Evans and Steeples, 1987). Water flooding to enhance recovery had been in operation since 1966. As shown in figure A13*A*, water injection typically operated at 52 bars THP within the Lansing Group (depths of 1,050–1,130 m) and 22 bars within the Sleepy Hollow sandstone (Reagan) formation (1,150–1,170 m depth), which corresponded to 172 and 142 bars BHP, respectively. Most of the well located earthquakes occurred within the confines of the producing field and at depths of less than 2 km (Rothe and Lui, 1983) in an area where well-defined subsurface faults (fig. A13*B*) were present, based on structure contour maps. Maximum magnitude of the induced seismicity was 2.9. In a later monitoring program, an additional 250 microearthquakes were detected within the active field between April 1982 and June 1984 (fig. A12*B*; Evans and Steeples, 1987),

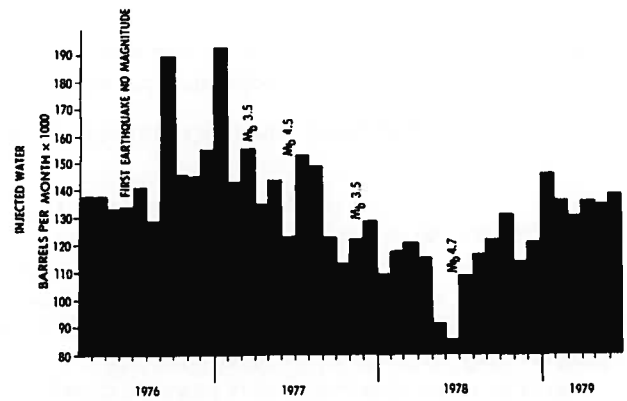


Figure A9. Cumulative monthly volume (barrels) of water injected in the Cogdell Canyon Reef oil field, Texas, and times of reported felt earthquakes (from Harding, 1981a). M_b, body-wave magnitude.

when the average THP in the field reached as high as 56 bars.

Southwestern Ontario, Canada

Oil and gas production from the Gobles oil field, which is located in southwestern Ontario about 55 km east-northeast of London (fig. A14*A*) began in 1960 (Mereu and others, 1986); the producing horizon is 884 m deep. Because formation fluid pressure was lower than expected, water-flooding operations to enhance recovery began in 1969. Historically, this area of southwestern Ontario has had a very low level of seismic activity. In December 1979, a M 2.8 earthquake was detected in the vicinity of the oil field. From July 1980 through August 1984, a portable network of stations recorded 478 earthquakes within and around the producing area (fig. A14*B*). All the locatable events were shallow and exhibited travel-times consistent with hypocenters at a focal depth coincident with the producing horizon. No spatial correlation with specific wells was identifiable, however, and, although earthquake activity varied considerably in time, fluctuations in activity rate did not correlate with injection pressure, which, for the most part, remained nearly constant. This area is located just west of the Dale brine field in western New York and just north of injection-induced seismicity in northeastern Ohio (see section "Recent Seismicity and Injection Operations—Northeastern Ohio").

Matsushiro, Japan

Besides the Rangely oil field experiment, one of the few attempts to specifically manipulate earthquake behavior by fluid injection occurred near Matsushiro, Japan. In 1970, 2.9 million L of water was injected at a depth of 1,800 m,

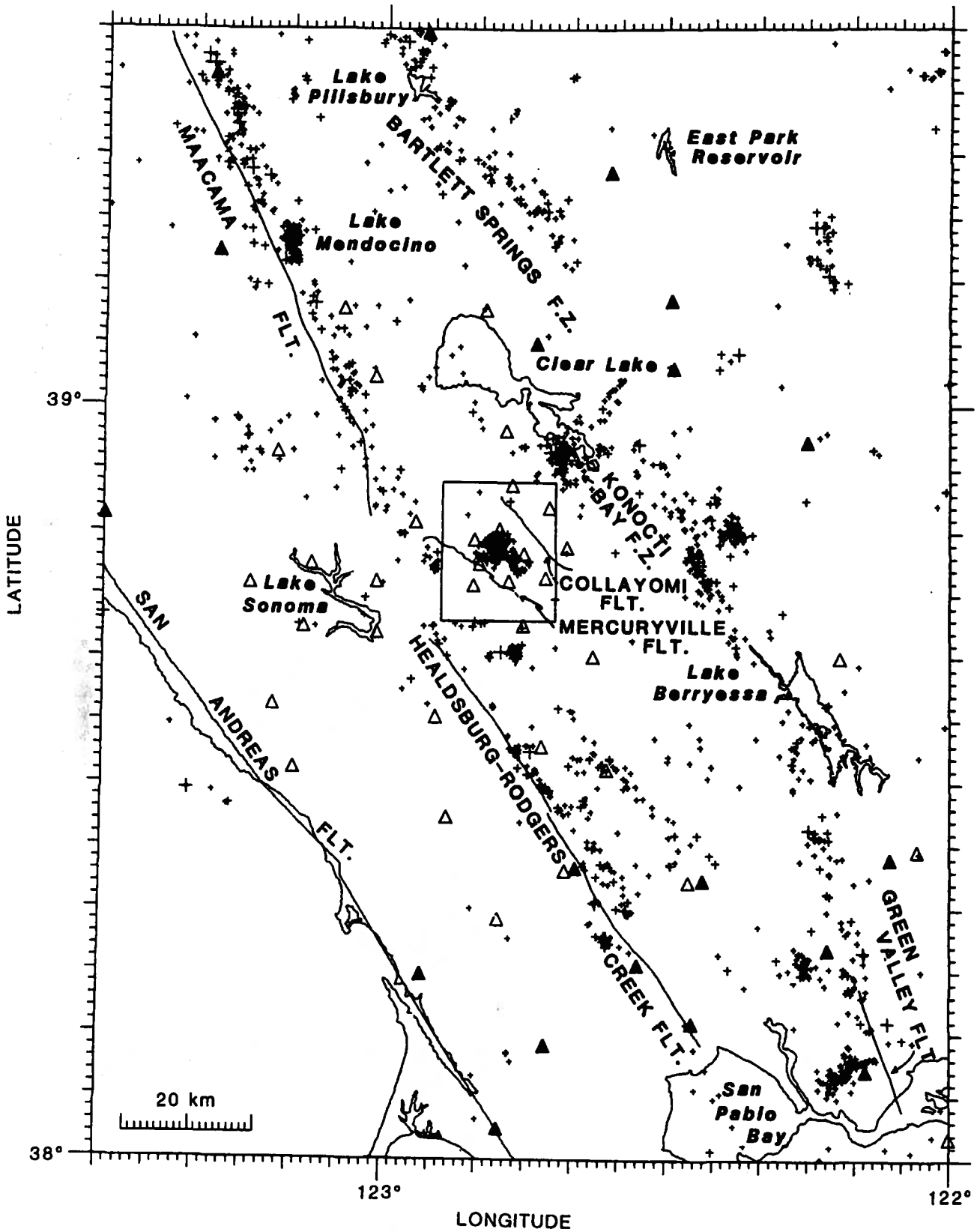


Figure A10. The Geysers geothermal area, California, and surrounding region. Epicenters outside the box represent well located earthquakes from January 1976 through December 1984. Seismicity inside the box is from the period January 1984 through October 1985. Open box, geothermal area; +, $M_L \geq 1.5$ epicenters; open triangles, locations of CALNET stations; and solid triangles, locations of stations used for locations of regional seismicity. Reprinted from Oppenheimer (1986) and published with permission.

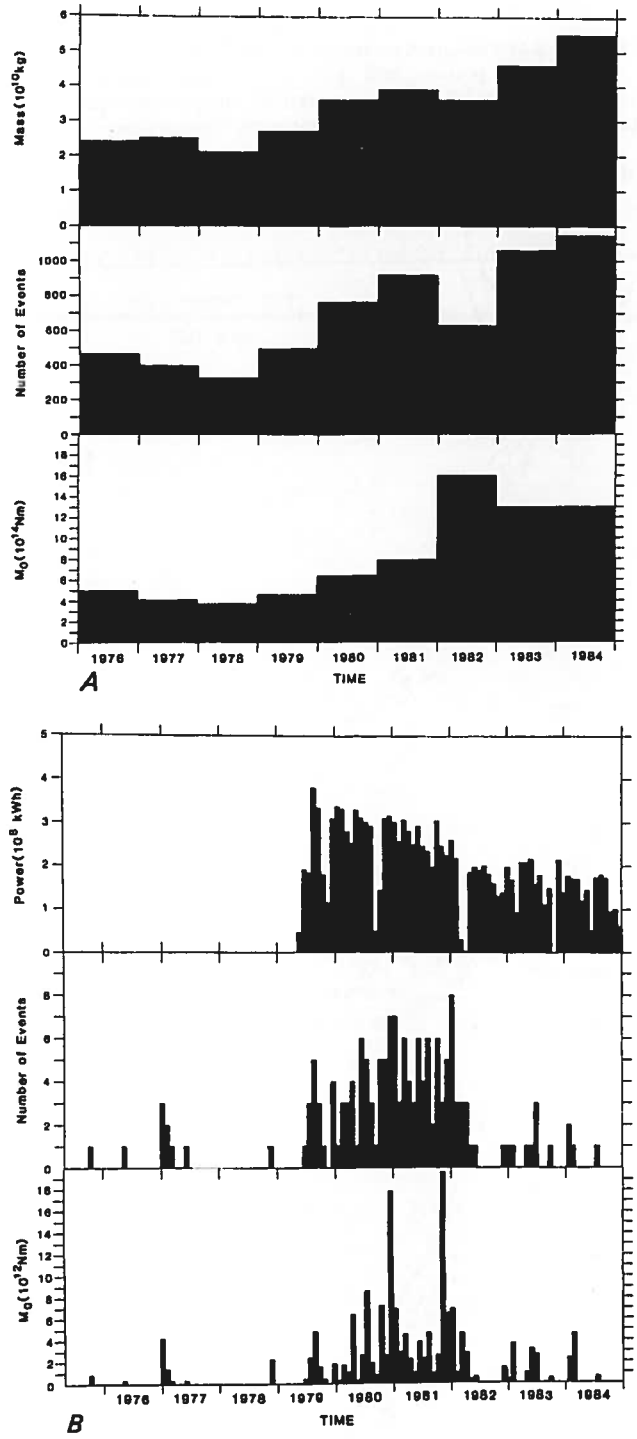


Figure A11. Water withdrawn and power generated as compared with the rates of seismicity at The Geysers geothermal field, California. *A*, Yearly net mass of water withdrawn. *B*, Monthly power generated. Both are compared with numbers and moments of earthquakes. Reprinted from Oppenheimer (1986) and published with permission.

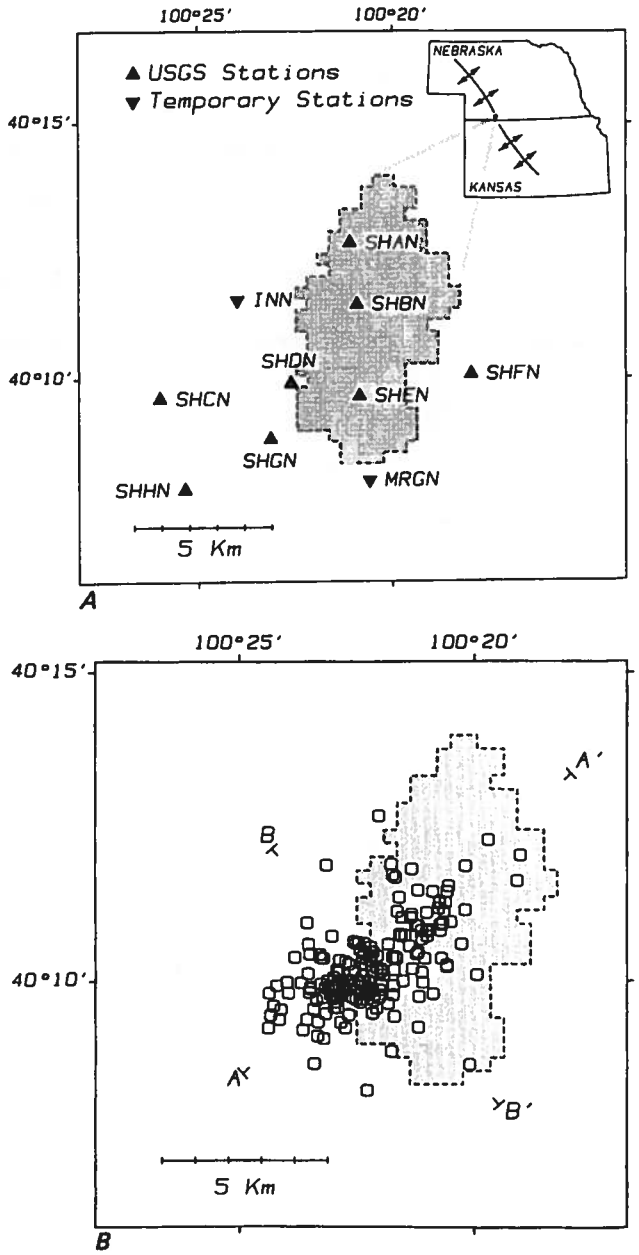


Figure A12. Seismic monitoring stations and earthquake epicenters, Sleepy Hollow oil field, Nebraska. *A*, Seismic monitoring stations. Shaded region, producing area of the field; and triangles, stations. *B*, Earthquake epicenters in the vicinity of the field between April 1982 and June 1984. Reprinted from Evans and Steeples (1987) and published with permission.

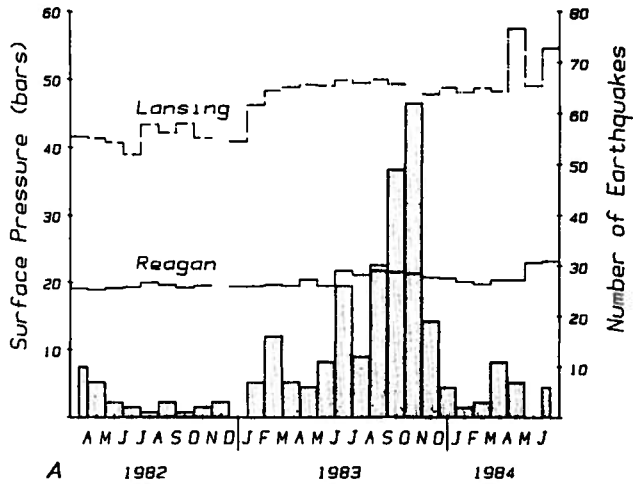
THP's of 14 to 50 bars, and injection rates of 120 to 300 L/min (Ohtake, 1974). During the 2 months (mo) of the experiment, several hundred small earthquakes were triggered within 4 km of the well and at depths of 1.5 to 7.5 km. A delay of 5 to 9 days (d) was observed between the onset of the increased seismicity and the increased injection pressure. Activity was significantly greater during injection than either before or after the experiment. Much of the induced seismicity was localized along the northeast-dipping Matsushiro fault zone, whereas most of the background seismicity was scattered in the hanging wall (Ohtake, 1974). No attempts were made to determine the *in situ* state of stress or the critical threshold for failure as indicated by the Mohr-Coulomb failure criterion, but the observed time delay for the onset of seismicity and the subsequent migration in depth of the earthquakes were consistent with inferred values of permeability and the time required for pore pressure effects to migrate to the area where the earthquakes were observed.

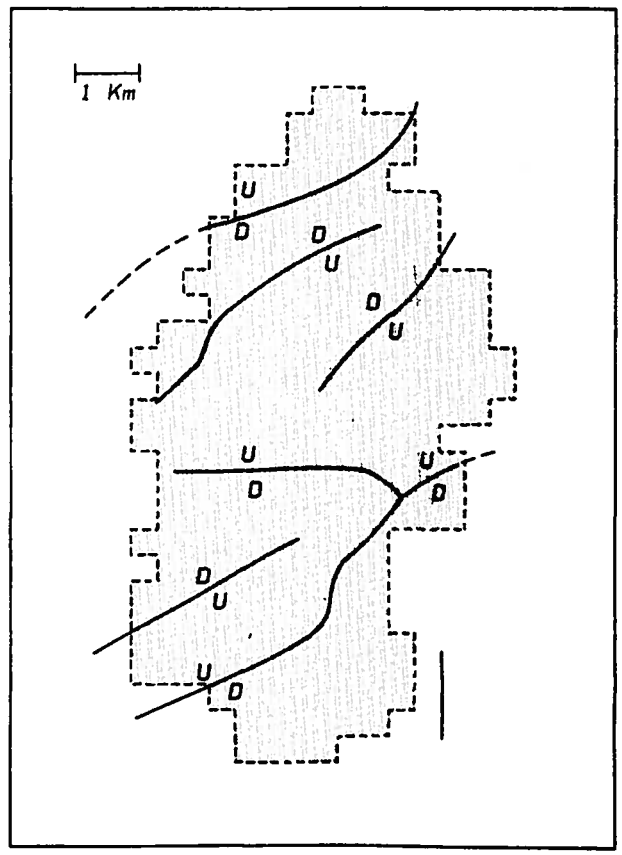
Less Well Documented or Possible Cases

Western Alberta, Canada

On March 8, 1970, a M 5.1 earthquake occurred near Snipe Lake (fig. A15; Milne, 1970). No significant earthquakes had previously occurred in the area, and, on the basis of the limited felt area and preliminary determinations of focal depth (<9 km), the 1970 event appeared to have been relatively shallow (Milne and Berry, 1976). At the time of the earthquake, 646 oil and gas wells were in operation within 80 km of Snipe Lake. Production began in 1954, and water injection to maintain field pressure had been in effect in 56 wells since 1963. Although little else is known about this event, this earthquake is considered to be the first and largest known Canadian example of an earthquake induced by fluid injection in a producing oil field because it occurred within an oil-producing area where fluid injection was actively taking place (Milne and Berry, 1976).

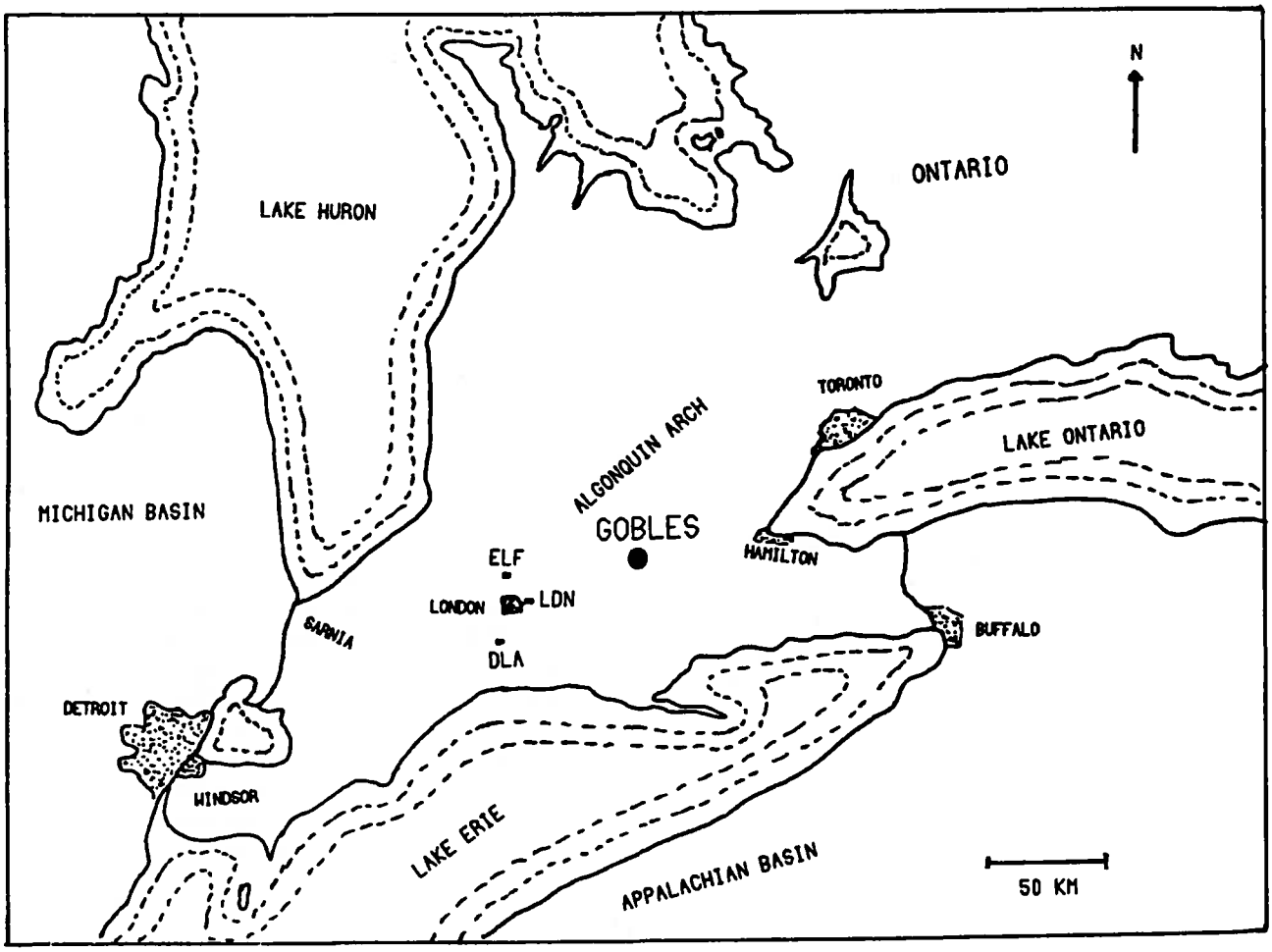
Confirmation that well activities in western Alberta are triggering earthquakes was documented near Rocky Mountain House (fig. A15; Wetmiller, 1985, 1986), where a microearthquake survey was conducted in 1980. In 23 d of operation, a seven-station network detected 146 earthquakes, of which 67 events were locatable. The largest earthquake recorded was a magnitude 3.4. All the locatable earthquakes occurred in a very small source area (fig. A16*A*) that was about 4 km long by 4 km wide by 1 km thick at a depth of 4 km. This source region coincides with the base of the Paleozoic section and is the site of the Strachan D-3A gas field, which is a Devonian-aged limestone-reef sour gas reservoir and western Alberta's major producer of natural gas. Production began in the field in the early 1970's, and a marked increase in seismicity, including earthquakes as large as M 4.0, began in 1974 (fig.





B

Figure A13. Formation fluid pressures and mapped faults, Sleepy Hollow oil field, Nebraska. *A*, Average monthly pressures within the two formation reservoirs used for injection and the number of earthquakes per month. Ten injection wells were added in May and June 1983. *B*, Mapped faults in the Precambrian basement in the vicinity of the field (shaded area). Reprinted from Rothe and Lui (1983) and published with permission.



A

Figure A14. Location and earthquake epicenters, Gobles oil field, southwestern Ontario, Canada. Seismic stations of the University of Western Ontario permanent seismic array are shown. *A*, Location of the field (solid circle). *B*, Earthquake epicenters in the vicinity of the field relative to location of local monitoring stations (solid squares). Reprinted from Mereu and others (1986) and published with permission.

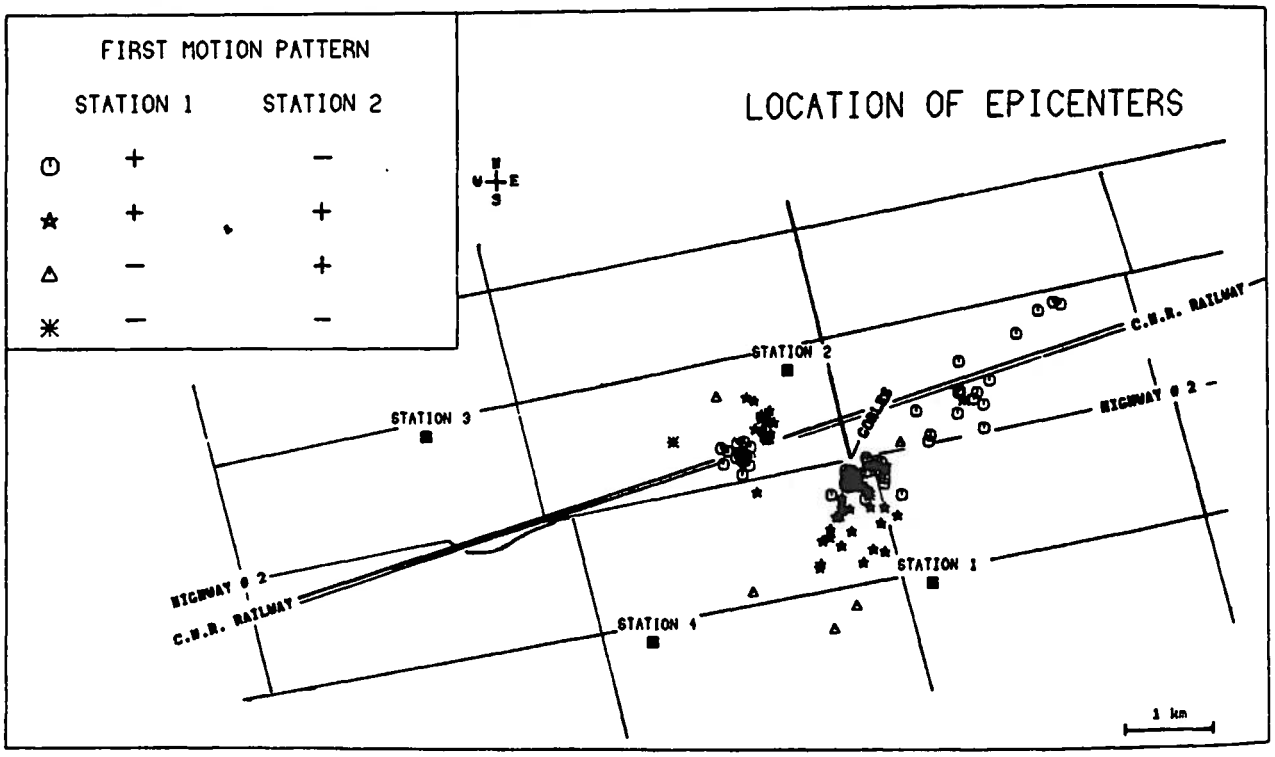
A16*B*; Wetmiller, 1986). The timing and the spatial correspondence of the microearthquake activity directly in or below the actual zone of production strongly suggests that the local seismicity is being triggered by gas production. The predominant thrust-faulting focal mechanisms exhibited by the earthquakes, however, indicate that the seismicity may be related to crustal unloading, which is similar to the situation of possible induced earthquakes near the Gazli gas field in Soviet Uzbekistan (Simpson and Leith, 1985), rather than to other cases of shallow normal-faulting events associated with subsidence of petroleum fields without secondary fluid injection (Yerkes and Castle, 1976; Pennington and others, 1986).

Since 1984, a six-station seismic network has been operating in the Cold Lake area of Alberta (Kapotas and Kanasewich, 1989), where heavy oil is being extracted by using an *in situ* process of steam injection. Local microearthquake activity ranges from 20 to more than 100 events per year. The induced tremors are mostly less than M 2 and, on the basis of geomorphological characteristics of the bedrock topography, appear to follow a major inferred subsurface fault structure through the area of heavy-oil production. Within the network, induced earthquakes occur at shallow focal depths consistent with formation levels of steam injection and oil extraction. Southeast of the array, earthquakes are also detected in association with fluid injection operations to dispose of excess oil field brine (Kapotas and Kanasewich, 1989).

Historical Seismicity and Solution Salt Mining

Western New York

The identification of recent induced seismic activity with the Dale brine field (Fletcher and Sykes, 1977) and



B

Figure A14. Continued.

with secondary recovery operations in southwestern Ontario (Mereu and others, 1986) suggests that a relation may exist between the older historical earthquakes in western New York and the adjacent solution mining operations in production at the time. Solution salt mining operations have been in operation in the northwestern region of the State since the late 19th century (Dunrud and Nevins, 1981). In 1929, a large (M 5.2) earthquake occurred near Attica (fig. A3), that caused significant damage in the epicentral region [VIII on the Modified Mercalli Intensity Scale (MM), Appendix C]. Subsequent earthquakes in 1966 (M 4.6) and 1967 (M 3.8) also generated relatively high intensities for their size (Herrmann, 1978). These high intensities were attributed to the shallow focal depths of the earthquakes (about 2 km, or roughly on the same order as the depth of the active solution salt mining wells). Past investigators have attributed these earthquakes near Attica to tectonic slip along the Clarendon-Linden fault system (fig. A3); however, the shallow focal depths and the proximity to protracted mining operations suggest that these earthquakes also may have been triggered by the adjacent mining operations. Unfortunately, the lack of detailed records of injection activities or direct measurements of the state of stress in the epicentral region make any definitive correlation between these older historical earthquakes and mining operations difficult.

Northeastern Ohio

The association of solution mining with the occurrence of small earthquakes in western New York State (Fletcher and Sykes, 1977) and the extensive salt mining operations in northeastern Ohio (Clifford, 1973) suggested the possibility that some of the earthquake activity in Ohio also may be related to solution salt mining (fig. A17). Solution mining for salt began in northeastern Ohio in 1889 (Clifford, 1973; Dunrud and Nevins, 1981) and continues to the present, although several previously active operations have been closed down. The target horizon for the mining operations is the Silurian Salina Formation at a depth of 600 to 900 m, depending on the distance from Lake Erie. On the basis of their spatial proximity and temporal association, it could be argued that several earthquakes in the northeastern region of the State are related to active solution salt mining operations. In particular, earthquakes in 1898, 1906, and 1907 (Stover and others, 1979), which were located within the Cleveland metropolitan area, as well as earthquakes in 1932 and 1940, which were about 50 km south of Cleveland, are possible examples. However, in view of the large number of earthquakes reported before the initiation of solution mining and the apparent occurrence of at least some earthquakes in northeastern Ohio beyond the range of the expected influence of mining operations, it seems reasonably clear that at least some of the earthquakes are

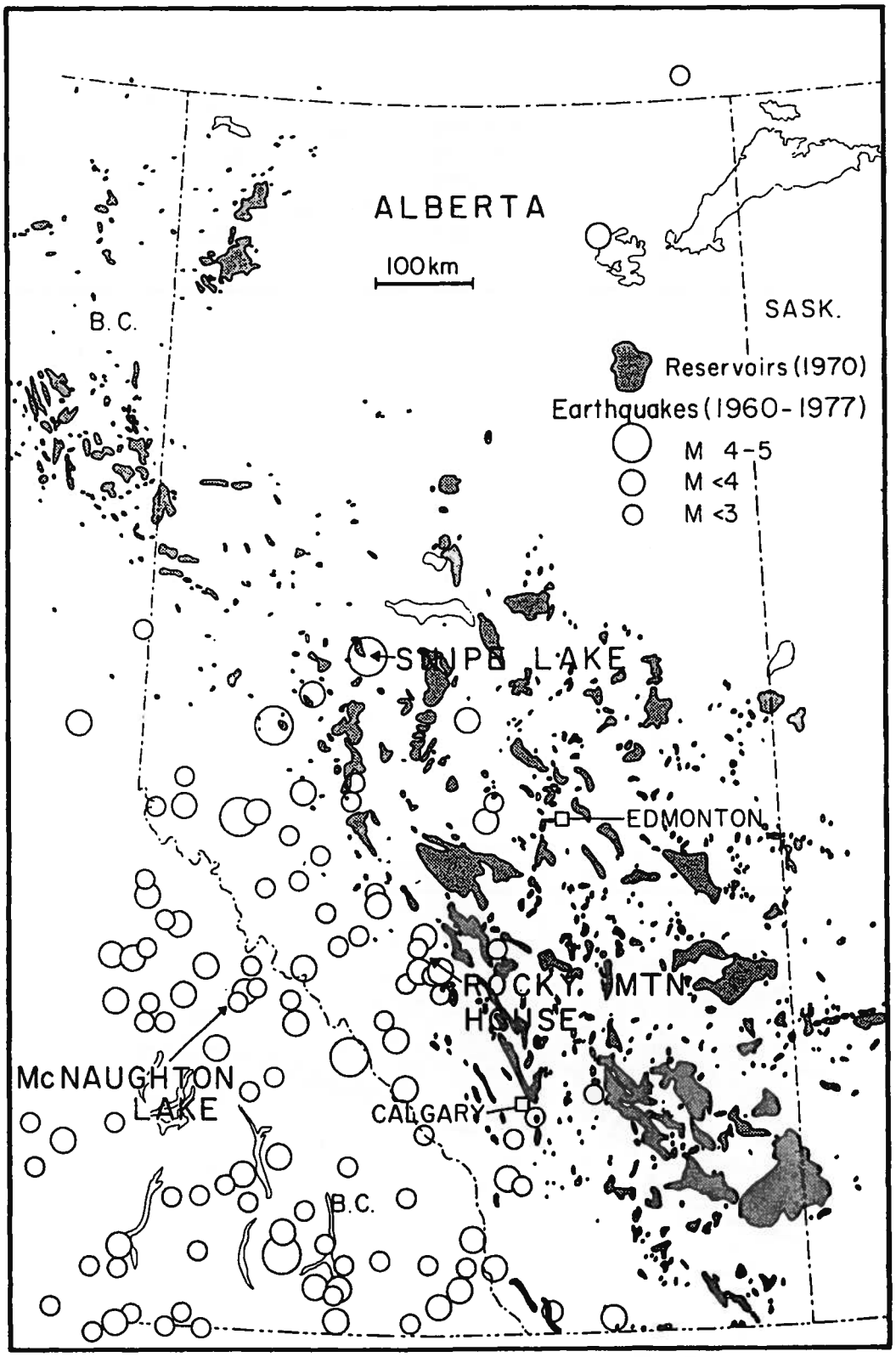


Figure A15. Earthquakes in Alberta, Canada (1960–77), and locations of active oil and gas reservoirs (shaded areas). Reprinted from Wetmiller (1986) and published with permission.

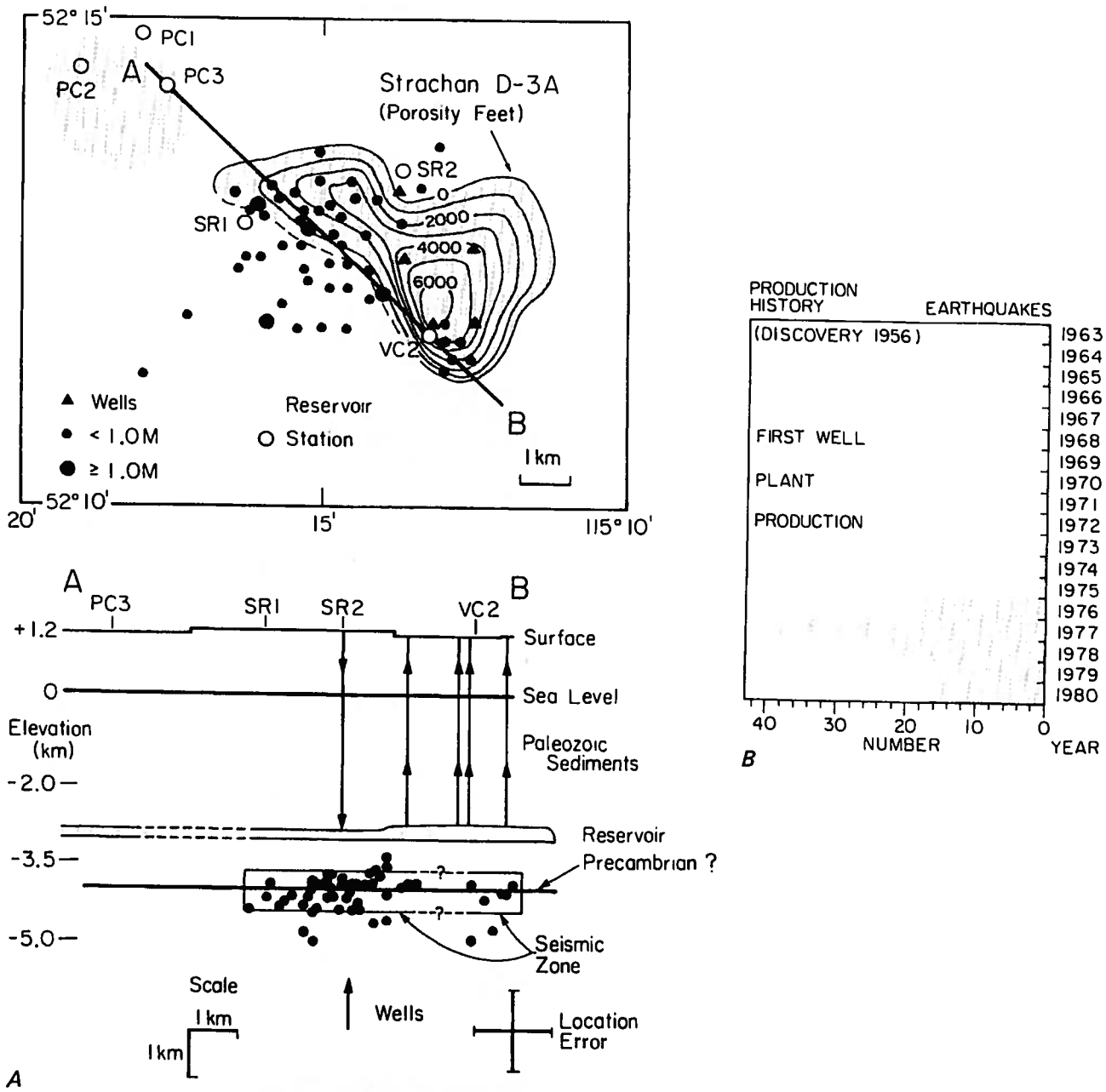


Figure A16. Locations of microearthquakes, production history, and earthquake activity, Strachan D-3A reservoir and gas field, western Alberta, Canada. *A*, Detail of the distribution in area and cross section of the microearthquakes (solid circles) located by the 1980 field survey within the reservoir and main production wells (solid triangles). *B*, Production history and annual earthquake activity at the field. Reprinted from Wetmiller (1986) and published with permission.

natural and that solution mining is not a necessary condition for the occurrence of earthquake activity.

Recent Seismicity and Injection Operations in Northeastern Ohio

On January 31, 1986, at 11:46 EST, an earthquake of magnitude 5.0 occurred about 40 km east of Cleveland, Ohio, and about 17 km south of the Perry Nuclear Powerplant (fig. A18). Within hours, a dense network of portable stations was installed to monitor possible aftershock activity (Wesson and Nicholson, 1986). As of April 15, only 13 aftershocks were detected, 6 of which occurred within the first 8 d. At the time of the mainshock, three deep injection wells for the disposal of hazardous and nonhazardous waste were operating within 15 km of the epicentral region and,

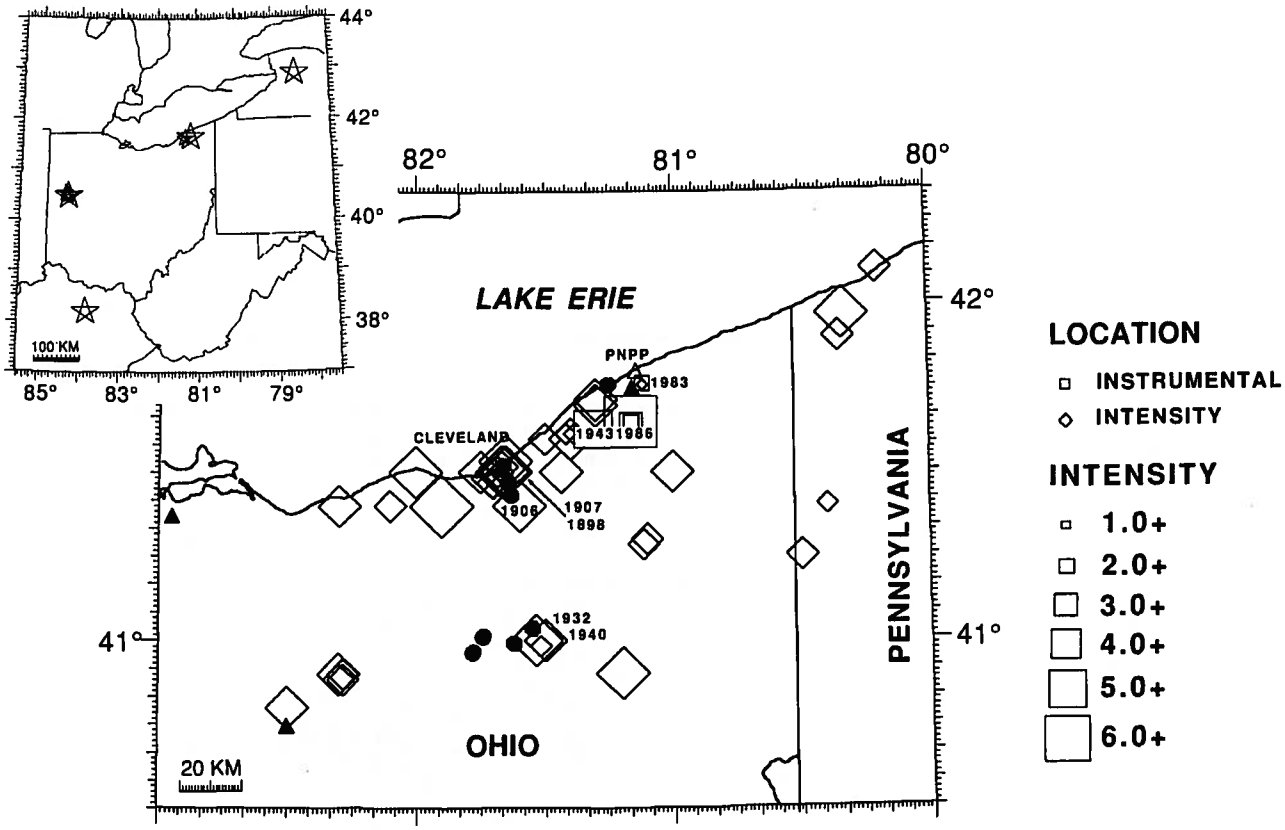


Figure A17. Locations of the Perry Nuclear Powerplant, the January 31, 1986, earthquake, and the significant historical seismicity and dates of occurrence, northeastern Ohio. Most of the seismicity precedes initiation of injection activities. PNPP, powerplant; large square, January 31 earthquake; solid octagons, sites of solution salt mining, typically in operation from 1900 to 1940; solid triangles, deep waste injection wells drilled from 1968 to 1971; diamonds, poorly located earthquakes, typically based on felt reports; squares, instrumentally located earthquakes; and stars, recent regional M ≥ 4.5 earthquakes (from Nicholson and others, 1988).

since 1975, have been responsible for the injection of nearly 1.2 billion L of fluid at a nominal depth of 1.8 km. Injection pressures at typical injection rates of 320 L/min reached a maximum of 112 bars THP.

Although the distance between the major injection wells and the January 31 earthquake (12 km) is greater than the corresponding distances in either the Denver or the Dale earthquakes, the total volume of fluid injected and the injection pressures involved are proportionately greater. Estimates of stress inferred from commercial hydrofracturing measurements suggest that the state of stress in northeastern Ohio is close to the theoretical threshold for failure along favorably oriented preexisting fractures, as determined by the Mohr-Coulomb failure criterion (fig. 5). The maximum horizontal compressive stress is greater than the vertical stress of 460 bars, the minimum horizontal stress is about 300 bars, and, before injection, the initial formation pore pressure was measured at about 200 bars (Wesson and Nicholson, 1986). This implies that, at a nominal injection pressure of 110 bars, the zone immediately surrounding the well bottom would be in a critical stress state for favorably oriented fractures that have cohesive strengths of as much as 40 bars and a coefficient of friction (μ) of 0.6 (fig. 5). Calculations of the pressure effect in the epicentral region based on modeling the fluid flow away from the wells and comparison with the history of pressure increase at the wells with time and continued pumping suggest that a radial flow model (instead of the narrow confined aquifer implicated in the Denver case) is the most appropriate. This model implies that, as a result of fluid injection since 1975, the expected fluid pressure increase in the epicentral region of the 1986 earthquakes would have been only a few bars. Since 1983, however, several small earthquakes have occurred at shallow depths and within less than 5 km from the wells (fig. A18)—where the calculated pressure increase as a result of fluid injection is about 15 bars or greater (Nicholson and others, 1988).

The increased depth and distance from the wells to the 1986 mainshock epicenter and its aftershocks, the lack of large numbers of small earthquakes typical of many induced sequences, the history of small to moderate earthquakes in the region before the initiation of injection, and

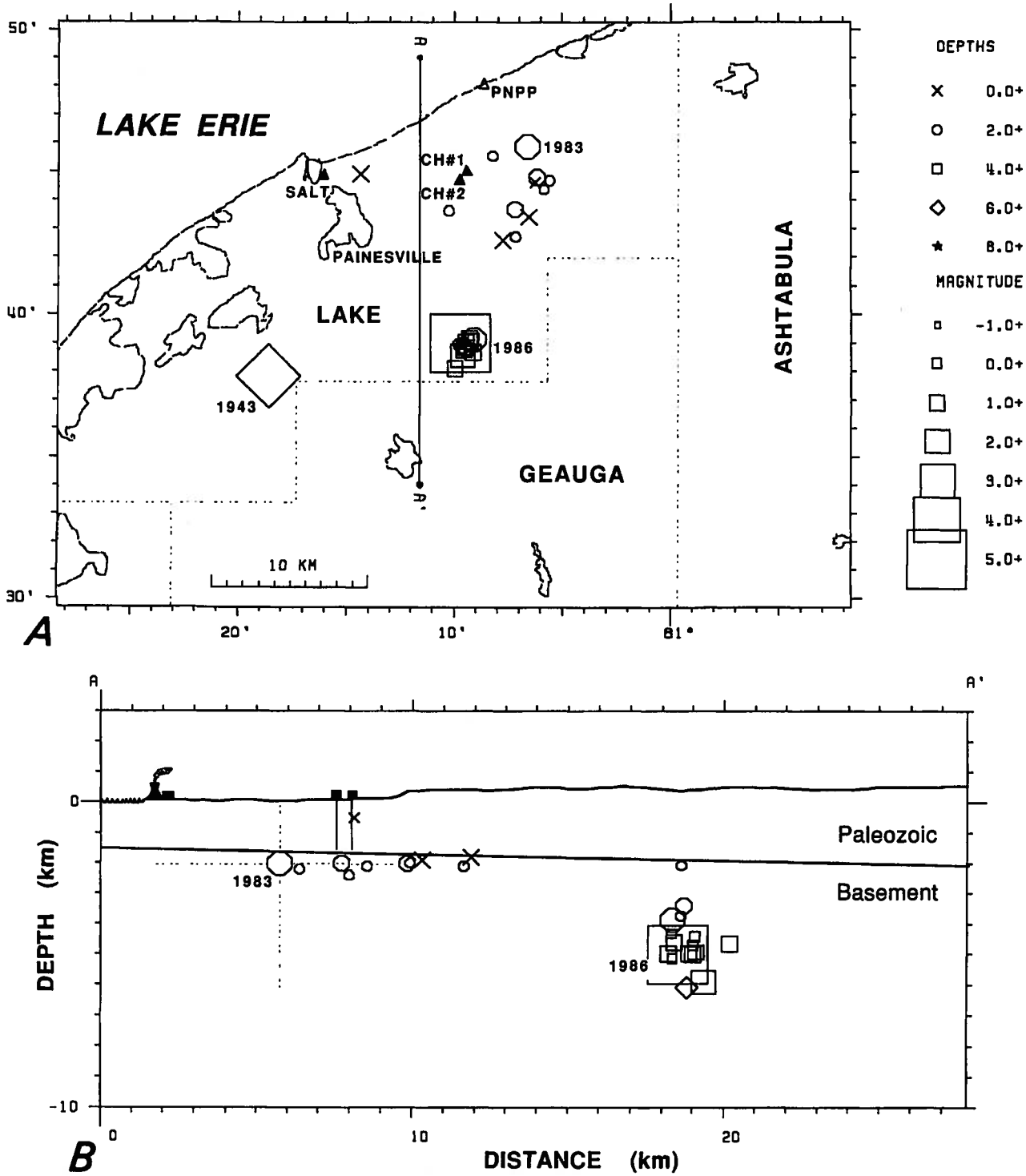


Figure A18. Deep injection wells and earthquake epicenters, Lake County, Ohio. *A*, Location of deep injection wells and earthquake epicenters through early 1987. Large uncertainties in location are associated with the 1943 and the 1983 earthquake epicenters. Solid triangles, injection wells; CH#1 and CH#2, deep waste-disposal wells; SALT, Painesville brine well; PNPP, Perry Nuclear Powerplant. *B*, Vertical cross section, no exaggeration, along the line *A–A'* shown in *A* (from Nicholson and others, 1988).

the attenuation of the pressure field with distance from the injection wells all argue for a "natural" origin for the January 31 earthquake. In contrast, the proximity to failure conditions at the bottom of the wells and the spatial association of at least a few small events suggest that triggering by well activities can not be precluded.

Ashtabula, Ohio

Confirmation that deep well fluid injection in northeastern Ohio has the potential for triggering earthquake activity was demonstrated dramatically on July 13, 1987. A M 3.6 earthquake occurred near Lake Erie, just east of Ashtabula and about 40 km northeast of the location of the January 31, 1986, earthquake (fig. A19). Except for one earthquake in 1857, no other earthquakes were known to have occurred within 30 km of Ashtabula. In the weeks following the mainshock, an unusually large number of aftershocks (more than 70 events) were generated (Armbruster and others, 1987). All the well located earthquakes were clustered in a narrow east-west-striking vertical plane about 1.5 km long that extended from about 1.6 to 3.2 km in depth (fig. A20; Armbruster and others, 1987; Seeber and others, 1988). The earthquakes occurred less than 1 km from the bottom of a hazardous-waste-disposal well that had been in operation only since July 1986. The injection well is about 1.8 km deep and operates at a nearly uniform flow rate of 114 L/min and at an injection pressure of about 100 bars THP (Ernie Rotering, Ohio EPA, written commun., 1987). Between July 1986 and June 1987, well operations were responsible for nearly 62 million L of hazardous fluid waste being injected into the basal sandstone layer (the Mount Simon Formation). The proximity to the active injection well and the temporal correlation of the seismicity with the initiation of well activities (about a year earlier) strongly suggests that the Ashtabula earthquakes of July 1987 were induced (Seeber and others, 1988).

Los Angeles Basin, California

The massive withdrawal of oil from one of the largest fields in the Los Angeles Basin, the Wilmington oil field (fig. A21), resulted in significant subsidence within the city limits of Long Beach. Up to 8.8 m of surface subsidence was observed over an elliptically shaped area between 1928 and 1970 (Mayuga, 1970). This rapid subsidence, which reached a maximum rate of 71 centimeters per year in 1951 9 mo after peak oil production (fig. A22), resulted in several damaging earthquakes, specifically in the years 1947, 1949, 1951, 1954, 1955, and 1961. In all cases, the earthquakes were unusually shallow (approximately 500 m deep) and generated high intensities for their size. The largest earthquake occurred on November 17, 1949, and caused nearly 200 wells to go off production, many of them permanently (Richter, 1958). Damage was estimated to be in excess of $9 million. The area affected equaled over 5.7 square kilometers (km^2) and involved measured displacements of 20 centimeters. This would correspond to an earthquake that had a moment magnitude of 4.7 and is consistent with a magnitude of 5.1 estimated from the

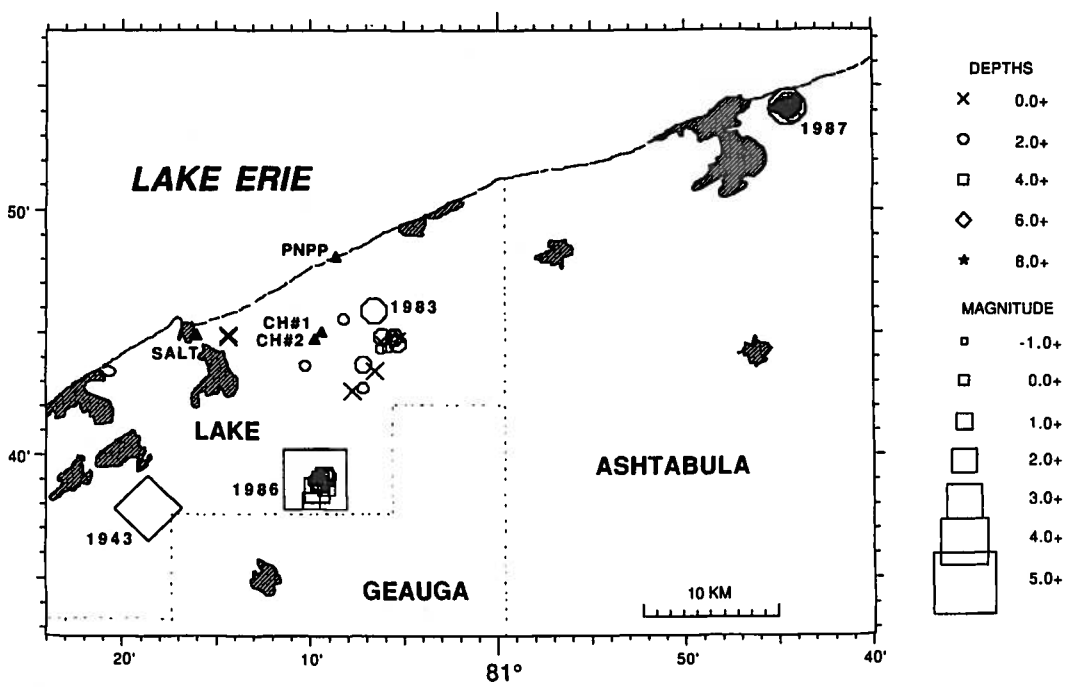


Figure A19. Location of the 1987 induced earthquake sequence in northeastern Ohio near Ashtabula relative to the 1986 earthquakes in Lake County.

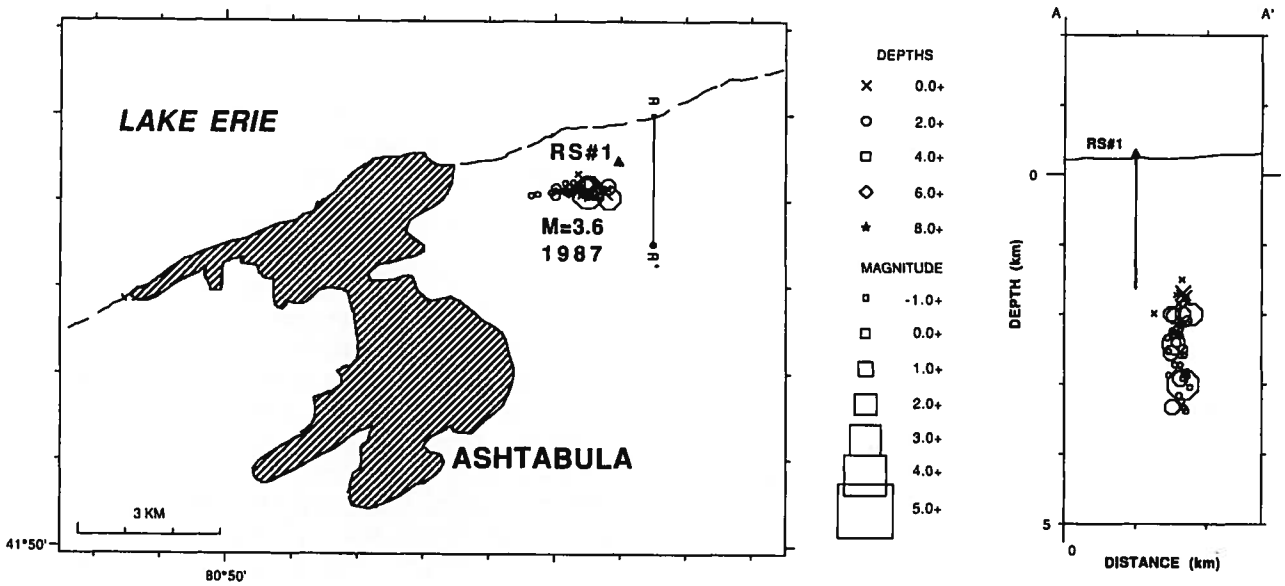


Figure A20. The 1987 Ashtabula, Ohio, earthquake hypocenters relative to the location of a nearby active, high-pressure, waste-disposal injection well (triangle, RS#1). Earthquake data provided courtesy of John Armbruster (Lamont-Doherty Geological Observatory, written commun., 1987).

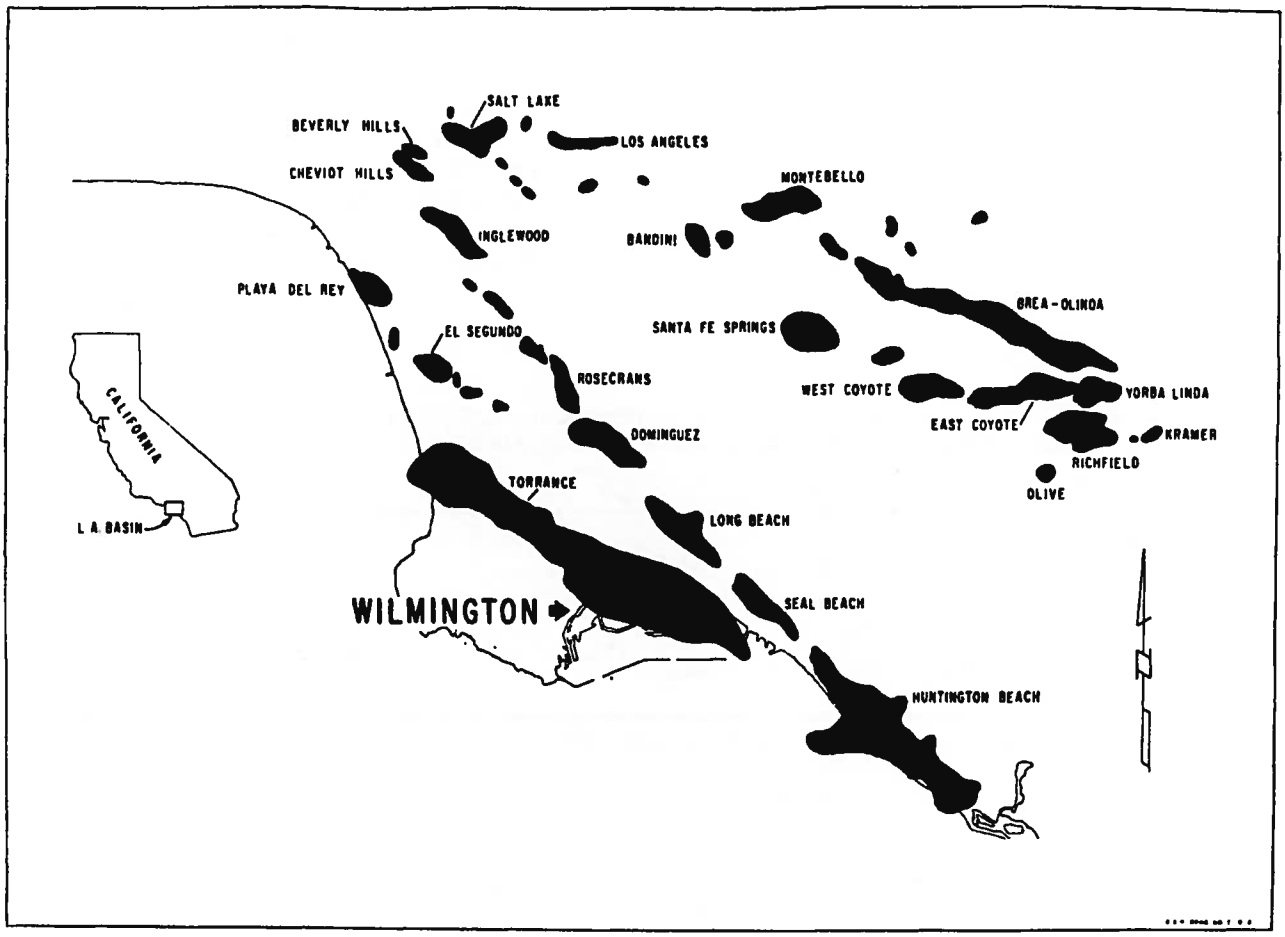


Figure A21. Distribution of the oil fields (shaded areas) in the Los Angeles Basin, Calif. (from Mayuga, 1970).

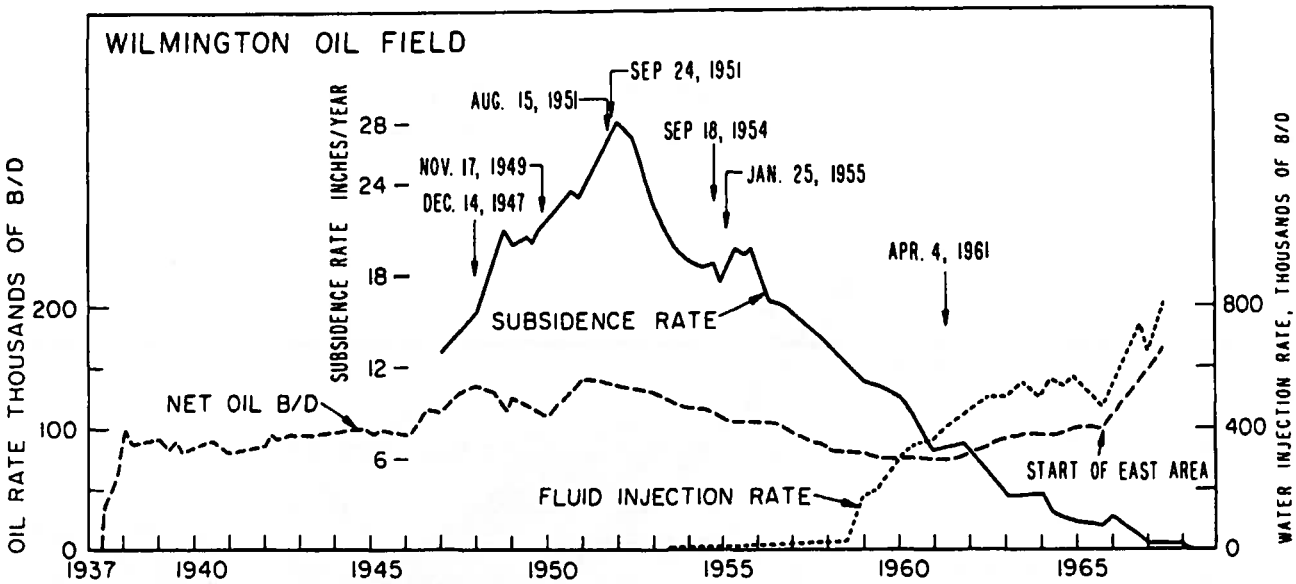


Figure A22. Subsidence rate in the center of the Wilmington oil field, California, compared with oil production and water injection rates. Arrows, major damaging earthquakes. Reprinted from Kovach (1974) and published with permission.

unusually well developed surface waves generated by the event (Kovach, 1974).

Water flooding of the field and adjacent areas was initiated in 1954 in an attempt to halt subsidence and to enhance the secondary recovery of oil. Teng and others (1973) reported on the seismic activity associated with 14 oil fields operating within the Los Angeles Basin where water-flooding operations were taking place. As of 1970, total fluid injection was 250,000 million L at depths that ranged from 910 to 1,520 m.

Although much of the seismicity in the area is natural and occurs predominantly at depths as deep as 16 km along the Newport-Inglewood Fault (Hauksson, 1987), seismic activity during 1971 appeared to correlate, at least in part, with injection volumes from nearby wells (fig. A23; Teng and others, 1973). However, many of the earthquakes detected were small (M<3.2) and occurred at depths of 5 km or more, which made it difficult to distinguish them from the natural background seismicity. Subsequent injection operations have stabilized to the point where fluid injection nearly equals fluid withdrawal and little, if any, seismic activity can be directly attributable to injection well operations (Egill Hauksson, University of Southern California, oral commun., 1986).

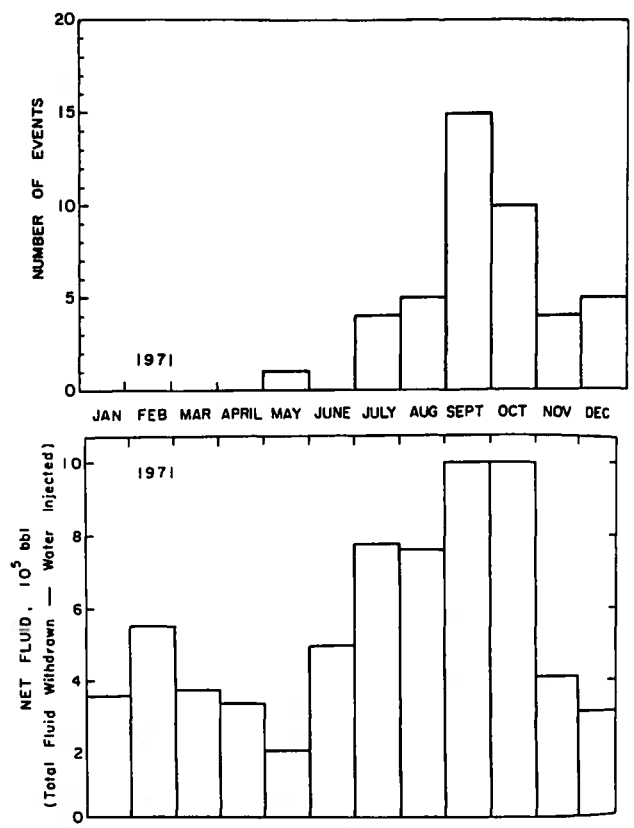


Figure A23. Seismicity and volumes of fluid injected along the Newport-Inglewood Fault, Los Angeles County, Calif., in 1971. Reprinted from Teng and others (1973) and published with permission.

Northern Texas Panhandle and East Texas

In 1984, a small network of monitoring stations was operated under contract to the Office of Nuclear Waste Isolation, U.S. Department of Energy, in the Palo Duro Basin of the northern Texas Panhandle (Stone and Webster

Engineering, written commun., 1985). Between April 27 and October 5, 1984, 34 small earthquakes were detected near the Mansfield station in eastern Oldham County (Davis, 1985). The largest of these events occurred on May 21 and had a local magnitude of 3.1 (pl. 1). Before this episode of seismicity, only one other earthquake was known to have occurred in this part of Texas—a M 3.4 event on April 3, 1983 (Davis, 1985). Several small oil fields had been discovered recently in eastern Oldham County and were producing at the time both earthquakes occurred. In particular, the Lambert No. 1 field, located about 7 km from the Mansfield station, began injection of water for secondary recovery in September 1979 at an average rate of 39,750 liters per day. Definitive correlation of the seismicity with oil field operations, however, was not possible because of the poor earthquake location capability of the wide-aperture network.

In East Texas, a sequence of four earthquakes occurred near Gladewater on March 19, 1957. The largest of these events had an estimated magnitude of 4.3 and generated a felt area of 47,000 km^2 (Nuttli and Herrmann, 1978). Little else is known about this sequence; however, Docekal (1970) recognized that the earthquake epicenters corresponded to an area of active oil production located in East Texas on the western flank of the Sabine Uplift and speculated on whether the earthquakes may have been induced. Water flooding to enhance production had been in effect in at least one field since 1942 at injection pressures of greater than 100 bars (Texas Railroad Commission, 1971). More recently, commercial stimulation of the Cotton Valley tight gas sands, which also are located in East Texas, triggered microearthquake activity at a depth of 2.6 to 3.7 km (Lacy, 1985).

Oklahoma

On October 30, 1956, a M 4.2 to 4.7 earthquake occurred near Catoosa, about 20 km east of Tulsa in northeastern Oklahoma (fig. A24; Nuttli and Herrmann, 1978). This event generated a relatively high maximum intensity (MM VII) for its size and felt area, which suggested a shallow focal depth (Nuttli and Zollweg, 1974). The maximum intensity reported for this event was based on damage to the Coshow No. 2 oil and gas well, which was active at the time of the earthquake (Brazee and Cloud, 1958). The well was forced to shut down because apparent displacements in the producing formation, as a result of the earthquake, disrupted the wellbore. Producing wells within the Catoosa District gas field were operational by 1941, and water flooding to enhance secondary recovery was conducted at one time, but details of the operation are not available (Robert McCoy, Oklahoma Corporation Commission, oral commun., 1987). In March 1960, two smaller earthquakes were felt in the same general area (fig. A24; Luza and others, 1978) shortly after an industrial-waste-disposal well became operational in January (Johnson and others, 1980). Since then, however, no significant seismic activity has been detected in the region, even though gas-production and waste-disposal operations have continued and sensitive seismic monitoring equipment has been operating in nearby Tulsa since 1961 (Luza and Lawson, 1983).

In Carter and Love Counties, southern Oklahoma, 400 earthquakes were detected from May 1, 1977, to December 31, 1978 (Luza and Lawson, 1980). Most of these events were too small to locate (fig. A24); however, of the few that were, nearly all occurred in areas of active oil and gas production, and all occurred at relatively shallow focal depths. On June 23, 1978, commercial stimulation of a 3,050-m-deep well near Wilson triggered 70 earthquakes in 6.2 hours (hr) (Luza and Lawson, 1980).

A similar situation occurred in May 1979, when a well located about 1 km from the Wilson monitoring station (fig. A24) was stimulated over a 4-d period in a massive hydraulic fracturing program. Three different formations were eventually hydrofractured on three separate occasions at average depths of 3.7, 3.4, and 3.0 km (J.E. Lawson, Jr., Oklahoma Geophysical Observatory, written commun., 1987). Maximum injection pressures reached 277 bars THP, and the instantaneous shut-in pressure (ISIP) at the greatest depth was measured to be 186 bars THP. The well was fractured from the bottom up. The first fracturing episode was followed about 20 hr later by about 50 earthquakes over the next 4 hr; the second fracture (at a depth of 3.4 km) was followed immediately by about 40 earthquakes in the subsequent 2 hr; and no increase in activity was noticed following the third fracture (J.E. Lawson, Jr., Oklahoma Geophysical Observatory, written commun., 1987). The largest earthquake in any of the sequences had a magnitude of 1.9; two of the earthquakes were felt. The largest total volume of fluid injected during any one procedure amounted to 5.7×10^4 L at an average injection rate of 230 L/min.

Oil has been produced in this same area since 1953. Earthquakes in the southern portion of the State have been detected since 1974, and earthquakes in Love County have been detected ever since a local monitoring station was installed in 1977 (fig. A24; Luza and others, 1978). Secondary recovery operations in Love County began in May 1965 (Tim Baker, Oklahoma Corporation Commission, oral commun., 1987). It must be noted, however, that similar commercial hydrofracturing operations in other nearby wells did not trigger noticeable increases in seismic activity, as did the massive hydraulic fracturing program in 1978 and 1979.

Whether additional earthquakes that have occurred in Oklahoma (fig. A24) are associated with oil and gas production is difficult to assess. Over 3,100 oil and gas fields exist within the State (most of which are still active), and nearly every felt or located earthquake has been found

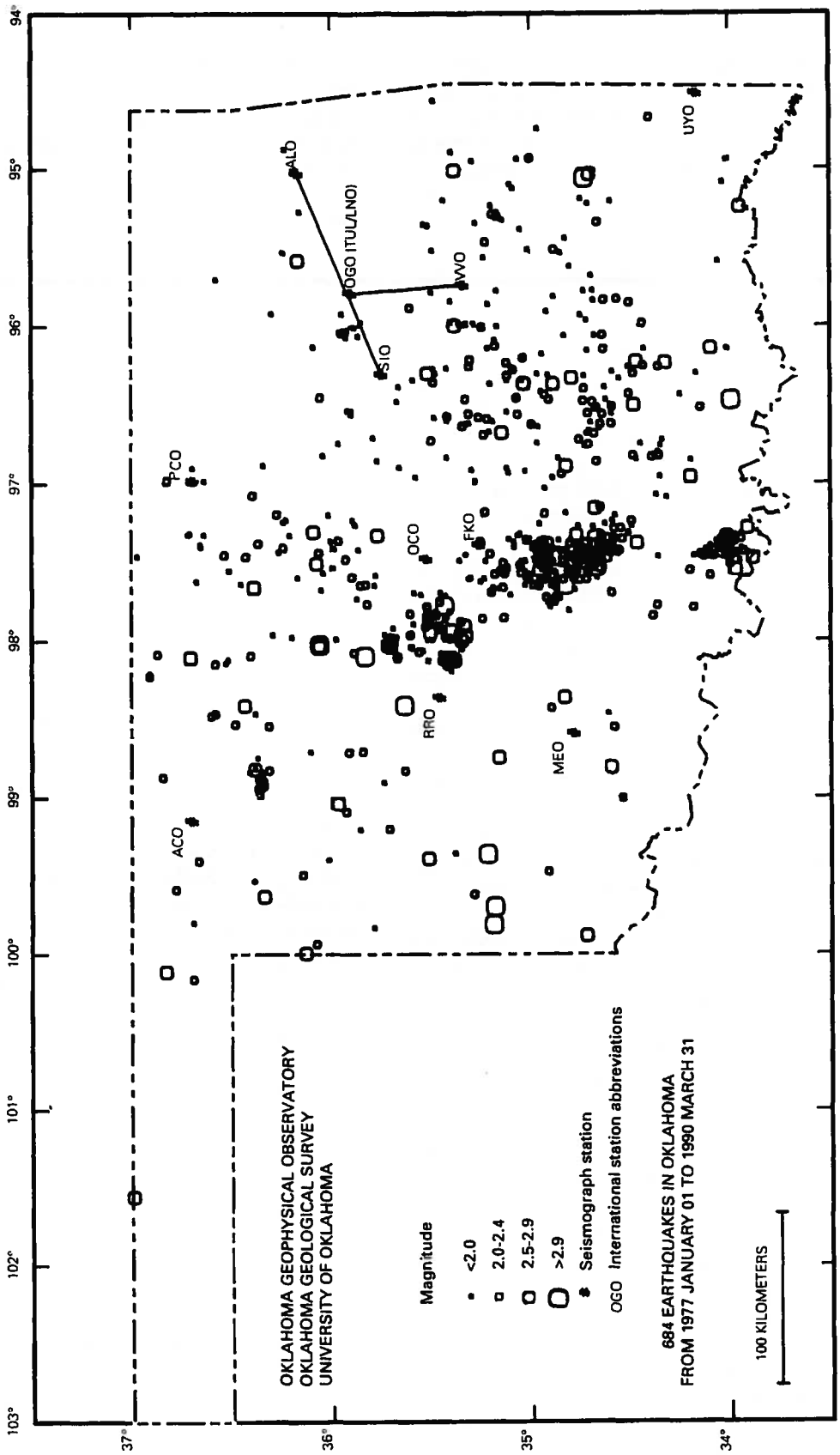


Figure A24. Earthquake epicenters in Oklahoma (684) from January 1, 1977, to March 31, 1990) (J.E. Lawson, Jr., Oklahoma Geophysical Observatory, written commun., 1990).

to occur in close proximity to at least one of them. The converse, however, is not true. Since the early 1900's, oil and gas production has been active in large areas of Oklahoma that have yet to show any detectable signs of seismic activity. Furthermore, many of the regions without earthquakes are actively water flooding to enhance secondary recovery, while many of the seismically active areas are not. Some of these later cases, where seismicity is occurring in areas without fluid injection, may be related to subsidence from massive oil and gas withdrawal, as in the cases of the Flashing gas field in southern Texas or the War-Wink oil and gas field in West Texas. A possible example is a series of nine earthquakes that occurred between October 12 and 18, 1968. All were concentrated in the vicinity of the East Durant gas field, Bryant County (fig. A24), which had been in production since 1958. The largest earthquake in the series was a magnitude 3.5 and generated a maximum intensity of MM VI at the epicenter (Luza and others, 1978).

Gulf Coast Region—Louisiana and Mississippi

In 1978, a magnitude 3.5 earthquake was felt strongly in Melvin, Ala. (pl. 1). Portable monitoring equipment was installed shortly after the earthquake, but only one small aftershock was detected. On the basis of the hypocenter determined for this one event, both earthquakes appeared to be at a focal depth of about 1 km and within 1 to 2 km of the Hunt oil field, which is located just across the State border in Mississippi (J.E. Zollweg, U.S. Geological Survey, oral commun., 1978, 1987). Four earthquakes of similar magnitudes (3.0–3.6) had been detected in the same area since 1976. Although no injection procedures were apparently in operation at the time of the 1978 earthquake, water flooding to enhance extraction had occurred previously.

A similar situation was noted in 1983, when a M 3.8 earthquake was detected in southwestern Louisiana near Lake Charles (pl. 1). Oil and gas operations had been active in the region for several decades, as well as injection activities from a nearby waste-disposal well, but lack of station coverage precluded accurate determination of the earthquake's location and focal depth and so made any direct correlation with particular well operations unresolvable. However, a small microearthquake network, which was installed in 1980 to monitor potential seismicity associated with a geothermal energy project located farther south, has continued to detect a low level of seismic activity in the Lake Charles region, presumably associated with the 1983 earthquake (Stevenson, 1985).

APPENDIX B—SUMMARY OF RESERVOIR-INDUCED SEISMICITY

The phenomenon of seismicity induced by the impoundment of reservoirs is more widespread and better documented than that of injection-induced seismicity; however, the mechanism of reservoir-induced seismicity is more complicated and not as well understood (Gupta and Rastogi, 1976; Simpson, 1986a). Reservoir-induced earthquakes were first described in association with the filling of Lake Mead, Nev. (Carder, 1945), but it was not until the late 1960's, when earthquakes larger than M 5.5 occurred at four major reservoirs (Hsinfengkiang, China, Kremasta, Greece, Lake Kariba, Rhodesia, and Koyna Reservoir, India), that sufficient concern was raised to warrant investigation of the mechanism controlling reservoir-induced seismicity. The largest of the earthquakes believed to have been induced by the impoundment of a reservoir occurred at Koyna Reservoir in 1967 and had a magnitude of 6.5. It caused over 200 deaths, 1,500 injuries, and considerable damage to the nearby town and the dam. Thus, the hazard associated with reservoir-induced seismicity is significant.

Unlike injection operations that only affect pore pressure, the presence of a large reservoir modifies the environment in several ways. First, the large mass of the reservoir represents a large increase in the imposed load, which increases the *in situ* elastic stresses. The load of water also affects the pore pressure directly (by the infiltration of the reservoir water and subsequent raising of the water table) and indirectly (through the closure of water-saturated pores and fractures in the rock beneath the reservoir load). This coupling between the elastic and the fluid effects in the rock, as well as the poorly understood response of inhomogeneities in material and hydrologic properties of the rock to changes in stress induced by the reservoir load, make modeling the impact of reservoirs much more difficult than for cases of fluid injection (Simpson, 1986a). Nevertheless, there are enough similarities between injection- and reservoir-induced earthquakes that they both provide a number of constraints on the mechanism of triggered seismicity.

Although the magnitude of the net pore pressure change produced by reservoir impoundment is often considerably less than at many fluid injection sites, the larger physical dimensions of the reservoirs allows their influence to extend over much broader areas. There are, however, a number of cases of reservoir-induced seismicity in which the load effect from the reservoir is believed to be minimal. These cases include some of the largest earthquakes associated with reservoir impoundment and are usually characterized by a large distance between the earthquake and the reservoir, as well as a long time interval between impoundment and the earthquake occurrence; for example, 1975 M_s 5.7 Oroville, Calif., and 1981 m_b 5.3 Aswan, Egypt.

If these cases do indeed represent seismicity induced by the reservoir, then the triggering mechanism is believed to be similar in many respects to that of injection-induced seismicity. In these cases, the mainshocks occurred along major mapped surface faults that intersected the reservoir. Thus, increased fluid pressure as a result of impoundment may have been able to migrate out along the fault zones, which reduced effective stress levels and thereby enhanced the probability for failure in an earthquake. Because the changes in pore pressure as a result of impoundment are believed to be relatively small at the increased distances involved in these cases, this suggests that the states of stress in those areas were already near critical levels for failure prior to impoundment (Simpson, 1986a).

A particularly good example of reservoir-induced seismicity occurred at the Nurek Reservoir, Tadjikistan, Soviet Central Asia (fig. B1; Simpson and Negmatullaev, 1981). In this case, the water height and the rate of change in water height proved to be critical parameters (fig. B2). At Nurek and at several other similar sites of reservoir-induced seismicity, changes in water height of only a few meters, which correspond to pressure changes of less than 1 bar, have triggered swarms of small earthquakes (fig. B2). This observation suggests that seismicity can be triggered on faults that otherwise remain stable, even at stress levels extremely close to failure (Leith and Simpson, 1986). In many cases of reservoir-induced seismicity, an accurate assessment of the magnitude of the critical stress change necessary for failure is difficult to determine because major heterogeneities in elastic and hydrologic properties of the rock may tend to concentrate or amplify changes in pore pressure caused by compaction and the redistribution of pore fluids in response to changes in water level (Simpson, 1986b). In the case of fluid injection, however, the total mass of the fluid involved is relatively small, and so the need to consider the coupled interaction among applied load, elastic stresses, and pore pressure is generally absent.

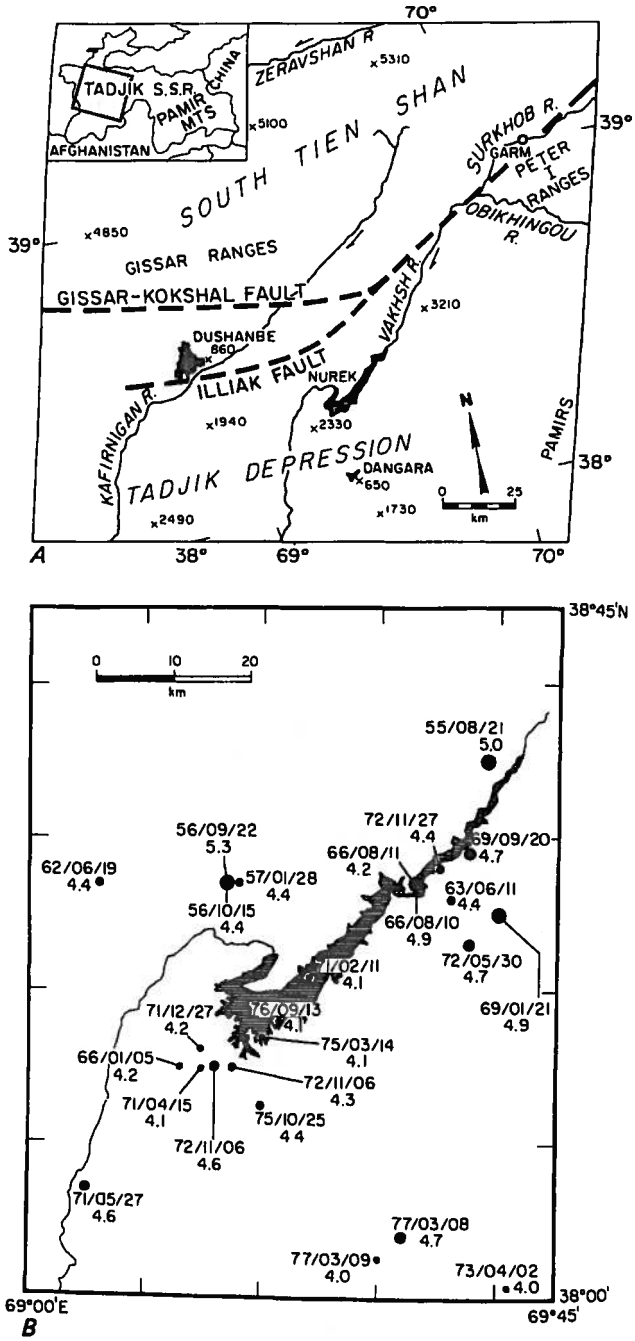


Figure B1. Location and historical seismicity, Nurek Reservoir, Tadjikistan, Soviet Central Asia. *A*, Location map of the reservoir. *B*, Historical seismicity in the vicinity of the dam. Reprinted from Simpson and Negmatullaev (1981) and published with permission.

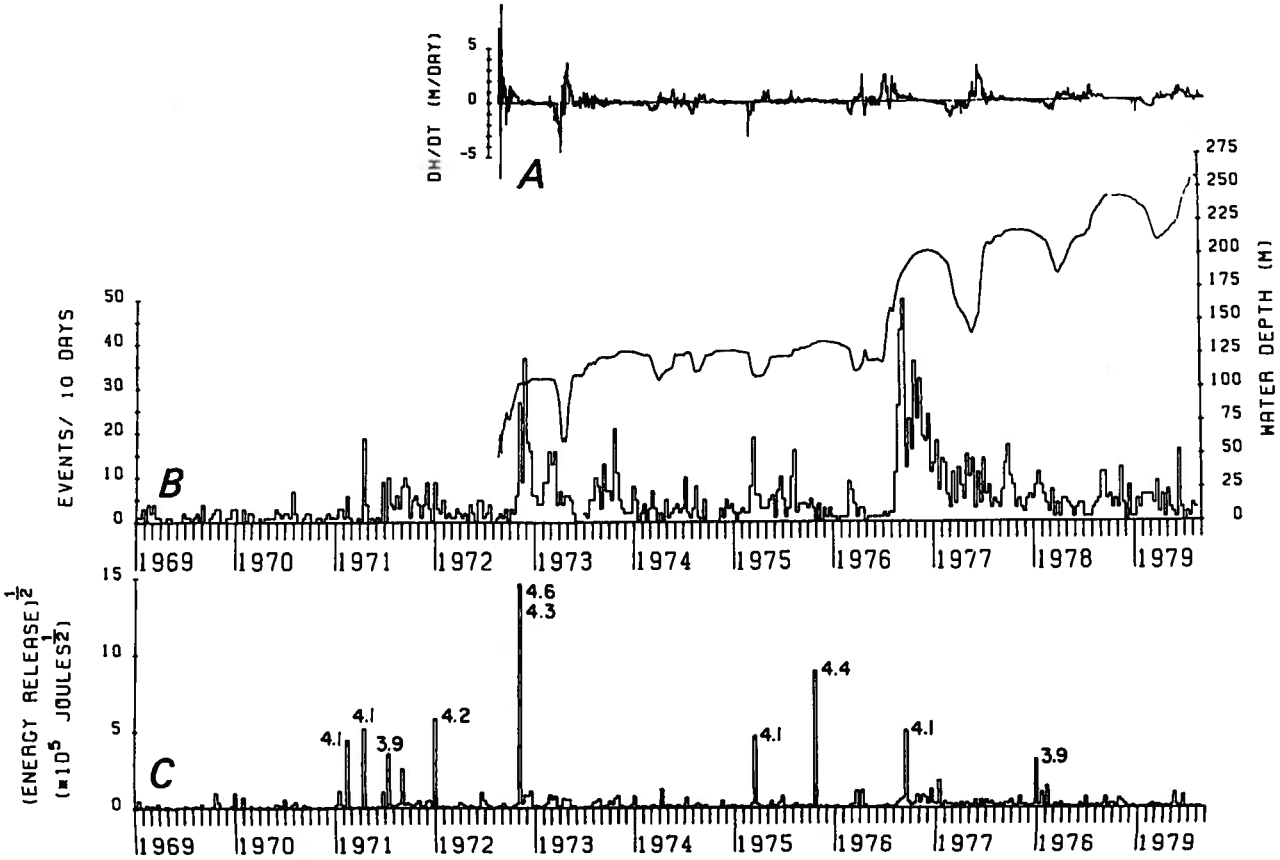


Figure B2. Temporal variations in seismicity, seismic energy release, water height, and daily changes in water level (DH/DT), Nurek Reservoir, Tadjikistan, Soviet Central Asia. Reprinted from Simpson and Negmatullaev (1981) and published with permission.

APPENDIX C—MODIFIED MERCALLI INTENSITY SCALE

This scale measures the intensity of ground shaking as determined from observations of the effects of an earthquake on people, structures, and the Earth's surface. This scale assigns to an earthquake event a Roman numeral from I to XII.

I Not felt by people, except rarely under especially favorable circumstances.

II Felt indoors only by persons at rest, especially on upper floors. Some hanging objects may swing.

III Felt indoors by several. Hanging objects may swing slightly. Vibration like passing of light trucks. Duration estimated. May not be recognized as an earthquake.

IV Felt indoors by many, outdoors by few. Hanging objects swing. Vibration like passing of heavy trucks or sensation of a jolt like a heavy ball striking the walls. Standing automobiles rock. Windows, dishes, doors rattle. Wooden walls and frames may creak.

V Felt indoors and outdoors by nearly everyone; direction estimated. Sleepers awakened. Liquids disturbed, some spilled. Small unstable objects displaced or upset; some dishes and glassware broken. Doors swing; shutters, pictures move. Pendulum clocks stop, start, change rate. Swaying of tall trees and poles sometimes noticed.

VI Felt by all. Damage slight. Many frightened and run outdoors. Persons walk unsteadily. Windows, dishes, glassware broken. Knickknacks and books fall off shelves; pictures off walls. Furniture moved or overturned. Weak plaster and masonry cracked.

VII Difficult to stand. Damage negligible in buildings of good design and construction; slight to moderate in well-built buildings; considerable in badly designed or poorly built buildings. Noticed by drivers of automobiles. Hanging objects quiver. Furniture broken. Weak chimneys broken. Damage to masonry; fall of plaster, loose bricks, stones, tiles, and unbraced parapets. Small slides and caving in along sand or gravel banks. Large bells ring.

VIII People frightened. Damage slight in specially designed structures; considerable in ordinary substantial buildings, partial collapse; great in poorly built structures. Steering of automobiles affected. Damage to or partial collapse of some masonry and stucco. Failure of some chimneys, factory stacks, monuments, towers, elevated tanks. Frame houses moved on foundations if not bolted down; loose panel walls thrown out. Decayed pilings broken off. Branches broken from trees. Changes in flow or temperature of springs and wells. Cracks in wet ground and on steep slopes.

IX General panic. Damage considerable in specially designed structures; great in substantial buildings, with some collapse. General damage to foundations; frame structures, if not bolted, shifted off foundations and thrown out of plumb. Serious damage to reservoirs. Underground pipes broken. Conspicuous crack in ground; liquefaction.

X Most masonry and frame structures destroyed with their foundations. Some well-built wooden structures and bridges destroyed. Serious damage to dams, dikes, embankments. Landslides on river banks and steep slopes considerable. Water splashed onto banks of canals, rivers, lakes. Sand and mud shifted horizontally on beaches and flat land. Rails bent slightly.

XI Few, if any, masonry structures remain standing. Bridges destroyed. Broad fissures in ground; earth slumps and landslides widespread. Underground pipelines completely out of service. Rails bent greatly.

XII Damage nearly total. Waves seen on ground surfaces. Large rock masses displaced. Lines of sight and level distorted. Objects thrown upward into the air.

APPENDIX D—GLOSSARY

[Terms set in bold type are defined elsewhere in the glossary. Sources: Ziony (1985), Bates and Jackson (1987), and Nance (1989)]

Acceleration. The time rate of change of velocity of a reference point during an **earthquake**. Commonly expressed in percentage of gravity (g) equal to 980 centimeters per square second.

Active fault. A **fault** that is considered likely to undergo renewed movement within a period of concern to humans. *Also called* capable fault.

Aftershock. An **earthquake** or tremor that follows a larger earthquake or mainshock and originates at or near the **focus** of the larger earthquake. Generally, **major earthquakes** are followed by many aftershocks, which decrease in frequency and magnitude with time. Such a series of tremors may last many days for small earthquakes or many months for large ones.

Amplification. An increase in **seismic** signal **amplitude** as waves propagate through different earth materials.

Amplitude. Zero-to-peak value of any wavelike disturbance; corresponds to half the height of the crest of a wave above the adjacent trough.

Aquifer. A geological subsurface formation containing and transmitting ground water, usually restricted to a body of rock that is sufficiently permeable to yield useful quantities of water to wells or springs.

Aseismic. (1) Not associated with an **earthquake** or earthquake activity. (2) An area that is not subject to earthquakes.

Attenuation. A decrease in **seismic** signal **amplitude** as waves propagate from the seismic source. Attenuation is caused by geometrical spreading of **seismic wave** energy and by the absorption and scattering of seismic energy in different earth materials.

Basement rock. Relatively hard, undifferentiated solid rock that underlies commonly softer sedimentary rock, unconsolidated sediment, alluvium, or soil. *Also called* bedrock.

Body wave. A **seismic wave** that travels through the interior or body of the Earth and is not related or confined to a specific boundary surface. **Primary** and **secondary waves** are examples of body waves.

Bottom-hole pressure. The fluid pressure measured in the bottom of a well. It consists of the wellhead pressure (**top-hole pressure**) plus a term to account for the weight of the column of fluid in the well. The abbreviation is BHP.

Breakdown pressure. The hydraulic pressure needed to **fracture** the intact rock of a borehole wall. The symbol is P_b. *Also called* fracture pressure.

Coefficient of friction. Constant of proportionality for that part of the shear strength of a rock or other intact solid that depends on the **normal stress** applied across the potential shear surface or **fracture**. The symbol is μ.

Cohesion. The **shear** strength of a rock not related to internal friction; that is, dependent on applied **normal stress**. The symbol is τ_0. *Also called* inherent shear strength.

Compressibility. The relative change of volume with pressure on the **aquifer** matrix. Reciprocal of the elastic bulk modulus of the medium. For solids, the symbol is α; for fluids, the symbol is β.

Core-induced fractures. Vertical fractures found in oriented bottom-hole cores caused by the downcutting drill bit. *Also called* petal-centerline fractures.

Creep. Slow, more or less continuous movement that may occur either along faults owing to ongoing **tectonic** deformation or along slopes owing to gravitational forces.

Crust. The outermost major layer of the Earth, ranging from about 9 to 60 km thick worldwide; characterized by **primary-wave** velocities of less than 8 kilometers per second (km/s).

Density. Mass per unit volume. The symbol is ρ.

Deviatoric stress. The difference in magnitude between the maximum (σ_1) and minimum (σ_3) **principal stresses**.

Dip. Inclination of a planar geologic surface (for example, a **fault** or formation) from the horizontal.

Displacement. The difference between the initial position of a reference point and any later position. (1) In seismology, displacement is typically calculated by integrating an accelerogram twice with respect to time and is expressed in centimeters. (2) In geology, displacement is the permanent offset of a geologic or manmade reference point along a fault or landslide.

Dynamic viscosity. A measure of the internal resistance of a fluid to flow. The symbol is η. *Also called* viscosity coefficient or absolute viscosity.

Earthquake. Groups of **elastic waves** propagating in the Earth, generated by a sudden disturbance of the Earth's elastic equilibrium, usually caused by a sudden movement in the Earth's **crust**.

Earthquake hazard. Any physical phenomenon associated with an **earthquake** that may produce adverse effects on human activities.

Effective stress. In the presence of a fluid, **stress** is partly compensated by the buoyancy of the fluid pressure. This reduces the effective magnitude of the stress by an amount equal to the **pore pressure**.

Elastic rebound theory. The theory that movement along a **fault** is the result of an abrupt release of a progressively increasing elastic **strain** between the rock masses on either side of the fault. Such movement (or faulting) returns the rocks to a condition of little or no strain and converts the stored elastic strain energy into

kinetic energy (motion along the fault), heat caused by friction, new fractures, and the generation of **elastic waves**, which radiate outwards from the point of rupture, the **hypocenter**.

Elastic wave. A wave that is propagated by some kind of elastic deformation; that is,a deformation that disappears when the forces causing the deformation are removed. A **seismic wave** is a type of elastic wave.

Epicenter. The point of the Earth's surface vertically above the **hypocenter** or **focus** of an **earthquake** (where a **seismic** rupture initiates).

Fault. A **fracture** or fracture zone along which there has been **displacement** of the sides relative to one another parallel to the fracture plane or planes.

Fault trace. Intersection of a **fault** with the ground surface; also, the line commonly plotted on geologic maps to represent a fault.

Favorably oriented fracture. A **fracture** whose orientation in an existing **stress** field is close to the orientation for maximum **shear stress** resolved across the fracture plane; typically within the range 30° to 45° relative to the maximum **principal stress** direction (σ_1).

Focal depth. The depth of the **hypocenter** or **focus** of an **earthquake**.

Focal mechanism. An analysis to determine the attitude of the causative **fault** and the direction of slip along the fault during an **earthquake** from the radiation pattern of **seismic waves** generated. The analysis most commonly uses the direction of first motion of **primary waves** recorded at numerous **seismograph** stations and yields two possible orthogonal orientations for the fault rupture and the direction of seismogenic slip. From these data, inferences can be made concerning the principal axes of **stress** in the region of the earthquake. *Also called* fault-plane solution.

Focus. The source of a given set of **elastic waves**; the true center of an **earthquake**, within which the **strain** energy is first converted to elastic wave energy. *See also* **Hypocenter**.

Foreshock. A small tremor that precedes a larger **earthquake** or mainshock by seconds to weeks and that originates at or near the **focus** of the larger earthquake.

Fracture. (1) A breakage in the rock strata due to mechanical failure by applied **stress**. (2) Deformation due to momentary loss of **cohesion** or loss of mechanical resistance to differential stress and a release of stored elastic energy.

Fracture-opening pressure. The injection pressure needed to just open a newly created **hydraulic fracture**. The symbol is P_{fo}.

Frequency. (1) Rate of occurrence. (2) Number of cycles occurring in unit time. Hertz, which is the unit of frequency, is equal to the number of cycles per second.

Geophysical survey. The use of one or more techniques of physical measurement to explore Earth properties and processes. For subsurface exploration, this usually involves indirect methods, such as gravity measurements, to infer rock densities, and so forth.

Head. (1) The elevation to which water rises at a given point as a result of reservoir **pore pressure**. (2) Water-level elevation in a well or elevation to which water of a flowing artesian well will rise in a pipe extended high enough to stop the flow.

Hydraulic conductivity. The ease with which water is conducted through an **aquifer** and is defined as the rate of flow of water through a unit cross section under a unit **hydraulic gradient** at the prevailing temperature. The symbol is **K**. *Also called* coefficient of permeability.

Hydraulic fracture. An artificial **fracture** generated in the rock around a well by high pressure fluid injection. *Also called* hydrofracture.

Hydraulic gradient. In an **aquifer**, the rate of change to **total head** per unit distance of flow at a given point and in a given direction.

Hydrostatic pressure. The pressure exerted by the water at any given point in a body of water at rest. For ground water, the hydrostatic pressure is equal to the weight of the water above the reference point or reference horizon, or the product of the fluid **density** (ρ), the **acceleration** of gravity (g), and the fluid depth.

Hypocenter. The point in the Earth where an **earthquake** rupture initiates.

Induced seismicity. **Earthquake** activity triggered by environmental changes caused by man; usually associated with either the injection or extraction of large amounts of fluid in the ground or the impoundment of a **reservoir**.

Instantaneous shut-in pressure. The fluid pressure recorded in the wellbore after a new **hydraulic fracture** is opened, injection is stopped, and the well is "shut-in" or closed. Under ideal conditions, this is a measure of the minimum **principal stress** (σ_3) acting to close the fracture. The abbreviation is ISIP.

Intensity. A subjective measure of the damage of an **earthquake** at a particular place as determined by its effects on people, structures, and earth materials. Intensity depends not only on the earthquake **magnitude**, but also on the distance from the point of reference to the **epicenter**, the earthquake **focal depth**, the type of faulting, and the local geology. The principal scale used in the United States today is the Modified Mercalli Intensity Scale (Appendix C).

Intrinsic permeability. The characteristic resistance to fluid flow of a porous medium alone, independent of the properties of the fluid. The symbol is k.

Isoseismal. A line connecting points on the Earth's surface at which **earthquake intensity** is the same. It is usually a closed curve around the **epicenter**.

Lithostatic pressure. The vertical pressure at any point at depth in the rock due to the overburden or weight of the overlying rock mass. *See also* **Vertical stress.**

Magnitude. A number that characterizes the size of an **earthquake**, usually based on measurement of the maximum **amplitude** recorded by a **seismograph** for **seismic waves** of a particular **frequency**. Scales most commonly used are (1) **local magnitude** (M_L), (2) **surface-wave magnitude** (M_S), and (3) **body-wave magnitude** (m_b). None of these scales satisfactorily measures the largest possible earthquakes because each relates to only the amplitude of certain frequencies of seismic waves and because the spectrum of radiated seismic energy changes with earthquake size. To compensate, the **moment magnitude (M)** scale, based on the concept of seismic moment, was devised and is uniformly applicable to all sizes of earthquakes.

Body-wave magnitude. This scale measures the maximum **amplitude** of waves that pass through the interior—the body—of the Earth and that have a period between 1 and 10 seconds (s). The symbol is m_b.

Local magnitude. This scale is commonly referred to as Richter magnitude. Although only accurately applied to California earthquakes, it is still quite useful today for describing smaller and more moderate earthquakes but not for measuring truly large earthquakes. It provides a good estimate to engineers of the high-frequency **accelerations** generated by an earthquake. The symbol is M_L.

Moment magnitude. This is perhaps the most meaningful scale today for large and great earthquakes, in that it reflects the total energy released. The measurement takes into account the surface area of the **fault** that moved to cause the earthquake, the average **displacement** along the fault plane, and the rigidity of the fault material. Seismic moment (M_o) is the result, and the moment magnitude is simply a scaled logarithm of this value. This scale was developed only in the late 1970's, which is why great earthquakes, such as that in Alaska in 1964, which was originally evaluated as a magnitude M_S 8.5, have been upgraded—Alaska now has an moment magnitude rating of 9.2. The symbol is **M** or M_w.

Surface-wave magnitude. This scale was formulated to describe earthquakes at distant locations. The scale principally measures **surface waves** of 20-s period or a wavelength of approximately 60 km. The symbol is M_S.

Major earthquake. An **earthquake** having a **magnitude** of 6.5 or greater.

Maximum horizontal stress. The maximum component of **principal stress** in the horizontal plane. The symbol is S_H.

Mean stress. The average of the three **principal stresses.**

Microearthquake. A small **earthquake** usually observable only with sensitive instruments. Typically corresponds to an earthquake of **magnitude** 2 or less. *Also called* microseismic event.

Minimum horizontal stress. The minimum component of **principal stress** in the horizontal plane. The symbol is S_h.

Mohr circle. A graphical representation of the state of **stress** at a particular point and at a particular time. The coordinates of each point on the circle are the **shear stress** (τ) and the **normal stress** (σ_n) on a particular plane.

Mohr-Coulomb failure criterion. The condition whereby failure (slip) is expected on a preexisting **fault** whenever the combinations of **shear stress** (τ) and **normal stress** (σ_n) resolved across the fault plane (as defined by the loci of points on the **Mohr circle**) meet or exceed the Coulomb criteria for frictional failure; that is, the shear stress is equal to the inherent fault **cohesion** (τ_o) plus the product of the **coefficient of friction** (μ) and the effective **normal stress** ($\sigma_n - p$). This level of **shear stress** is called the critical stress (τ_{crit}).

Normal fault. A steeply to slightly inclined **fault** in which the block above the fault (the hanging wall) has moved downward relative to the block below (the footwall).

Normal stress. The component of **stress** oriented normal (perpendicular) to a given **fault**, fracture plane or slip surface. The symbol is σ_n.

Permeability. The capacity of a porous rock or soil for transmitting fluid or gas; it is a measure of the relative ease of fluid flow under unequal pressure.

Plate tectonics. A widely excepted theory that considers the Earth's **crust** and upper mantle to be composed of a number of large, rigid plates that move relative to one another. Interaction along plate boundaries is then the major cause of **earthquakes** and volcanic activity.

Pore pressure. Pressure of water in pores of a saturated medium. The symbol is p.

Pore space. Space occupied by voids within the rock matrix capable of holding either fluid or gas.

Porosity. Percentage ratio of void volume to the bulk (total) volume of rock or soil sample. It is a measure of the fluid bearing capacity of the medium. The symbol is n.

Primary wave. A type of elastic **body wave** that propagates by alternating compression and expansion of material in the direction of propagation. It is the fastest of the seismic waves (typically traveling at speeds of 5–6.8 km/s in the crust and 8–8.5 km/s in the upper mantle, just below the crust), and is analogous to a traveling sound wave. The abbreviation is P wave.

Principal stress. A **stress** that is perpendicular to one of three mutually orthogonal planes on which the **shear stress** is zero and in whose direction stresses are purely

compressive; a stress that is normal to a principal plane of stress. The three principal stress are identified as σ_1, maximum or greatest principal stress; σ_2, intermediate principal stress; and σ_3, minimum or least principal stress.

Rake. The direction of **displacement** (slip) resolved across a **fault** plane, measured in degrees from the horizontal.

Reservoir. (1) A recipient for the collection of liquid. In geology, a subsurface rock formation that has sufficient **porosity** and **permeability** to except and retain a large amount of fluid or gas under adequate trap conditions. (2) A manmade body of water impounded behind a dam.

Reverse fault. A moderately inclined fault in which the block above the fault (the hanging wall) has moved upward relative to the block below the fault (the footwall).

Secondary recovery. Production of oil or gas as a result of artificially augmenting the **reservoir** energy, usually by injection of water or other fluid at high pressure. Secondary-recovery techniques are generally applied after substantial reservoir depletion. *See also* **Water flooding**.

Secondary wave. A type of **seismic body wave** that propagates by a shearing motion of material, so that wave motion or oscillation is perpendicular (transverse) to the direction of propagation. It does not travel through liquids or through the outer core of the Earth. Its speed is typically 2.8 to 4 km/s in the crust and 4.3 to 4.5 km/s in the upper mantle, just below the crust. This wave arrives later than the faster **primary wave**. The abbreviation is S wave.

Seismic. Pertaining to an **earthquake** or earth vibration, including those that are artificially produced.

Seismicity. Earthquake activity; the geographical and the historical distribution of earthquakes.

Seismic risk. The probability of social or economic consequences of an **earthquake**.

Seismic wave. An **elastic wave** generated by a sudden impulse, such as an **earthquake** or an explosion.

Seismogram. A record of ground motion or of vibration of a structure caused by an **earthquake** or an explosion; the record produced by a **seismograph**.

Seismograph. An instrument that detects, magnifies, and records ground vibrations, especially **earthquakes**. The resulting record is a **seismogram**.

Separation. In geology, the distance between any two parts of a reference plane (for example, a sedimentary unit or a geomorphic surface) offset by a **fault** measured in any plane. Separation is the amount of apparent fault **displacement** and is nearly always less than the actual slip.

Shear. A mode of failure whereby two adjacent parts of a solid slide past one another parallel to the plane of failure.

Shear stress. The component of **stress** that acts tangential to a plane through any given point in a body. The symbol is τ.

Shear wave. A secondary or transverse **elastic wave**.

Slip rate. The average **displacement** at a point along a **fault** as determined from geodetic measurements from offset manmade structures or from offset geologic features whose age can be estimated. It is measured parallel to the dominant slip direction or estimated from the vertical or the horizontal **separation** of geologic, geodetic, or other markers.

Storativity. The capacity of an **aquifer** to accept (store) or release fluid under a change in applied **pore pressure** (p) and is defined as the amount of fluid in storage released from a column of aquifer with unit cross section under a unit decline in pressure **head**. The symbol is S. *Also called* storage coefficient.

Strain. The amount of any change in dimensions or shape of a body when subjected to deformation under an applied **stress**.

Stress. The force per unit area acting on a surface within a body. Nine values are required to characterize completely the state of stress at a point: three normal components (which are purely compressive) and six shear components, relative to three mutually perpendicular reference axes.

Strike. The orientation of the line of intersection of any plane with the horizontal measured in degrees from true north; the direction or trend taken by a structural surface, such as a **fault** plane, as it intersects the horizontal.

Strike-slip fault. A **fault** in which movement is principally horizontal, parallel to the **strike** of the fault.

Subsidence. Downward settling of the Earth's surface with little or no horizontal motion. May be caused by natural geologic processes (such as sediment compaction or **tectonic** activity) or by human activity (such as mining or withdrawal of ground water or petroleum).

Surface faulting. Displacement that reaches the ground (or sea floor) surface during slip along a **fault**. Commonly accompanying moderate and large **earthquakes** having **focal depths** to 12 km. Surface faulting may also accompany **aseismic tectonic creep** or natural or man-induced **subsidence**.

Surface wave. Seismic wave that propagates along the Earth's surface.

Tectonic. Pertaining to either the forces or the resulting structural features from those forces acting within the Earth; refers to crustal rock-deformation processes that affect relatively large areas.

Tensile strength. The maximum applied **tensile stress** that a body can withstand before failure occurs. The symbol is T_0.

Tensile stress. A **normal stress** that tends to cause separation across the plane on which it acts.

Top-hole pressure. The fluid pressure measured at the wellhead. The abbreviation is THP.

Total head. The sum of the elevation **head**, pressure head, and velocity head of a liquid. For ground water, the velocity-head component is generally negligible.

Transmissivity. The rate at which water is transmitted through a unit width of **aquifer** under a unit **hydraulic gradient**; it is equal to the product of the **hydraulic conductivity** and the thickness of the aquifer. The symbol is T.

Vertical stress. The **stress** at any point at depth in the rock due to the overburden or weight of the overlying rock mass; equal to the product of the average **density** of the overlying column of rock, the **acceleration** of gravity, and the depth. The symbol is S_v. *See also* **Lithostatic pressure**.

Water flooding. A **secondary recovery** technique in which water is injected into a petroleum **reservoir** to force additional oil out of the reservoir rock and into producing wells.

Water table. The upper surface of a body of unconfined ground water at which the water pressure is equal to the atmospheric pressure.

Wellbore breakouts. Deformation of the wellbore wall caused by spalling of weak material induced by compressive **shear** failure. *Also called* borehole elongations.

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The Impact of Injection on Seismicity at The Geysers, California Geothermal Field

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Abstract

Water injection into geothermal systems has often become a required strategy to extended and sustain production of geothermal resources. To reduce a trend of declining pressures and increasing non-condensable gas concentrations in steam produced from The Geysers, operators have been injecting steam condensate, local rain and stream waters, and most recently treated wastewater piped to the field from neighboring communities. If geothermal energy is to provide a significant increase in energy in the United States (US Department of Energy (DOE) goal is 40,000 megawatts by 2040), injection must play a larger role in the overall strategy, i.e., enhanced geothermal systems, (EGS). Presented in this paper are the results of monitoring microseismicity during an increase in injection at The Geysers field in California using data from a high-density digital microearthquake array. Although seismicity has increased due to increased injection it has been found to be somewhat predicable, thus implying that intelligent injection control may be able to control large increases in seismicity.

Background

Water injection into geothermal systems has become a nearly universal and often required strategy for extended and sustained production of geothermal resources. To reduce a trend of declining pressures and increasing non-condensable gas concentrations in steam produced from The Geysers, operators have been injecting steam condensate, local rain and stream waters, and most recently treated wastewater piped to the field from neighboring communities. Monitoring of microearthquakes related to production and injection has been conducted since the mid 1970's. MEQ has been applied as a general indicator of fluid paths and general response to injection at The Geysers for over 20 years [1]; [2]; [3]; [4]; [5]; [6]; [7]; [8]; [9]; [10]; [11]; [12]; [13]; [14]. A dramatic increase in planned injection rates and spatial extent of injection due to the recent completion of a wastewater pipeline (from Santa Rosa, CA) has raised

concerns regarding the societal and economic impact of injection related seismicity. An obvious question to be asked is will the rate and size of the MEQ events place an upper bound on injection at The Geysers, or vice versa, will there be larger and larger events as injection increases? Although the Santa Rosa injection has only been going on for a few years the operators are evaluating a 50 percent increase over the initial injection (41millions liters/day). Without this injected water the thermal capacity of The Geysers will be underutilized and The Geysers will not be able to provide as much energy as possible. Vapor-dominated geothermal reservoirs such as The Geysers by their very nature are water-short systems. If The Geysers were produced without simultaneously injecting water, reservoir pressures and flow rates from production wells would decline fairly rapidly, and would reach uneconomically small levels while enormous heat reserves would still remain in the reservoir rocks. Furthermore, the Northwest Geysers, which contains a significant portion of the recoverable geothermal energy, is currently underutilized due to high concentrations of non-condensable gas and corrosive HCl. Mitigation of these deleterious components through water injection would significantly increase The Geysers resource. Therefore, the key to sustaining and enhancing energy recovery from The Geysers is water injection.

Water injection is not automatically beneficial. Injected water may migrate along major fractures and quickly reach production wells, which may degrade production by lowering fluid enthalpy and temperature. At its best, injected water will be completely vaporized by contact with hot rocks before it reaches production wells, supplying additional steam, and increasing reservoir pressures and production well flow rates with minimal or even positive societal impact. Injection can also improve the quality of produced fluid from a chemical viewpoint, by reducing concentrations of non-condensable gases such as CO_2 and corrosive gases such as HCl. It is not new knowledge that seismicity at The Geysers is linked to injection and production. Several studies have demonstrated that MEQs at The Geysers geothermal area are associated with both water injection and steam extraction [2]; [10]; [16]; [12]; [17]; [15]; [18]; [19]. These studies include correlation of spatial and temporal MEQ distributions with injection/production data. In a recent paper, [19] the authors make a comprehensive correlation study based on induced seismicity and operational data from 1976 to 1998. They found three types of induced seismicity at high significance:

i) Shallow, production-induced seismicity that has a long time lag on the order of 1 year.

ii) Deep, injection-induced seismicity with short time lag, < 2 months.

iii) Deep, production-induced, seismicity with short time lag, < 2 months that appears to diminish in the late 1980s.

For each of these three types of induced seismicity they also proposed failure mechanisms based on analytical modeling and reasoning.

For shallow induced MEQs, [19] the authors found that MEQ distribution closely matches mapped low pressures in the reservoir and the areas of maximum volume strain inferred from surface deformation data, suggesting that these events are caused by poroelastic stressing. The observations are consistent with a contracting reservoir, which as it shrinks, induces stresses and strains in the surrounding crust. Shear stresses on faults outside the reservoir can increase, causing subsidence. However, these results [19] suggests that shallow earthquakes are production-induced and is in contrast with results of [20]. Studying one specific case in detail, they found that shallow MEQs are well correlated to injection, rather than production, and with a relatively short time lag of about 1 week. For shallow MEQs there might be a long-term effect caused by the overall steam-production and local short-term responses related to injections. In addition, [21] hypothesized that there is a back front of seismicity produced that will cause extended periods of seismicity after injection has ceased. This was found during hydraulic fracturing cases not located at The Geysers.

For deep induced MEQs occurring after the 1980s there seems to be a consensus that these are correlated to local injection rates with some time lag [12]; [16]; [22]; [17]; [15]; [18]. For example, [12] showed that plumes of MEQs are clustered around many injection wells, and the seismic activity around each injection well correlates with its injection rate. Also, it has been hypothesized that injection-induced MEQs are probably caused by thermo-elastic perturbation due to cold-water injection into a hot reservoir [19]. When cool water flows into hot rock fractures, the fracture faces contract by cooling, loosening the frictional forces across the fractures and thereby allowing stress release by seismic slip. Although [19] studied other mechanisms (e.g. loss of effective stress due to hydraulic pressure in the fracture), they concluded that it is the temperature contrast between the injected water and the hotter rock fracture surfaces that is probably the dominant mechanism driving Geysers injection-induced seismicity. Finally, some have attributed deep production-induced seismicity to thermo-elastic stressing caused by evaporative cooling [19]. They concluded that an evaporative-thermoelastic model could explain why

deep production correlated seismicity declined in the mid 1980s as the reservoir dried out and evaporative cooling diminished.

It has also been found that where clusters extend some distance from the injectors, the production wells tend to show "heavy" isotopic signature of flashed injectate [12]. They therefore hypothesized that MEQs are induced where injected water is present as liquid. It was suggested that the MEQs occurring in this liquid zone might be a result of the effects of hydraulic head and/or cooling due to the injected water [12]. Recently, this hypothesis was used to explain the vertical pattern of induced seismicity in the Northern Geyser reservoir [18]. Historic Geysers earthquakes and injection data shows an area of approximately 8 km^2 underlain by a cluster of MEQs in the depth range of 3 to 5 km below sea level. The cluster lies far below the normal 240 °C isothermal reservoir and is in the underlying High Temperature Zone (HTZ), where temperature gradients can exceed 100°C per km. Above this cluster there is a gap, 0.5 to 1 km thick, where few MEQs occur. Above the gap is a more typical pattern of the Geysers seismicity, including plumes of MEQs associated with injection wells. This was then used in a conceptual model to show that this pattern could be governed by the temperature contrast between injected water and the rock, and would imply that significant volumes of injected water have descended into the HTZ reaching a depth as great as 5 km below sea level [18]. Furthermore, monthly injection and seismic data from 1983 to 2002 was studied and was found that the deep injection induced seismicity was lagging behind by 3 months suggesting that it would take about 3 months for the injected water to descend to depths of 3 to 5 km.

The above studies have made progress in showing a general correlation of liquid injection and steam production with various types of induced MEQs at The Geysers. Furthermore, several plausible hypotheses have been proposed to explain the mechanisms producing those MEQs. The Geysers region is subject to active tectonic forces associated with the strike-slip relative motion between the North American and Pacific plates [18]; [11]. Many naturally occurring fractures may be stressed to near the failure point, so a small perturbation in the stress field could lead to failure. However, it is not at all certain that most MEQs at The Geysers are produced by shear slip along pre-existing fractures [23]; [17]. Others, [24] conducted highly accurate moment tensor analysis for thirty recorded earthquakes in the area and showed that most of the earthquakes have a non-shear component in their focal mechanisms. They suggested that sources may be explained by combinations of tensile cracks and shear movements

accompanied by fluid flow. Cracks open in the presence of high-temperature and pressure fluids, rapid flow in the new void, possibly accompanied by water flashing to steam. In general, rapid cooling along a fracture is capable of creating thermally induced fractures (TIFs) in the rock matrix adjacent to the fracture [25]. In any case, it is likely that thermo-elastic responses, induced by rapid cooling, play a major role in inducing MEQs at The Geysers.

Lacking, prior to the work described here, was a detailed field-wide MEQ response to a large influx of water, such as the Santa Rosa injection project. New technology in MEQ acquisition and analysis (wide band width, multi-component), while used in parts of The Geysers for short periods of time, was not in place prior to this project. These data can potentially provide an improved understanding of the basic mechanisms for the cause of the induced seismicity and the potential for injected water to efficiently mitigate high concentrations of non-condensable gases and corrosive HCl. Although the routine MEQ data are being collected and analyzed, new methods of MEQ analysis have been developed in the last several years which could be applied to further improve our understanding of such attributes as location, magnitude, source mechanisms, which in turn will allow an overall understanding of energy release in The Geysers and its relation to production and injection activities.

The most established use of earthquake data at The Geysers, the tracking of strain release and presumably injection flow paths, could be greatly enhanced if the many theories describing how earthquakes and injectate are related were better constrained by observation. This requires an improved understanding of the "triggering" mechanisms of both the injection and the production related induced seismicity and of any source mechanism peculiarities that naturally occurring earthquakes may have in geothermal regions. The locations of the earthquakes have also been used to characterize patterns of permeability in reservoirs. However, this is a very complex issue since in different circumstances earthquakes can be more closely associated with either relatively low or relatively high permeability. Because characterizing permeability of geothermal reservoirs is of great importance in targeting wells and predicting overall reservoir performance, reducing the uncertainty in such earthquake interpretations would have great value.

A recent success [26]; [27] has been reported in using microearthquakes as illumination sources to image physical properties within The Geysers reservoir area. For instance, "tomographic" imaging of seismic

wave velocity can be periodically repeated to map temporal changes in water saturation. A decline in water saturation is often accompanied by a decline in production pressure and an increase in non-condensable gas concentrations. Therefore, the existing earthquake array was designed to also provide the needed data to address such issues.

Last but not least, although seismicity is currently being used as a reservoir management tool, it is also becoming a negative issue with some of the more populated communities nearby geothermal fields. Events with magnitude 2 and above have raised concern to the residents near certain fields for not only their individual, but cumulative effect. In addition, some fear that as injection and production increases, the events will not only increase in numbers but increase in magnitude. In particular, the general public's perception is that this induced seismicity may cause damage to structures on the surface, similar to that caused by "natural" earthquakes. The communities affected are concerned and would like to see efforts on how and why do they occur and can one devise any procedures to reduce them. In addition, the operators also want to know how the seismicity is linked to reservoir performance and what can be learned from the seismicity.

It must be kept in mind that there are many different mechanisms that have been proposed for inducing earthquakes. Induced seismicity has not only been noted in geothermal reservoirs but in reservoir impoundment (water behind dams), waste injections, and oil and gas operations. Another type of induced seismicity is that associated with hydrofracturing. In this paper, however, we are only dealing with seismicity in naturally fractured systems although in such areas as Soultz in France, seismicity associated with hydrofracturing has become an issue.

Regional Seismicity

If one examines the subsurface in enough detail one can find fractures, joints, and/or faults almost anywhere in the world. A fault is not defined in terms of size, (definition of a fault is a displacement across a fracture or fracture zone), however, most mapped faults range in size from very small (few meters) to very large (hundreds of kilometers long). The size of an earthquake (or how much energy is released) depends upon how much slip occurs on the fault, how much stress there is on the fault before slipping, how fast it fails, and over how large an area it occurs. In most regions where there are economic geothermal resources there is usually tectonic activity, such as in the western United States. For example,

Figure 1 is a map of northern California and part of Nevada showing the location of earthquakes from 1900 to the present with magnitudes from 3.0 to 5.0. Also shown are some of the geothermal areas. It is not surprising that if the stresses are manipulated through injection and withdrawal of fluid that seismicity may change in these tectonic areas. Large or damaging earthquakes tend to occur on developed or active fault systems. In other words, large earthquakes rarely occur where there is not a fault large or long enough to release enough energy. It is difficult to create a large new fault, because there is usually a pre-existing fault that will slip first, rather than a new fault being created.

A critical question that needs to be addressed is how injection will affect the seismicity, what does it imply for injection strategy, and how will it impact the local community as well as field operations. The Geysers is a prime candidate for EGS due to the very high heat content (especially the northwest Geysers) and a general lack of fluid. Injection is one of the few economic means to mine this heat (versus subsurface installed heat exchangers for example). The northwest Geysers has had production in the past, but over the last several years been shut down and is now the target of increased production due to future injection. We view the Geysers in general as a laboratory for induced earthquakes due to its broad range of seismicity (from less than zero to above magnitude 4's as well as for the large number of events, from 2000 to 3000 locatable events per month). In addition, the northwest area is a unique opportunity to obtain the data before a large injection and increased production begins.

Objective of Microearthquke Monitoring Work

There are two prime objectives of this work: 1. To understand the impact of EGS operations on induced seismicity and its environmental impact on the surrounding community. 2. To use microearthquake monitoring to intelligently manage the effects of fluid injections and stimulations to aid in the optimization of Enhanced Geothermal Systems.

These two objectives are related but separate. In the first objective we are trying to understand at what level the seismicity becomes a hazard to the community (and possibly the geothermal operations) and how can one possibly mitigate the hazard without severely reducing the output of the field. In the second objective we are trying to understand the relation between the reservoir properties (physical and chemical) and the link to seismicity and what the seismicity is telling us about those properties in order to optimize and manage the reservoir. Both objectives must be met to meet overall EGS objectives.

Data Collection and Processing

The purpose of this effort was to design and install a seismic monitoring system covering all of The Geysers and its immediate surroundings with spatial resolution and detection threshold comparable or superior to the current array being maintained by the operators of the field (Calpine Inc). That array is an analog system with voltage-controlled oscillators (VCO) and discriminators using mainly single vertical component data. A second array of stations covering The Geysers is the network of stations operated by the USGS, again mainly vertical component with a bandwidth of less than 50 hertz. The system put in place that collected the current subject data was installed in two phases. The first phase installed 23 state-of-the-art, three-component short period seismometer sites continuously digitally telemetered at 500 samples per second (sps) for each of three channels to a central acquisition PC which would automatically trigger on events, pick arrivals, locate events and estimate origin time and magnitude. This first phase covered the existing production from the main Geysers geothermal field in order to monitor the effects of the Santa Rosa injection. The first phase of the array was completed and became operational in October of 2003. The second phase of the array installed five more stations to cover a new injection area in the northwest section of The Geysers, i.e., the "Aidlin" area. The Aidlin area is in a more remote area, somewhat separated from the "main" field with a reservoir volume high in non-condensible gases yet high in temperature. The Aidlin stations were added in June of 2004. Figure 2 shows the location of the new stations and the Calpine stations relative to The Geysers central area and the existing USGS array. Also shown in Figure 2 are the locations of several strong motion stations installed by Calpine near the bordering communities. The final entire array is shown in Figure 3. Figure 4 shows the difference in event detection between the USGS array and the LBNL array. The threshold of USGS locations is approximately magnitude 1.2 while the threshold of detection for the LBNL array is about magnitude zero. In September of 2004 a large fire swept through the southeast Geysers and destroyed several stations. A reconfiguration in 2005 left the five Aidlin stations and 18 stations covering the reset of The Geysers for a total of 23 stations. This did not affect the threshold of detection however.

To achieve the processing goals we needed to locate the earthquakes as well as possible, in both time and space, yet do so with a large numbers of events. We have demonstrated in past work at The Geysers that we can locate events to within 50 meters of precision and 100 meters of accuracy in The SE Geysers by using the technology used in this project, [17]. We also needed to detect and locate events down to very small events, possibly down to magnitude magnitude zero, or lower. We felt that this level of precision

and accuracy was necessary Geysers-wide to have the quality and volume of data to meet our objectives. The analysis and processing carried out consisted of "routine locations", magnitude determination and correlation with the injection parameters to establish relations between seismicity and reservoir performance. The general operation of the data flow is as follows. An event is defined as valid if six or more stations detect a trigger (a trigger is defined if the short term average of a 16 point rectified average of the data exceeds the long term average (4096 points) in a 0.5 second time window). This procedure follows the processing stream developed by [28]. The P-arrival times are then gathered (with criteria set out by [2]) and are used to locate the event with a 1-d model. In addition to the 1-d model, a three-dimensional inversion using cubic splines was also used to invert for a velocity model and locations. Figure 5 shows the difference in locations when one uses two different starting models for a three dimensional inversion. For one thousand events the residual difference of locations is mostly less than 100 meters (length of each line), with no particular preference in direction (circle in Figure 5). There are lines longer than 100 meters but those events are mostly for events on the edge of the array. It seems that due to the shear number of events are overwhelming the heterogeneity, thus making it difficult to tell the significant difference in small changes in the velocity model. Therefore, for the routine locations we decided to use a 1-d velocity model (model 1).

The magnitudes are determined with an average coda length of all the triggered stations. A duration magnitude was determined for the events by fitting the log duration from the LBNL events to the USGS magnitude for the same events. The magnitude is estimated for each event using equation (1).

(1) Magnitude = 0.37 log10 (duration (seconds)) - 1.39.

The duration is defined as the time at which the short-term average drops below 1.25 for more than 0.25 seconds i.e. following [2].

The location, P-times, magnitude and waveforms are then sent to the United States Geological Survey (USGS) via internet and provided on their internet site. In addition, all events located are then sent to the larger database at the University of California/USGS Northern California Data Center (NCDC).

On average over 3000 events are detected and located per month down to a magnitude of zero in real time. Due to the large volume of data it would be prohibitively expensive to provide "hand" processed results in real time. However, it is critical that for public and scientific reasons that this never-before-obtained resolution, three component, and bandwidth data set from The Geysers be made available in a timely fashion to the research community and other interested people. Therefore, a complete list of all events recorded is available at the NCDC such that the general public can request all time series and station data in a standard format.

Results

Our working hypothesis for the increased microearthquake activity at The Geysers is that the seismicity is due to a diverse set of mechanisms. That is, there is not one universal "triggering" mechanism (other than stress) but a variety of mechanisms in operation that may work independently, together, or superimpose to enhance or possibly reduce seismicity. For example, as one injects water into the reservoir there is obviously cooling, a change in pore pressure (at least locally around the well) and possibly wider ranging stress effects. There has also been a debate in the literature about the relation between the location of the microearthquakes and the location of the fluids. If the events are due to thermal contraction from cooling the rock matrix one would assume that would take a very long time, i.e. the thermal front travels orders of magnitude slower than the fluid front. As it is, the fluid front does not travel in one continuous manner but it fingers it way through the fractures in a lace-like manner. Unlike the rock matrix, fracture surfaces can cool very quickly as they are contacted by the fluid front. By examining the spatial and temporal rate of change in seismicity one may be able rule out or confirm certain mechanisms. Also, as the injections proceed effects may be felt on a field wide basis. As the local stresses change around each injection well they may superimpose upon the existing regional stresses or link up to form a larger local effect that in turn may affect a wider region within the field. Figure 6 shows the rate of seismicity from 1965 to the present (early 2006) at The Geysers as derived from the USGS database. The data are for magnitudes above 1.2 as determined from the USGS data set at the Northern California Earthquake Data Center. As can be seen, as the injection increases the seismicity increases, but not at all levels. If one only looks at the larger the seismicity has stayed fairly constant since 1985 (magnitude 3 events) There is also no clear relation between total injection and seismicity, except if one looks at all events above 1.2. Magnitude 4 events however have been increasing. As can be seen there are peaks in seismicity in 1986 and again in 1998, and more recently due to the latest injections. It is also

important to point out that as steam production has decreased since 1986 the overall rate of seismicity has remained fairly constant. Recent data does show that there has been an increase in seismicity due to the recent injection in 1997 and 2003. It should be noted that for 2005 the seismicity has already reached above past years levels. Figure 7 shows the trend in seismicity as recorded by the LBNL array between October 2003 and September 2006. The two "gaps" in seismicity are due to array problems from wild fires in the area. Also shown is the approximate start time of the Santa Rosa waste water injection (up to 11 millions gallons per day). The injection did not start exactly on any one date but was brought on line over several months time between October and December of 2003. As can be seen there is a definite increase in seismicity in 2004 continuing to the present. Figure 7 shows that initially the seismicity sharply increased, but has not been increasing as much as injection increases.

Figure 8 shows the injection history for the entire Geysers field from 2000 to mid 2006. The oscillations are due to injecting more water in the winter when it rains and there is also less evaporation from the cooling towers, thus there is more water available to be reinjected, compared to the summer when it almost never rains. Therefore there is much more injection in the winter months than in the summer months. This figure also shows the general upward trend in total injection. Figure 7, shows that at least in the number of events (versus total energy release) that there is not a strong correlation between the oscillation in the injection the oscillation in the seismicity. Figure 9 shows one month of data before the Santa Rosa injection (October 2003) and a typical one-month of data after the full injection start (April 2004). As can be seem there has been a definite increase in seismicity in the area of the injection wells. There is a definite clustering of events around the injection wells, but there is also seismicity in other areas. As stated before this is typical of seismicity at The Geysers, and some or all of the increase may just be normal seasonal variation as the non-Santa Rosa water injection ramps up. Low-magnitude seismicity increased in the SE Geysers when supplemental injection began there [17]; [14]; [15] and it is not surprising that is occurring now with the Santa Rosa injection. Looking at a longer period of time a similar pattern emerges. Figures 10, 11, 12 and 13 show The Geysers field, the location of injection wells for the Santa Rosa injection (blue squares), the LBNL array at the time and all the located events in two different time periods, October 2003 to September 2005 (two years), and from October 2005 to September 2006 (one year) . It should be noted that injection and production is occurring field wide but there is a strong correlation to not only the Santa Rosa injection well but to other injection wells (see Figure 3 for the location of other injection wells). Also shown in these figures are the locations of the

magnitude 4 events (large stars in Figures 10 and 12). It is interesting to note that there is only a loose correlation between the magnitude 4 events and the zones of injection. In fact it seems that the larger event s occur on the edges of the seismicity or away from it. Figure 11 shows the location of only the larger events (2, 3, and 4s) for the first period and Figure 13 shows the location of the larger events in the second time period. It is interesting to note the location of the 4's, and also a line of 3's in the southwest part of the filed away from the main cluster of events.

Also, as part of this study as was mentioned before, we expanded the array in early 2004 to cover the northwest area of The Geysers field, the Aidlin area. This is an area where the subsurface temperatures are very hot (well over 250 C) and there are large concentrations of non-condensable gases. In late 2004 injection began in this area (see Figure 14) at relatively small volumes, it held relatively steady at this rate until September of 2005 when the injection sharply increased. As can be seen from Figure 14 the seismicity generally tracked this injection. The three large increases in injection generally occur after injection changes. In some cases there is a lag in seismicity. Figure15 shows the plan view and an east-west cross section through the center of the cluster as well as the trace of the well. The seiamicity is near the bottom and extending away from the well. Also shown is the location of a magnitude 4 event that occurred in October of 2005, near the edge of the cluster of seismicity at a depth of 2.5 kilometers. Another magnitude event occurred in May of 2006, in the northwest Geysers but well away from the Aidlin cluster of events (see Figure 12.

Discussion and Conclusions

If past experience is any indication, the system will reach equilibrium as time proceeds and the seismicity may level off and possibly decrease (see Figure 6). It has been our experience that the initial injections will perturb the system, cause an increase in seismicity, then level off and/or decrease. This is again being noted in the Aidlin area. The time period will be a function of the size of the disturbance and the volume of the affected area. Rate of injection seems to be an important factor also. One hypothesis worth considering is that if the rate of increase injections is varied (give the system a chance to equilibrate) there may be less initial seismicity. The recent injections may reverse this trend but it is too early in the monitoring process to determine. Last but not least, what will be the impact of the maximum event size? The maximum event at the Geysers was in 1982 (4.6), but in the past year there have been 3 events of magnitude greater than 4.0 (see Figure 12). The maximum event will depend upon the size of the fault

available for slippage as well as the stress redistribution due to injection and production. To date there has been no faults mapped in The Geysers which would generate a magnitude 5.0 event or greater. This is not an absolute guarantee that one would not happen, but does lower the likelihood.

In order to realistically examine the overall benefit of injection one must look at both the public and private sectors. Access to high quality, state-of-the-art seismic information will be important for both public acceptance and industry reservoir management. For example, at The Geysers related geothermal industry benefits will include establishment of a non-industry monitoring and reporting system capable of providing the high quality, publicly credible, seismic data base needed to gain public acceptance of wastewater injection; and the basic scientific knowledge regarding the relations between seismicity and fluid movement in the crust.

The most established use of earthquake data in geothermal regions, the tracking of strain release and presumably injection flow paths, could be greatly enhanced if the many theories describing how earthquakes and injectate are related were better constrained by observation. This requires an improved understanding of the "triggering" mechanisms of both the injection and the production related induced seismicity and of any source mechanism peculiarities that naturally occurring earthquakes may have in geothermal regions. The locations of the earthquakes have also been used to characterize patterns of permeability in reservoirs. However, this is a very complex issue since in different circumstances earthquakes can be more closely associated with either relatively low or relatively high permeability. Because characterizing permeability of geothermal reservoirs is of great importance in targeting wells and predicting overall reservoir performance, reducing the uncertainty in such earthquake interpretations would have great value.

Specific to the Geysers, it is also likely that, during the monitoring of the seismicity, information will be gained which will be the prime motivator for operational decisions, which will increase net production. For example there is a large untapped portion, which could be exploited if proper injection and production strategies are designed. Due to concerns regarding MEQ generation one must also take into account the impact of injection on seismic as well as reservoir conditions. If injected under the right conditions and rates wastewater may mitigate deleterious high non-condensable and corrosive gas concentrations in the reservoir. *In situ* mitigation will alleviate the economic and technological issues presently preventing

exploitation of much of a high temperature reservoir characterized by high concentrations of CO_2, H_2S, and HCl in the vapor contaminates the production stream, requiring costly surface mitigation strategies, diminished well life times and retrofitting of power plants to handle the high gas contents.

In conclusion, it has been demonstrated that the seismicity is largely a function of fluid injection, although there is not a strict one to one correlation in time and space. We view this as positive because it indicates that balancing the injection and fluid withdrawal the seismicity can be controlled. The challenge is to optimize the production as well as control the larger events, which may have impact on the local community. In terms of the seismicity being a hazard to the community, the risk does not seem high. The region surrounding the Geysers is tectonically stressed, cut by numerous faults, and subject to a high level of earthquake activity. In the Geysers field, there are no mapped faults active in the last 10,000 years [11]. The Collayomi Fault, running approximately 1 mile NE of the field limit, is mapped as an inactive fault. The nearest active fault is the Mayacamas Fault, located 4 miles SW of the field limit. On the northeast side, the active Konocti Bay fault system is located approximately 8 miles north of the field limit. Therefore one must speculate if there even exists a fault large enough in the region to create a large event.

Last but not least it is concluded that injection-induced seismicity is observed in the form of "clouds" of earthquakes extending primarily downward from injection wells. At such a well, the cloud generally appears shortly after injection begins, and earthquake activity within each cloud shows good temporal correlation with injection rates. It has been demonstrated that injection-induced seismicity is generally of low magnitudes ($\leq$3.0). On a fieldwide basis, seismicity of magnitudes $\geq$1.5 has generally followed injection trends, but this correlation has not been observed for earthquakes of magnitudes $\geq$3.0.

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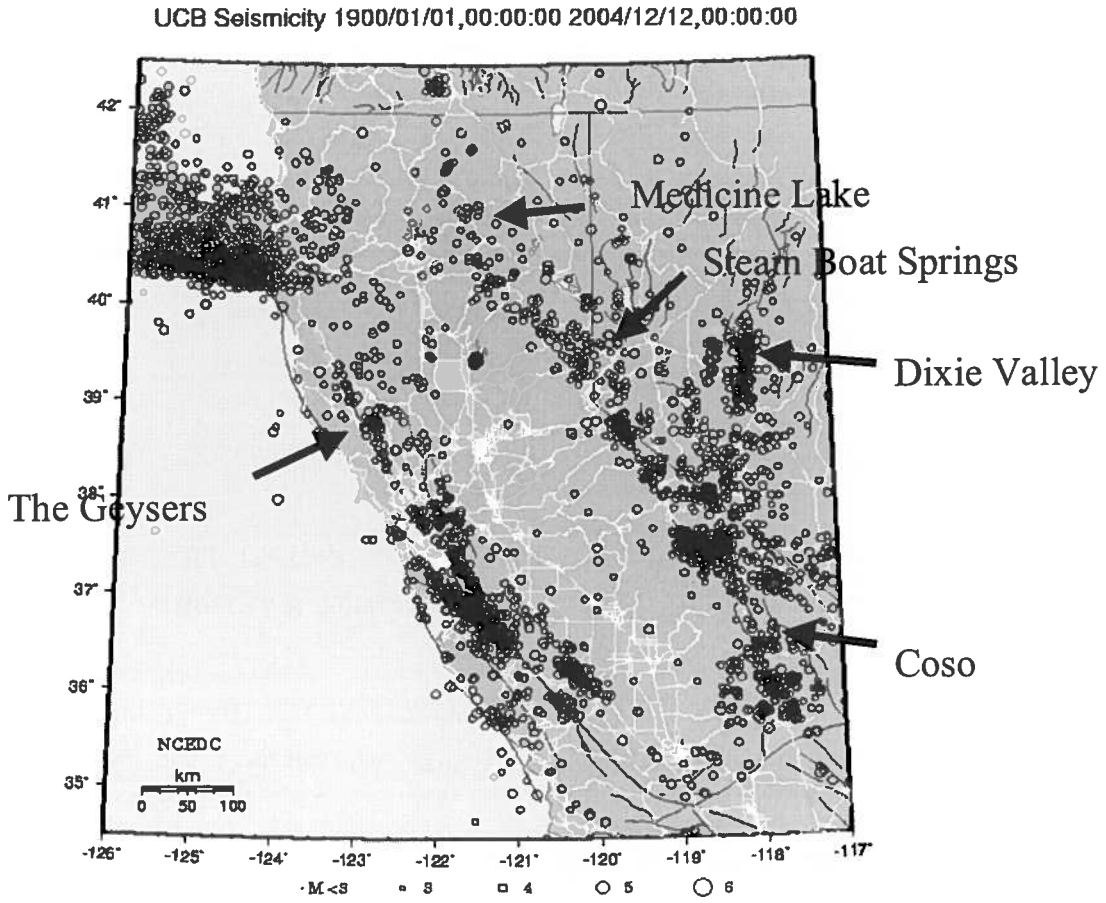


Figure 1. Seismicity from 1900 to 2005 (from magnitude 3.0 to 5.0) relative to some of the Western U.S. geothermal fields (From UCB Seismographic Station).

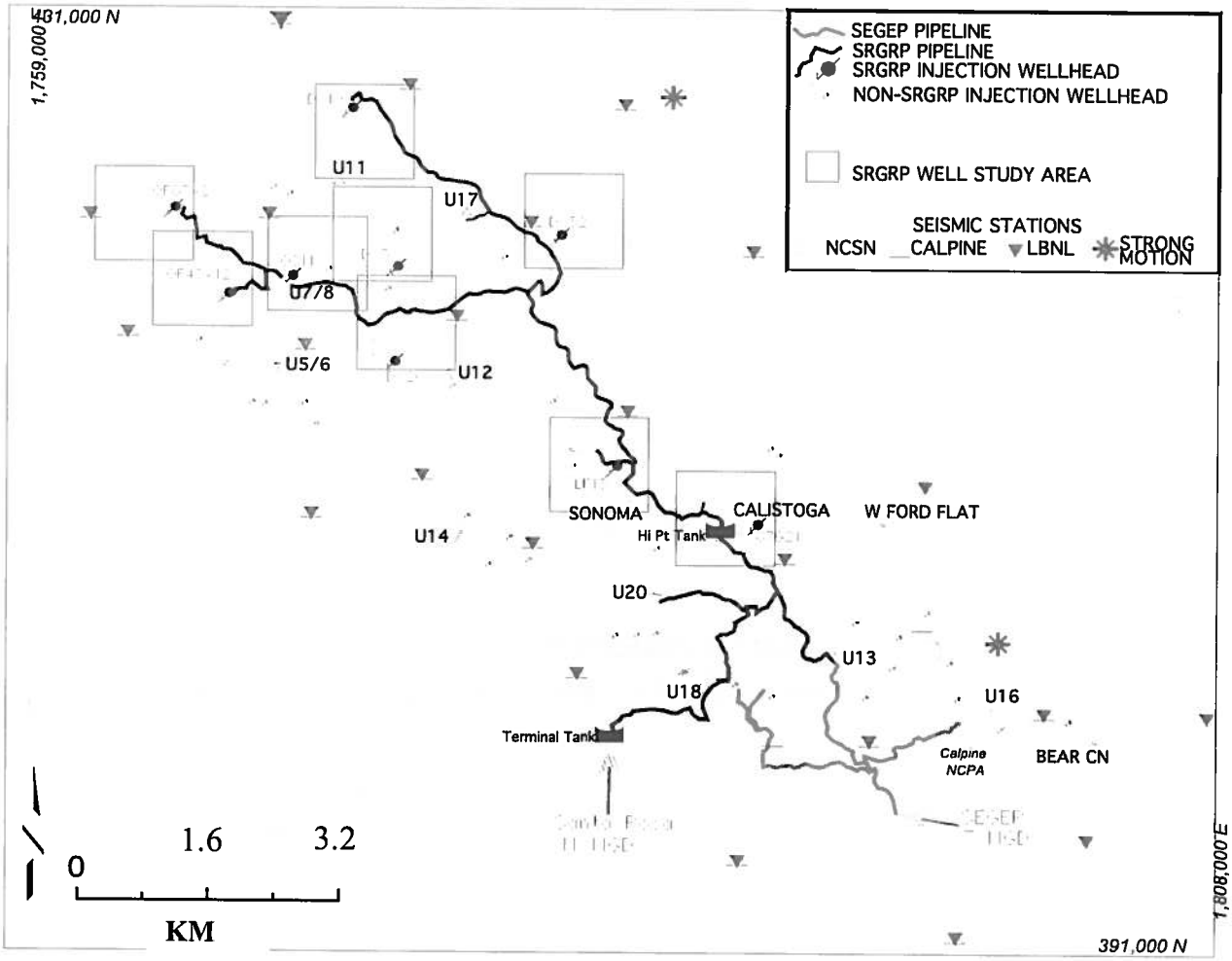


Figure 2. Location of USGS (NCSN) stations, current Calpine array (pen triangles), and the first phase of the new stations (solid inverted triangles). Also shown are the locations of the pipelines used for the water from Santa Rosa. And the pipeline installed prior to this study in 1997 to inject water into the southeast Geysers (SEGP) at a rate of 26 million liters/day (7 million gallons/day, from Stark 2003).

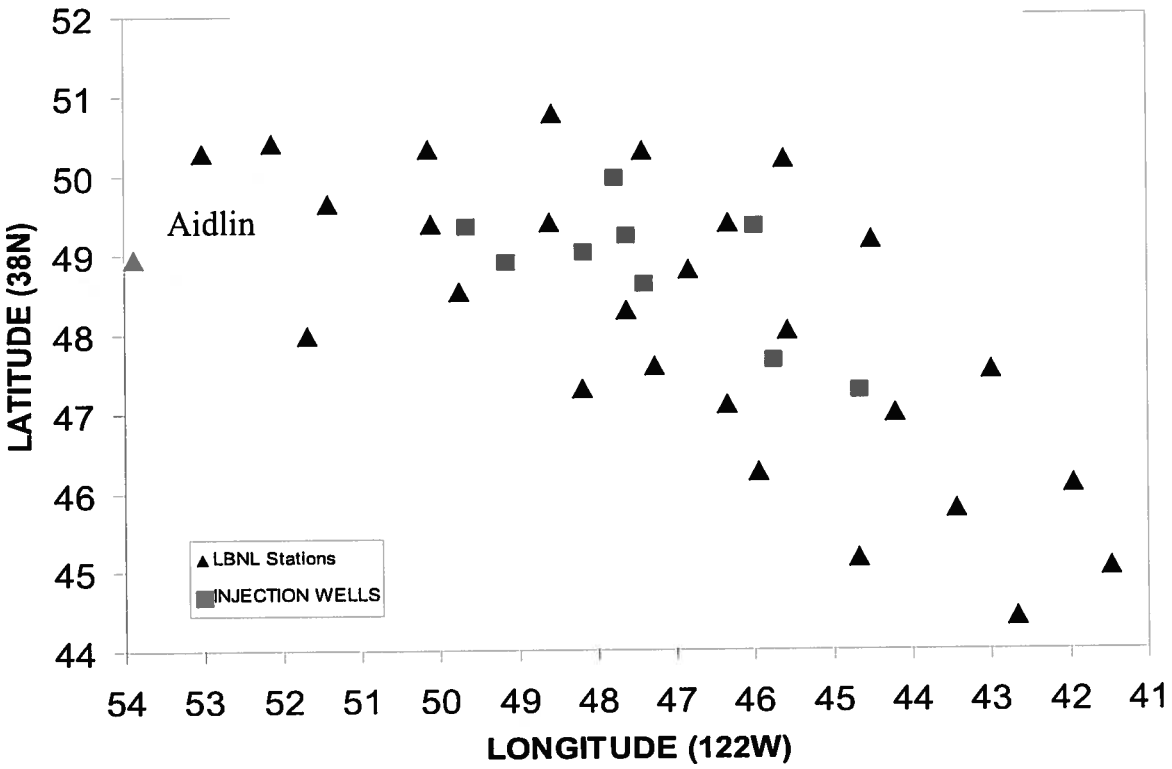


Figure 3. The entire current array including the Aidlin stations, the squares are the injection wells for the Santa Rosa water.

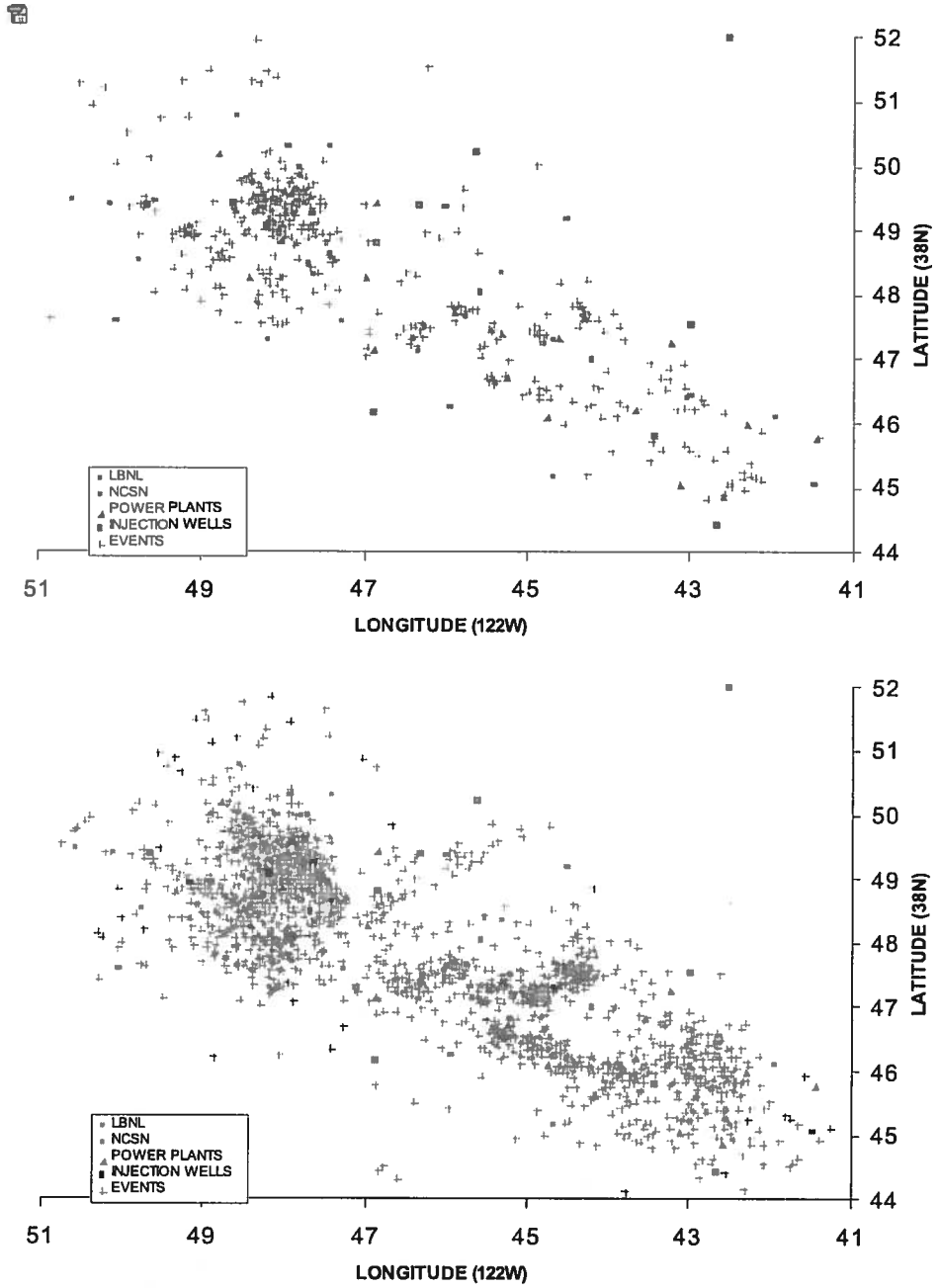
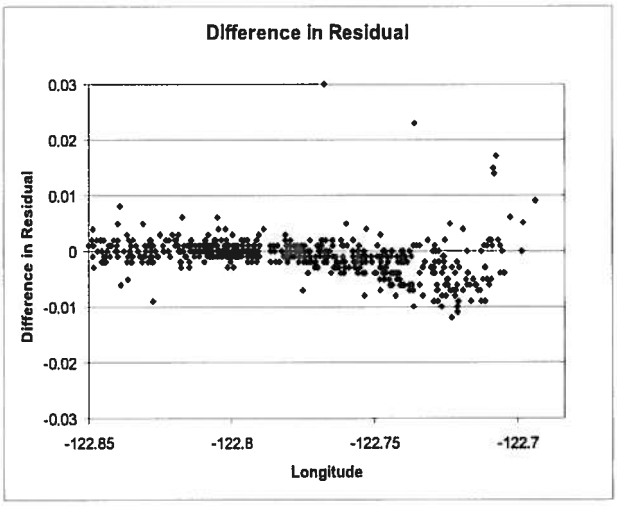
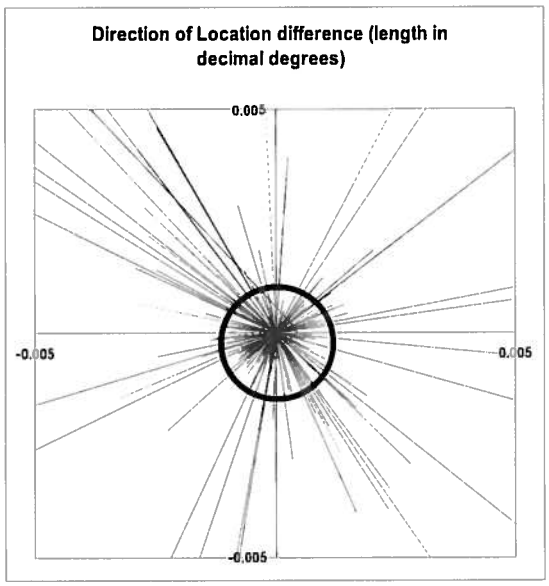


Figure 4. One month (April 2004) of data from the USGS array (top) and the LBNL array (bottom figure).





Velocity Model 1

Elevation (km)	Velocity (km/s)
-0.5	4.00
0.5	4.43
1.5	5.12
2.5	5.47
3.5	5.58
4.5	5.62
5.5	5.86

Velocity Model 2

Elevation (km)	Velocity (km/s)
-0.5	4.20
0.5	4.75
1.5	5.12
2.5	5.30
3.5	5.40
4.5	5.50
5.5	5.62

Figure 5. Change in residual and location found by using different velocity models. The average difference in location is 100 meters (radius of circle) with no preferential direction.

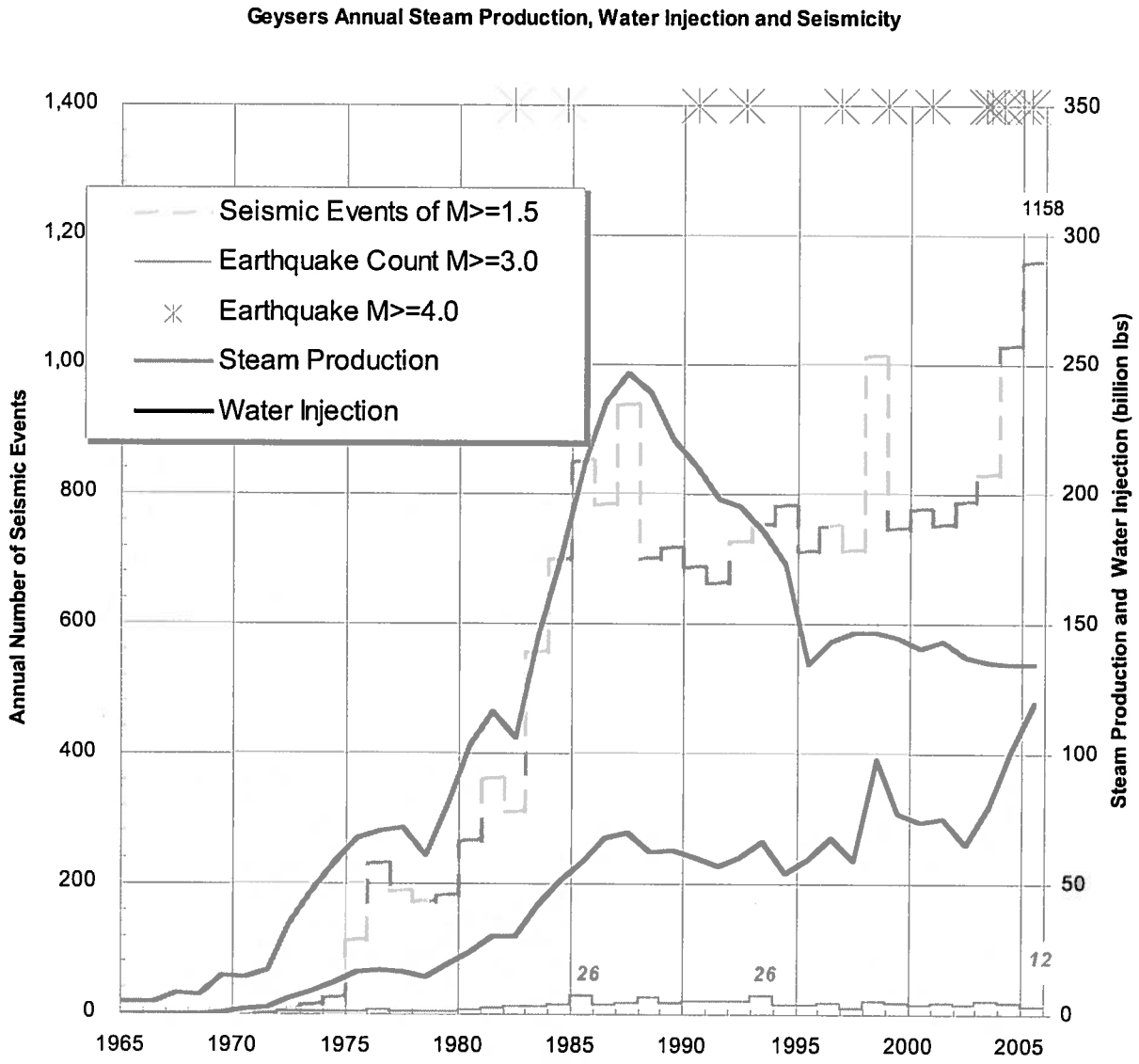


Figure 6. Historical seismicity at The Geysers from 1965 through October 2005 using all events above magnitude 1.2 from the USGS array (from M. Stark, Calpine Inc. and B. Smith, NCPA). The largest event recorded was a magnitude 4.6 in 1982. The injection and production is an average per year in billion gallons.

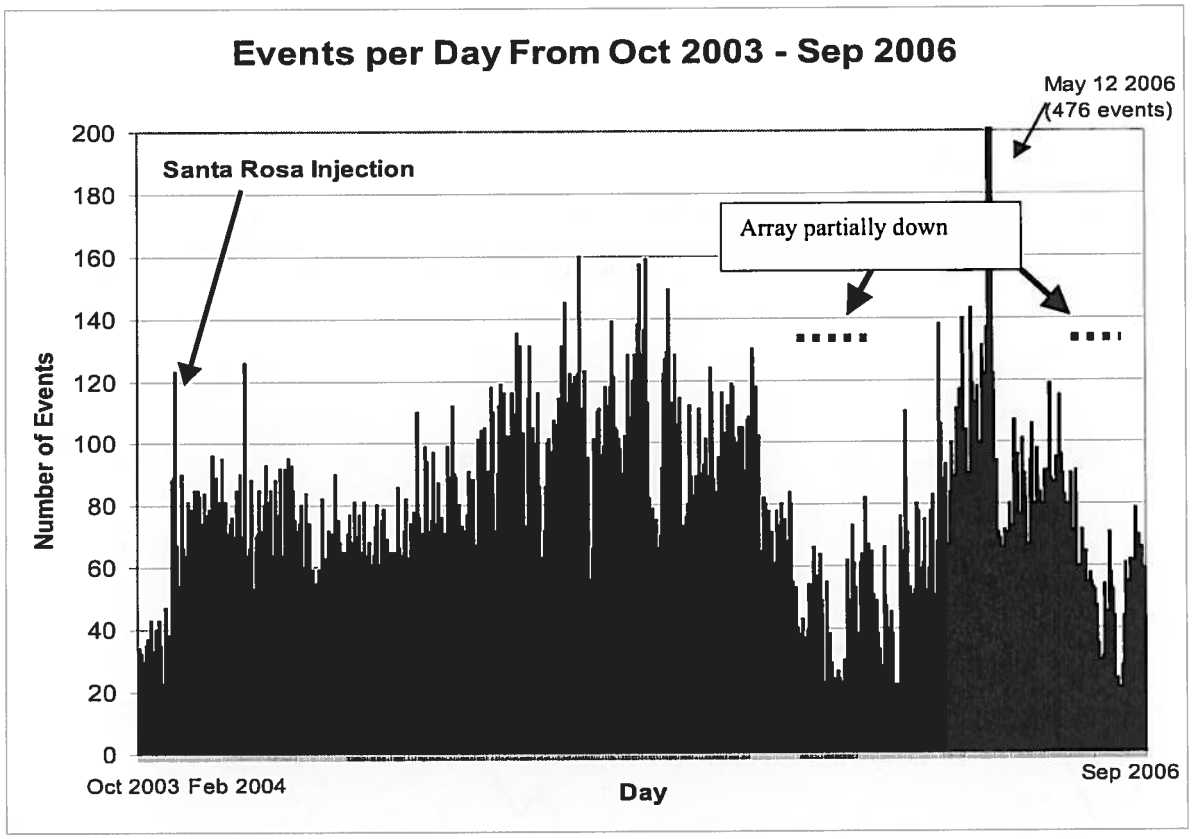


Figure 7. The rate of seismicity before and after the Santa Rosa injection as recorded by the LBNL array, the start of injection was December of 2003. The times marked with the array partially down was due to fires destroying parts of the array.

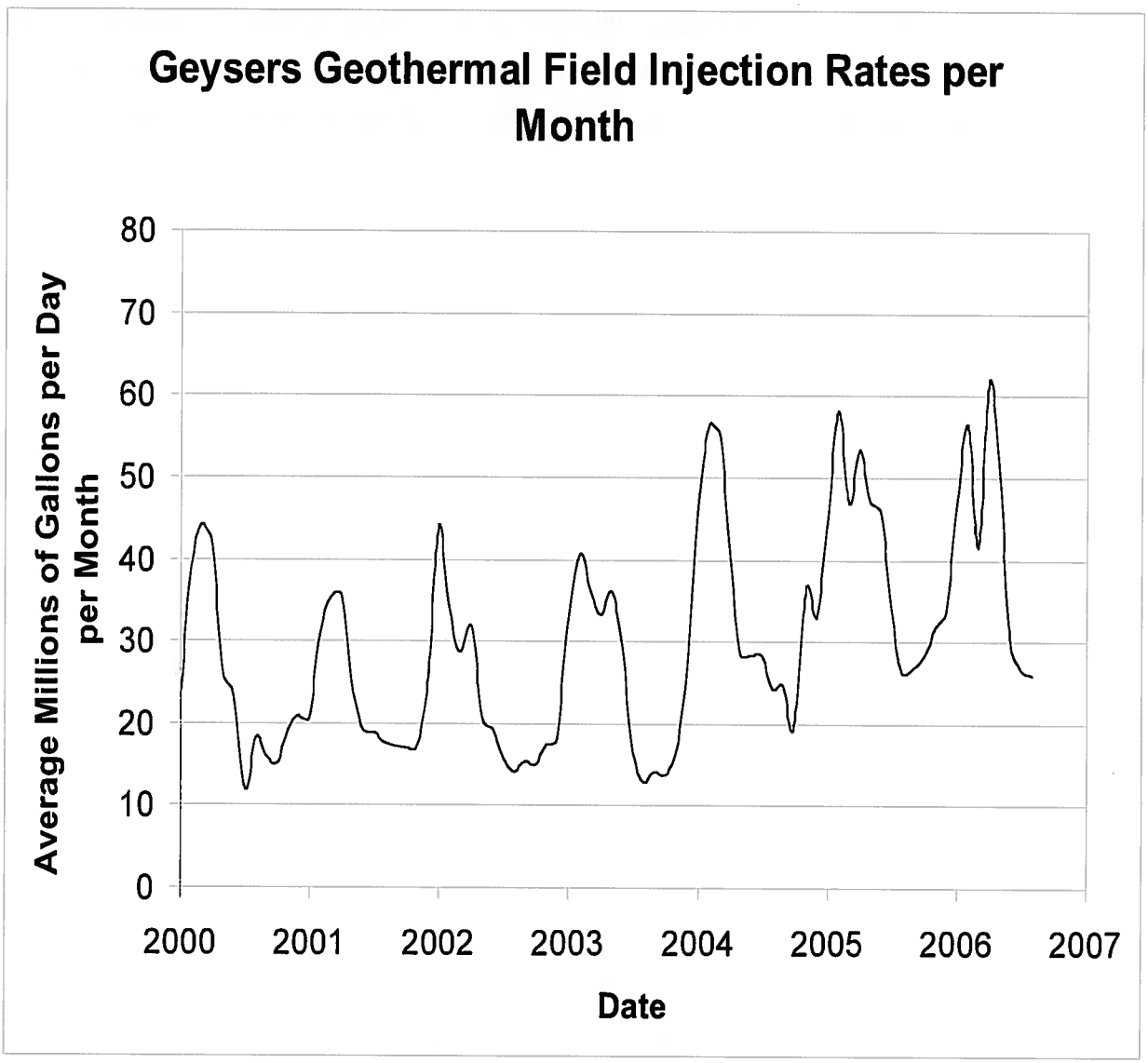


Figure 8. Total injections per day, averaged per month from 2000 through mid 2006 in millions of gallons for the entire Geysers field.

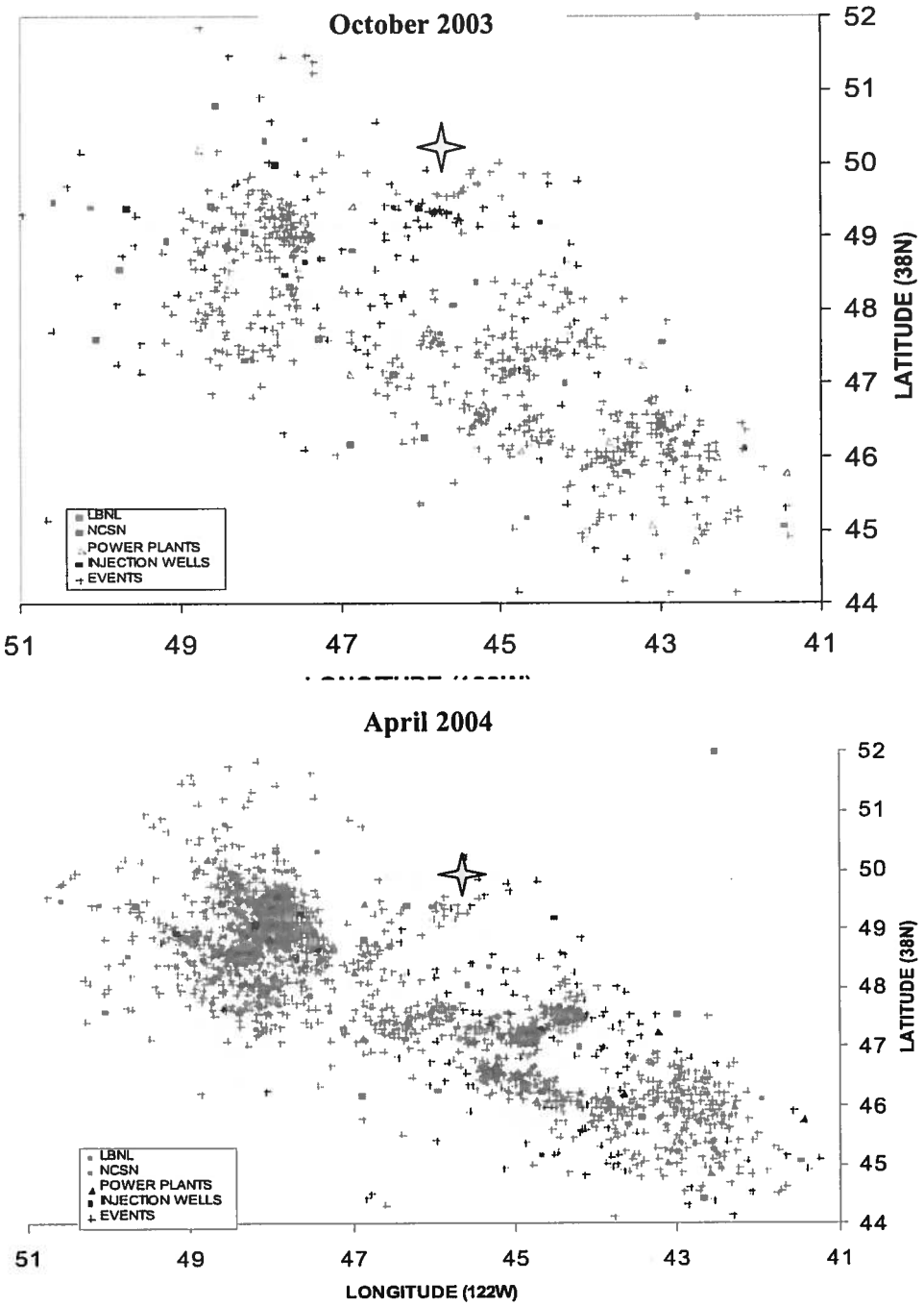


Figure 9. Top figure is one month of data recorded on the LBNL array before the Santa Rosa injection (October 2003) The bottom figure is one months of data (April 2004) after the Santa Rosa injection started. The star is the location of a February 2005 magnitude 4 event.

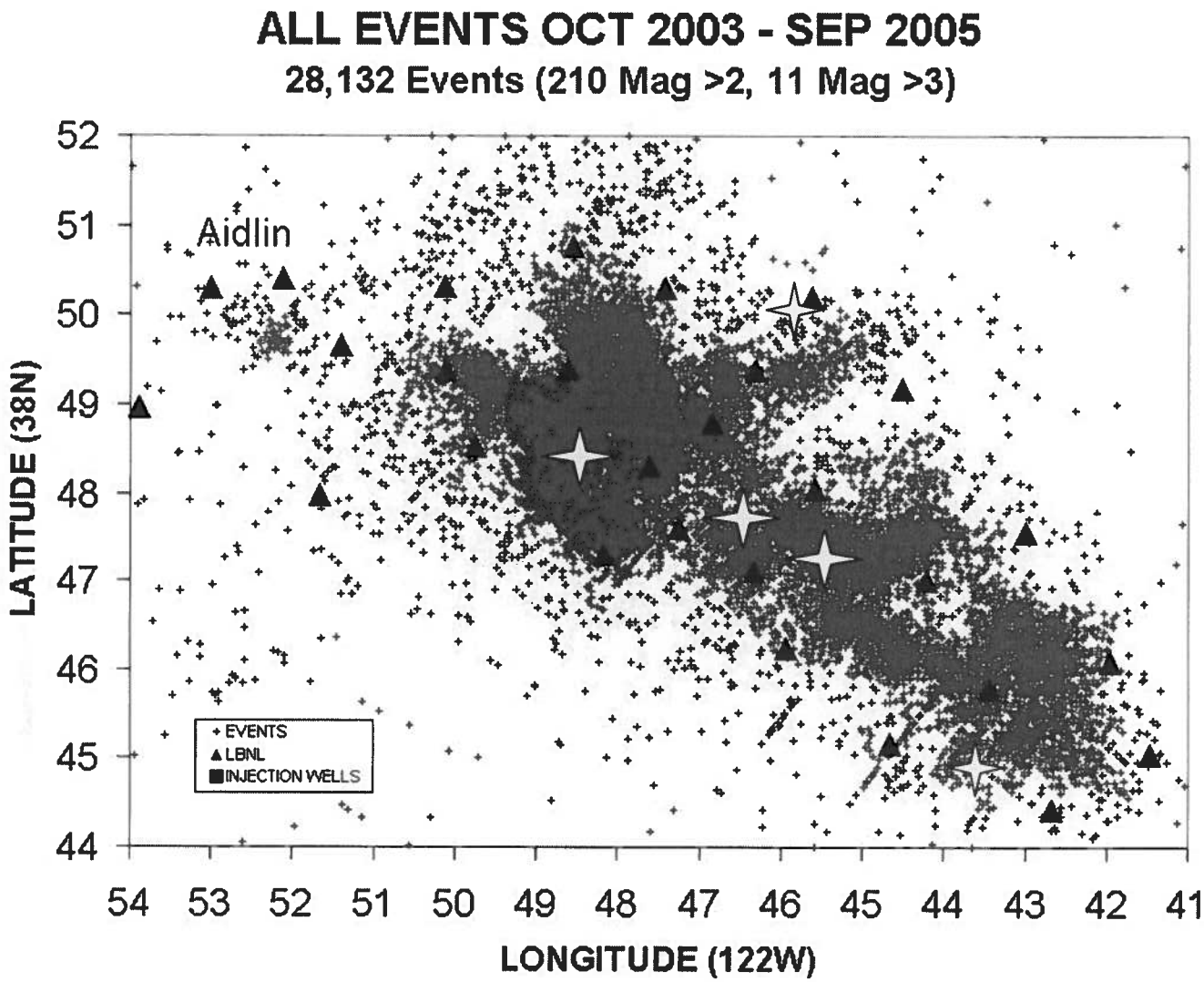


Figure 10. Locations of all events from October 2003 through October 2005, Geysers wide, note the relatively lack of events in the Aidlin area, this is prior to a large increase in injection in the Aidlin area, injection started in late 2005. The blue boxes are the injection wells for the Santa Rosa water injection. The large stars are magnitude 4 plus events (Feb. 2004, Dec. 2004, May 2005, Oct. 2005). The linear trends in the data are artifacts of the automatic location.

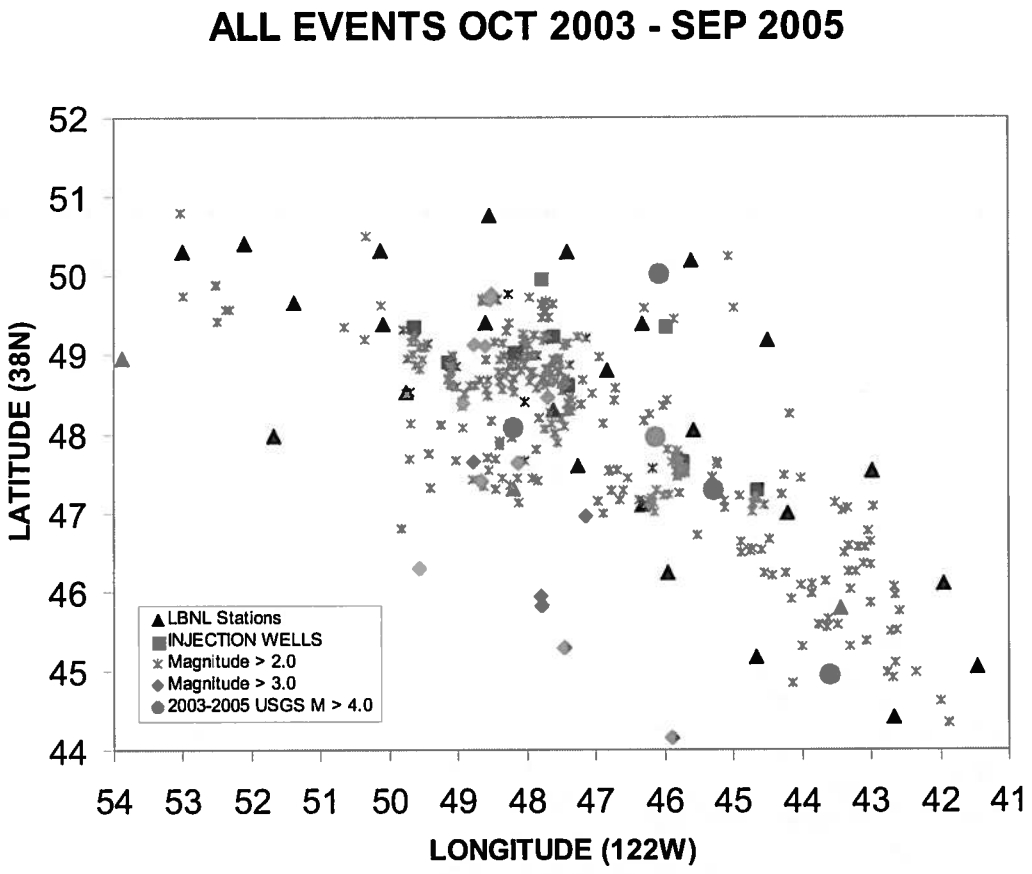


Figure 11. Location of magnitude 2, 3 and 4's from October 2003 through October 2005. The injection wells are only for the Santa Rosa water.

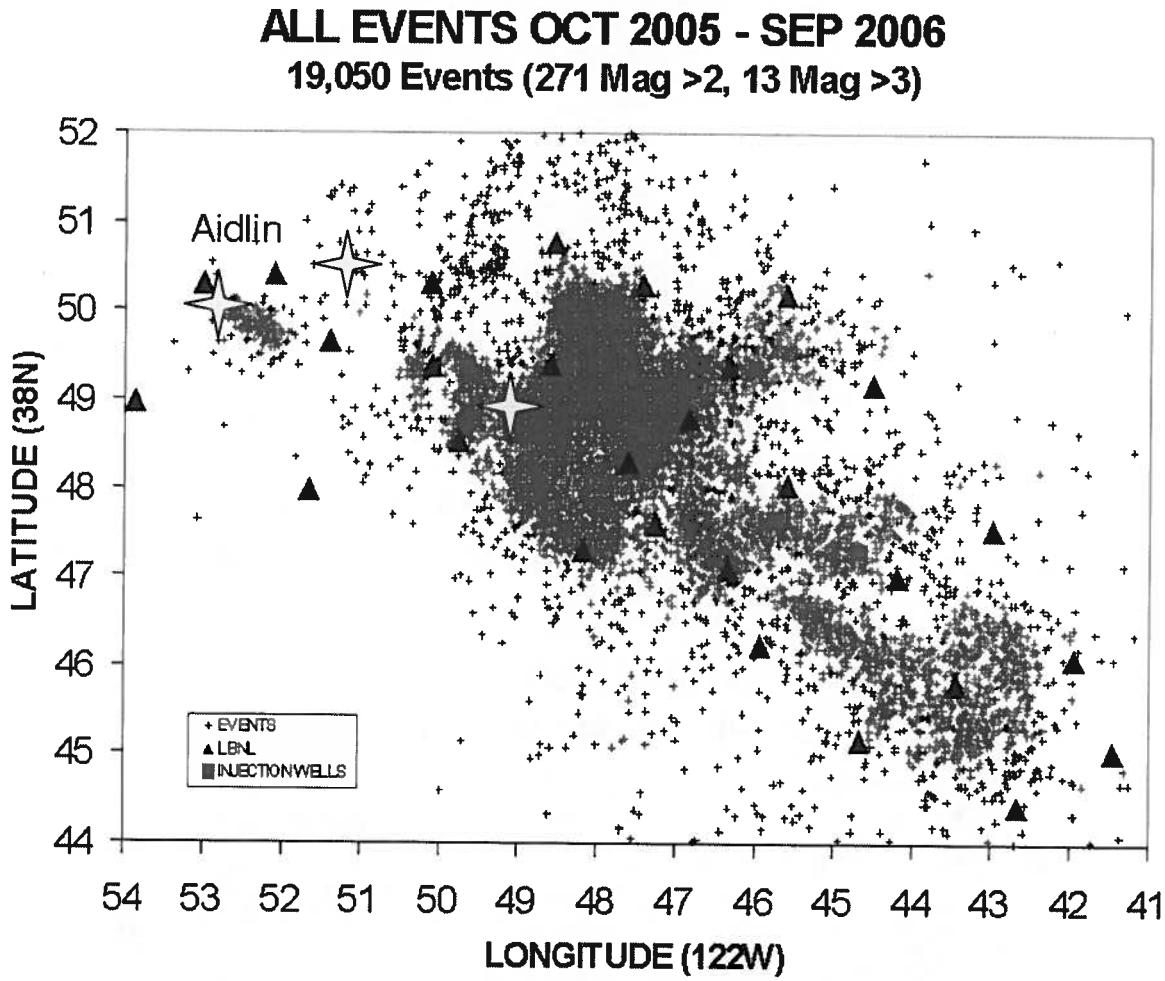


Figure 12. Locations of all events from October 2005 through August 2006, Geysers wide, note the increased clustering of events in the Aidlin area after injection has occurred. The blue boxes are the injection wells for the Santa Rosa water injection. The stars are magnitude 4 plus events (May 2006).

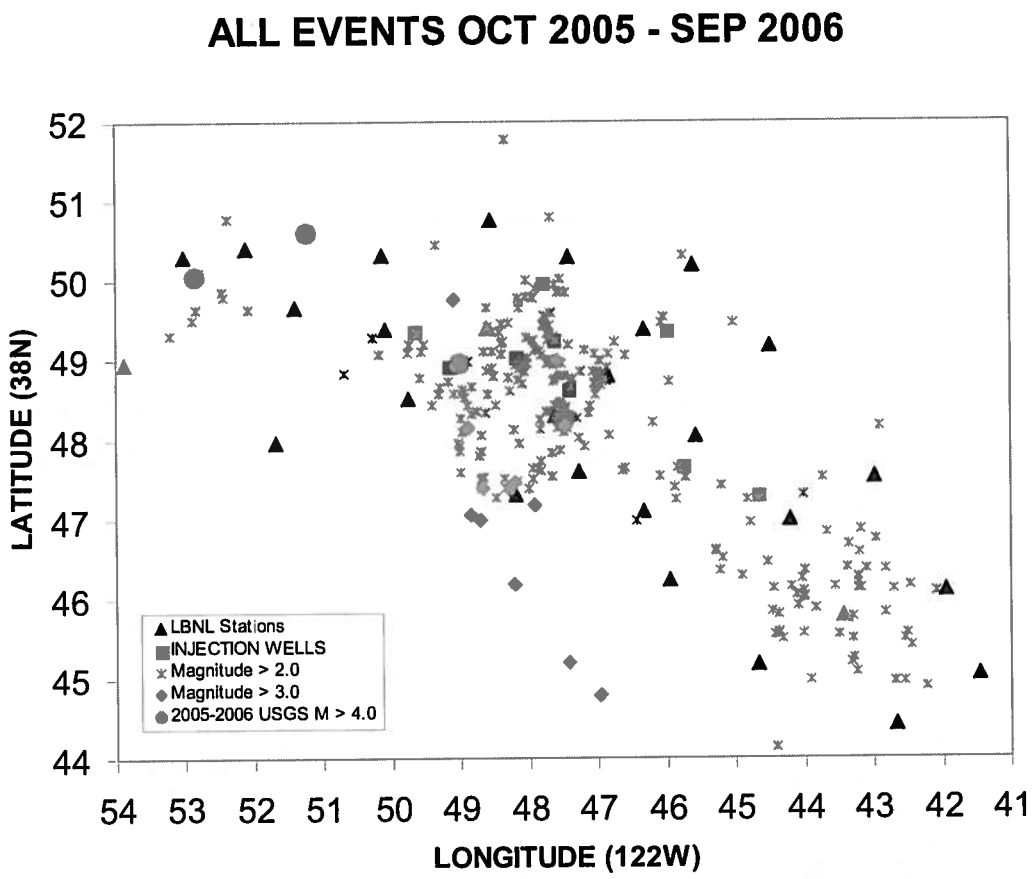


Figure 13. Location of magnitude 2, 3 and 4's from October 2003 through October 2005. The injection wells are only for the Santa Rosa water.

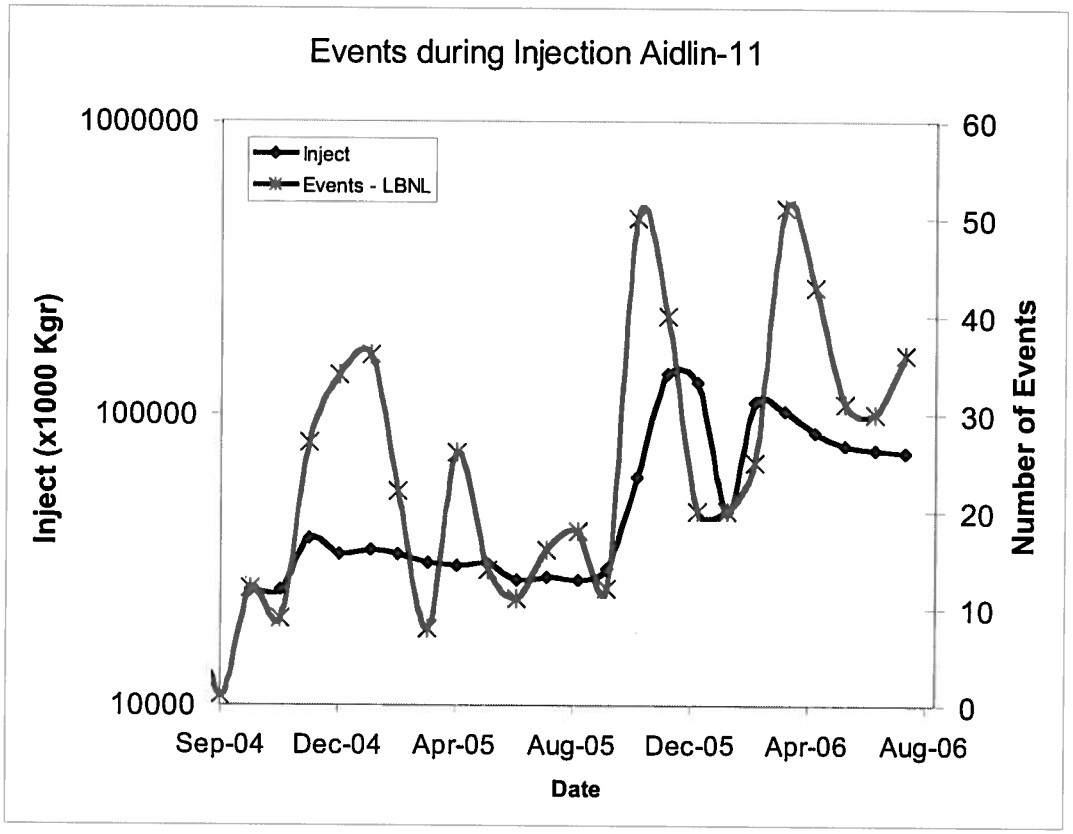


Figure 14. Injection history (total injection for each month) and seismicity (number of events per month) in the Aidlin area. Note that the injection volume is plotted on a log scale.

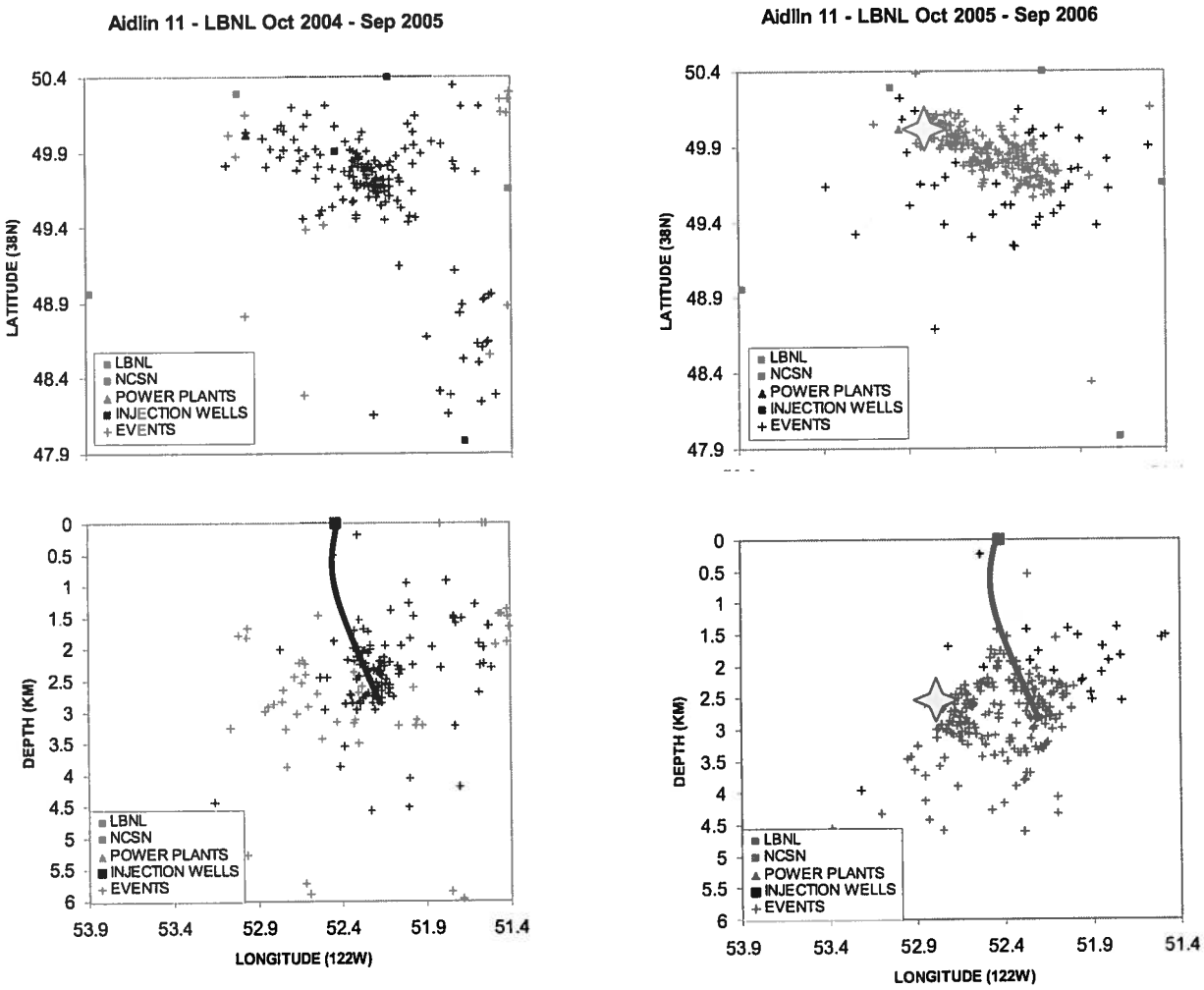


Figure 15. Location and depth of events in the Aidlin area of the Geysers. Also shown is the location of a magnitude 4 event in the vicinity that occurred in October of 2005.

EXHIBIT B

K. Shawn Smallwood, Ph.D.
3108 Finch Street
Davis, CA 95616

Collin Reinhardt, Project Manager
BLM, Bishop Field Office
351 Pacu Lane, Suite 100
Bishop, CA 93514

14 January 2013

RE: Casa Diablo IV Geothermal Development Project

Dear Mr. Reinhardt,

I would like to comment on the DEIR/DEIS prepared for the 33-MW Casa Diablo IV Geothermal Development Project (ESA 2012). My qualifications for preparing expert comments are the following. I earned a Ph.D. degree in Ecology from the University of California at Davis in 1990, where I subsequently worked for four years as a post-graduate researcher in the Department of Agronomy and Range Sciences. My research has been on animal density and distribution, habitat selection, habitat restoration, interactions between wildlife and human infrastructure and activities, conservation of rare and endangered species, and on the ecology of invading species. I have authored numerous papers on special-status species issues, including "Using the best scientific data for endangered species conservation," published in Environmental Management (Smallwood et al. 1999), and "Suggested standards for science applied to conservation issues" published in the Transactions of the Western Section of The Wildlife Society (Smallwood et al. 2001). I served as Chair of the Conservation Affairs Committee for The Wildlife Society – Western Section. I am a member of The Wildlife Society and the Raptor Research Foundation, and I've been a part-time lecturer at California State University, Sacramento. I was also Associate Editor of wildlife biology's premier scientific journal, The Journal of Wildlife Management, as well as of Biological Conservation, and I was on the Editorial Board of Environmental Management.

I have performed wildlife surveys in California for twenty-three years (Smallwood et al. 1996, Smallwood and Nakamoto 2009). Over these years, I studied the impacts of human activities and human infrastructure on birds and other animals, including on California mountain lions (Smallwood 1997), Swainson's hawks (Smallwood 1995), burrowing owls (Smallwood et al. 2007), and other species (Smallwood and Nakamoto 2009). I studied fossorial animals (i.e., animals that burrow into soil, where they live much of their lives), including pocket gophers, ground squirrels, kangaroo rats, voles, harvester ants, and many other functionally similar groups. I performed focused studies of how wildlife interact with agricultural fields and associated cultural practices, especially with alfalfa production. I have also performed wildlife surveys at many proposed project sites, including in the immediate area of the proposed project. My CV is attached.

I. INSUFFICIENCY OF DEIR/DEIS

A. The EIR/EIS Fails to Provide Adequate or Accurate Information on Special-Status Wildlife Species that may be Adversely Affected by the Project

Whereas I concur with the DEIR/DEIS's conclusion that northern goshawk is highly likely to occur on site (page 3.4-7), I disagree with most of the conclusions of occurrence potential of other special status species. For example, the bald eagle was given low potential to occur, because the DEIR/DEIS claimed that the project site does not offer foraging habitat. However, bald eagles forage in Crowley Lake, only 12 km away, and they likely forage in smaller water bodies within only 2-3 km from the project site. Bald eagles often roost in conifers nearby but not immediately adjacent to foraging areas, so it is not unreasonable to consider the project site as potentially useful to bald eagles. I14-81

I strongly disagree with the DEIR/DEIS that golden eagles are unlikely to occur at the project site (page 3.4-7). I have seen golden eagles foraging in areas similar to the conditions at the project site. I have witnessed golden eagle's hunting in conifer forests by beating their wings against tree branches while descending slopes, apparently as an attempt to flush potential prey items. There is nothing about the project site that would limit golden eagle occurrence. I14-82

The DEIR/DEIS attributed moderate potential for the occurrence of greater sage grouse, but I have been in greater sage grouse habitat many times, including at the project site. I do not see any reason why high occurrence potential should be attributed to greater sage grouse at the proposed project site. I14-83

Prairie falcons were concluded to have low potential due to lack of habitat at the project site. I have observed prairie falcons many times during my surveys, including in partially forested environments. The project site is a mix of forest and sage scrub, so a conclusion of low potential was not warranted. Prairie falcons have a moderate to high potential for occurrence at the project site. I14-84

In the absence of appropriate surveys, the DEIR/DEIS concluded that the occurrence potential was only moderate for two species of bats: Pallid bat and Townsend's big-eared bat. The DEIR/DEIS concluded that the occurrence potential was low for five species of bat: Silver-haired bat, Western red, Long-eared myotis, Long-legged myotis, and Yuma myotis. Little is known about the habitat use of these bats, because few studies have been performed. In the absence of appropriate surveys and scientific studies, the DEIR/DEIS was unjustified in concluding low or moderate occurrence potentials of these species. The prudent conclusion, and one that would be more consistent with the environmental protection objectives of CEQA, would be that all of these bat species likely use the project site. I14-85

The DEIR/DEIS concluded only a moderate potential for Sierra Nevada red fox to occur at the project site, but there is nothing about the site that would discourage Sierra Nevada red fox from occurring there. During my statewide surveys for mountain lions, I recorded fox tracks on one of my transects, which happens to have been immediately adjacent to the project site. I have surveyed that transect seven times since 1985. In 1992, I recorded fox tracks, although I cannot I14-86

be certain that these tracks were left by Sierra Nevada red fox (instead of gray fox). There is no reason why Sierra Nevada red fox would not occur at the project site, and my discovery of fox tracks in the area serves as potential evidence of their occurrence. I14-86 cont.

The DEIR/DEIS made no mention of American badger (*Taxidea taxus*), which is a California Species of Special Concern[1] (CSC). Nor did the DEIR/DEIS mention California mountain lion, which is a Specially Protected Species under state law. During my mountain lion surveys since 1985, I have detected tracks of both American badger and California mountain lion on my survey transect, only a mile or two from the proposed project site. I14-87

The proposed project site supports multiple special-status species of wildlife, some of which the DEIR/DEIS acknowledged, and some of which it dismissed without sound scientific reasoning. The DEIR/DEIS concluded that the following special-status species of wildlife have the potential to occur on the project site: northern goshawk, greater sage-grouse, pallid bat, Townsend's big-eared bat, western white-tailed jackrabbit, Sierra Nevada red fox, and Sierra marten. To this list, I add American badger, California mountain lion, Silver-haired bat, Western red, Long-eared myotis, Long-legged myotis, and Yuma myotis, golden eagle, bald eagle, and prairie falcon. The project's impacts would be significant to at least 17 special-status species. I14-88

B. Movement corridors and habitat fragmentation

The DEIR/DEIS did not discuss the project's contribution to habitat fragmentation, which is a process that has been recognized as the greatest threat to species' persistence in the wild (Wilcox and Murphy 1985). Habitat fragmentation results in the reduction of a net larger habitat area than can be measured by summing the remaining, apparent habitat patches (Wilcox and Murphy 1985, Saunders et al. 1991, Hall et al. 1997). The project, as proposed, would impose a sprawling barrier to wildlife movement due to the 6.5 acre power plant, an expanded well field totaling 45 acres, above-ground pipelines, 650 feet of new transmission totaling 0.75 acres of additional forest clearing, a new substation on 0.25 acres, 0.77 miles of new roadway, and 5.58 miles of road improvements. Furthermore, this sprawling addition of wildlife movement barriers is proposed to be oriented generally east-west across most of the low-lying portion of a natural movement corridor between the City of Mammoth Lakes and higher-elevation terrain to the east. The possible direct and cumulative impacts of this project as a movement barrier was not discussed in the DEIR/DEIS, leaving it inadequate as a CEQA review document. I14-89

II. CUMULATIVE IMPACTS

What remains of a naturally-occurring, north-south, wildlife movement corridor will be impeded by the proposed project. The DEIR/DEIS should have mapped the locations and extent of existing human infrastructure, as well as proposed and likely future clearing of habitat and imposition of additional human infrastructure. A map of existing and conceivable future projects would most effectively inform the readers of the DEIS/DEIR of the likely cumulative effects of the project on wildlife movement through the area. I14-90

[1] The California Department of Fish and Game continues to not list this species as CSC on its web site, but I have a copy of a letter from CDFG explaining that the listing omission was a mistake and that the American badger is indeed considered to be CSC.

III. MITIGATION

Project design Measure 1: The DEIR/DEIS states that a wildlife biologist will walk the length of the new pipeline to look for signs of impedance of wildlife movement caused by the pipeline. However, the DEIR/DEIS needed to clarify how the monitor would determine whether the pipeline is impeding wildlife movement. More details are also needed, including the time of year the biologist would survey the pipeline, and what steps could be taken to reduce the impact, should an impact be detected. I14-91

Project design Measure 2: Thresholds of success need to be established, and monitoring to measure effectiveness needs to be designed and implemented. A performance bond should be established, and it should be linked to the thresholds of success. I14-92

Project design measures 3 through 7: The DEIR/DEIS was vague about who will be responsible for implementing the proposed measures. Who will be responsible for monitoring their implementation and effectiveness? I14-93

WIL-2: Impacts could be minimized by removing accumulated water daily from lined well site basins, or by installing ramps. However, the DEIR/DEIS needs to include consequences for not taking these steps, and there needs to be mitigation monitoring to ensure that this measure is implemented. Again, a performance bond should be required, along with thresholds linked to these measures and consequences for not meeting the thresholds. I14-94

WIL-3: Whereas this measure would minimize impacts by retaining downed woody debris and snags to the degree feasible, it does nothing to offset project impacts. I14-95

WIL-4: Whereas it would be best to work with CDFG in designing and siting a new deer crossing, the DEIR/DEIS needs to identify an alternative plan in case the best-intended plan for a new deer crossing fails. Mule deer might not cooperate with the applicant's plan for a new deer crossing, or the crossing might be infeasible for reason(s) biologists do not understand. Again, a performance bond is needed for the project's impacts on mule deer movement patterns in the area, and monitoring linked to performance thresholds is needed. It needs to be explained what can and will be done should the new deer crossing fail. I14-96

WIL-5: Again, this measure looks reasonable as a logic exercise, but best laid plans do not always work out. A performance bond is needed, along with monitoring linked to thresholds of success, and along with alternative measures. I14-97

WIL-6: The DEIR/DEIS needs to be more explicit about what qualifies as a deer crossing or as a movement corridor. Is there a quantitative threshold of activity that can be added to the DEIR/DEIS? Leaving the definitions vague usually results in no action, in my experience. I14-98

WIL-7: Both pre- and post-construction surveys are needed for greater sage grouse, as well as for other special status species. These surveys are needed to detect project impacts, so that additional impact reduction measures can be taken, as well as compensatory mitigation. I14-99

The DEIR/DEIS proposed no compensatory mitigation of any kind. The project will reduce wildlife habitat, which should be mitigated. The project will also interfere with wildlife movement patterns, and this impact should also be mitigated through some form of compensation. I14-100

IV. MITIGATION MONITORING

It has long been known that mitigation pursuant to CEQA has often either failed or has not been implemented, but with no consequences to the take-permit holder (Silva 1990). There should be consequences for not achieving mitigation objectives or performance standards. The project proponents should be required to provide a performance bond in an amount that is sufficient for an independent party to achieve the mitigation objectives originally promised, and in this case, the promises should be much more substantial. A fund is needed to support named individuals or an organization to track the implementation of mitigation measures. Report deadlines should be listed, and who will be the recipients of the reports. In my professional opinion, the lack of specific mitigation monitoring details in the EIR/EIS renders it inadequate and uncertain, and makes it impossible to gauge whether or to what extent any mitigation measures will lessen potentially significant impacts on species, If these measures are not clearly laid out in the EIR/EIS, then there will be no basis to determine that impacts will be less than significant once implemented, and fail to provide enforceable performance measures by which the public and regulatory agencies can gauge their effectiveness. Furthermore, without adequate funding allocated in advance, there is no certainty that any proposed mitigation monitoring will actually take place. I14-101

Shawn Smallwood

Shawn Smallwood, Ph.D.

V. REFERENCES

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Kenneth Shawn Smallwood
Curriculum Vitae

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puma@dcn.org

Born May 3, 1963 in
Sacramento, California.
Married, father of two.

Ecologist

Expertise

- Finding solutions to controversial problems related to wildlife interactions with human industry, infrastructure, and activities; and,

- Using systems analysis and experimental design principles to identify meaningful ecological patterns that can inform conclusions and management decisions.

Education

Ph.D. Ecology, University of California, Davis. September 1990.
M.S. Ecology, University of California, Davis. June 1987.
B.S. Anthropology, University of California, Davis. June 1985.
Corcoran High School, Corcoran, California. June 1981.

Experience

- 337 professional publications, including:
- 61 peer reviewed publications
- 24 in non-reviewed proceedings
- 244 reports, declarations, and book reviews
- 8 in mass media outlets
- 75 public presentations of research results at meetings
- Reviewed many professional papers and reports
- Testified in 4 court cases.

Associate Editor, *Journal of Wildlife Management*, March 2004 to 30 June 2007.

Editorial Board Member, *Environmental Management*, 10/1999 to 8/2004.

Associate Editor, *Biological Conservation*, 9/1994 to 9/1995. Administered independent scientific reviews of submitted, professional papers in ecology and conservation biology, and made recommendations to the Editors.

Member, Alameda County Scientific Review Committee (SRC), 8/06 to 4/11. As part of a five member committee, I investigated the causes of bird and bat collisions in the Altamont Pass Wind Resource Area, and I recommended mitigation and monitoring measures. The SRC reviews the science underlying the Alameda county Avian Protection Program, and advises the County on how to reduce wildlife fatalities.

Research Ecologist, 2/06 to 12/07, under contract to East Bay Regional Parks District. Performed research of how fossorial mammals and raptors responded to grazing treatments and wind turbines at Vasco Caves Regional Preserve. I designed the study, trained the fatality monitors and behavior observers, mapped the burrows of fossorial mammals, analyzed the data, and took the lead on writing the report.

Consulting Ecologist, 7/04 to 12/07, California Energy Commission (CEC). In collaboration with Lawrence-Livermore National Lab, I performed independent research funded by the CEC on bird behavior in the Altamont Pass Wind Resources Area. I also provided consulting services as needed to the CEC. I produced several reports to the CEC and the CEC's Public Interest Energy Research program.

Consulting Ecologist, 11/99 to present, U.S. Navy. I provide endangered species surveys at multiple Navy facilities, hazardous waste site monitoring, and habitat restoration for the endangered Fresno kangaroo rat, California tiger salamander, California red-legged frog, California clapper rail, western burrowing owl, and other species. I have worked at Naval Air Station Lemoore; Naval Weapons Station, Seal Beach, Detachment Concord; Naval Security Group Activity, Skaggs Island; National Radio Transmitter Facility, Dixon.

Part-time Lecturer, 1/98 to 2005, California State University, Sacramento. I taught Contemporary Environmental Issues, Natural Resources Conservation (twice), Mammalogy, Behavioral Ecology, and Ornithology Lab.

Senior Ecologist, 1999 to 2005, BioResource Consultants. I planned and carried out research and monitoring projects, and analyzed complex data related to avian fatalities at wind turbines, avian electrocutions on electric distribution poles across California, and avian fatalities at transmission lines.

Systems Ecologist, 7/96 to present, Consulting in the Public Interest, www.cipi.com. I am part of a multi-disciplinary consortium of scientists facilitating large-scale, environmental planning projects and litigation. We provide risk assessments, assessments of management practices, and expert witness testimony.

Chairman, Conservation Affairs Committee, The Wildlife Society--Western Section, 1999-2001. I prepared position statements and led efforts directed toward conservation issues, including travel to Washington, D.C. to lobby Congress for more wildlife conservation funding.

Systems Ecologist, 1/95 until about 2000, Institute for Sustainable Development. I headed ISD's program on integrated resources management. I developed indicators of ecological integrity for large areas, using remotely sensed data, local community involvement and GIS.

Associate, 1997-1998, Department of Agronomy and Range Science, University of California, Davis. I worked with Shu Geng and Mingua Zhang on several projects related to wildlife interactions with agriculture and patterns of fertilizer and pesticide residues in groundwater across a large landscape.

Lead Scientist, 6/96 to 6/99, National Endangered Species Network. I headed NESN's efforts to inform academic scientists and environmental activists about emerging issues regarding the Endangered Species Act and other environmental laws pertaining to special status species. I also testified at public hearings on behalf of environmental groups and endangered species.

Ecologist, 1/97 to 6/98, Western Foundation of Vertebrate Zoology. I conducted field research to determine the impact of past mercury mining on the status of California red-legged frogs in Santa Clara County, California.

Senior Systems Ecologist, 7/94 to 12/95, EIP Associates, Sacramento, California. Provided consulting services in environmental planning. I also developed a quantitative assessment of land units for their conservation and restoration opportunities, using the ecological resource requirements of 29 special status species. I mapped vegetation and land use, and derived new spatial data from a GIS overlay of these variables with soil types, flood zones, roads, and other spatially referenced data. Using these derived data, I developed a set of indicators for prioritizing areas within Yolo County that will receive mitigation funds for habitat easements and restoration.

Post-Graduate Researcher, 10/90 to 6/94, with Dr. Shu Geng, Department of Agronomy and Range Science, *U.C. Davis*. Studied landscape and management effects on temporal and spatial patterns of abundance among pocket gophers and species of Falconiformes and Carnivora in the Sacramento Valley. I also developed and analyzed a data base of energy use in California agriculture, and I assisted with a landscape (GIS) study of groundwater contamination across Tulare County, California.

Co-teacher, 1/91 to 6/91 and 1/93 to 6/93, Graduate Group in Ecology, U.C. Davis. Co-taught conservation biology with Dr. Christine Schonewald.

Reader, 3/90 to 6/90, Department of Psychology, U.C. Davis. Assisted students of Psychobiology (taught by Dr. Richard Coss) with research and writing term papers.

Research Assistant, 11/88 to 9/90, with Dr. Walter E. Howard, Department of Wildlife and Fisheries Biology, U.C. Davis. Tested durable baits for pocket gopher control in forest plantations, and developed gopher sampling methods.

Fulbright Research Fellow, Indonesia, 7/88 to 11/88. Tested use of new sampling methods for monitoring the number of Sumatran tigers and six other species of endemic felids, and evaluated methods used by other researchers.

Research Assistant, 7/87 to 6/88, with Dr. Terrell P. Salmon, Wildlife Extension, Department of Wildlife and Fisheries Biology, U.C. Davis. Developed empirical models of mammal and bird invasions in North America, and a rating system for priority research and control of exotic species based on economic, environmental, and human health hazards in California.

Student Assistant, 3/85 to 6/87, with Dr. E. Lee Fitzhugh, Wildlife Extension, Department of Wildlife and Fisheries Biology, U.C. Davis. Developed and implemented a statewide mountain lion track count for long-term monitoring of numbers and distribution. I've continued the

statewide track count since 1985 (the last count was in 2008). I also developed quantitative methods to identify individual mountain lions by their tracks, and to differentiate mountain lion and dog tracks.

Projects

Research to reduce avian mortality due to wind turbines at Altamont Pass. I used GPS and GIS to map and study environmental impacts of 5,400 wind turbines. I related the number of raptor fatalities at wind turbines to the degree of aggregation of prey species around the turbines, as well as many other factors related to where the turbines are located, how they are designed and operated, and how raptors behave in the Altamont Pass Wind Resource Area. I also serve on the Alameda County Scientific Review Committee, charged with recommending scientific monitoring methods and mitigation measures for reducing avian mortality.

Research to reduce avian mortality on electric distribution poles. Since about 2000 I have performed research directed toward reducing bird electrocutions on electric distribution poles. I led fatality monitoring efforts at 10,000 poles multiple times in California, spanning Orange County to Glenn County, and I have produced two large reports.

Cook *et al.* v. Rockwell International *et al.*, No. 90-K-181 (D. Colorado). I provided expert testimony on the role of burrowing animals in affecting the fate of buried and surface-deposited radioactive and hazardous chemical wastes at the Rocky Flats Plant, Colorado. I provided expert reports based on four site visits and the most extensive document review of burrowing animals ever conducted. I conducted transect surveys for evidence of burrowing animals and other wildlife on and around waste facilities. I also discovered substantial intrusion of waste structures by burrowing animals. I testified in federal court in November 2005, and my clients were subsequently awarded a $553,000,000 judgment by a jury.

Hanford Nuclear Reservation Litigation. I am providing expert testimony on the role of burrowing animals in affecting the fate of buried radioactive wastes at the Hanford Nuclear Reservation, Washington. I provided three expert reports based on three site visits and extensive document review. I predicted and verified a certain population density of pocket gophers on buried waste structures, as well as incidence of radionuclide contamination in body tissue. I conducted transect surveys for evidence of burrowing animals and other wildlife on and around waste facilities. I also discovered substantial intrusion of waste structures by burrowing animals.

Expert Testimony and Declarations on Residential and Commercial Development Proposals. I have testified before the California Coastal Commission, California Energy Commission, County Boards of Supervisors, and City Councils, and I have participated with press conferences and have been deposed by attorneys. I prepared expert witness reports and court declarations, which are summarized under Reports (below).

Expert Testimony on Proposed Gas-fired Power Plants. I provided comments letters, declarations, expert reports, and oral testimony on the impacts and appropriate mitigation of about eight natural gas-fired power plants in California.

Expert Testimony on Proposed Wind Farms. I provided comment letters and oral testimony to

administrative law courts in Klickitat and Skamania Counties, Washington, which convinced the court in Skamania County to require the replacement of a negative declaration with an EIS. I provided written testimony and deposition in support of litigation brought against the development of wind turbines in Cook County, Texas, which resulted in a settlement. I also provided written comments on the first EIR for the Buena Vista Wind Energy Project in Contra County, California, prompting the withdrawal of that EIR and the preparation of an improved EIR which was later certified.

Protocol-level endangered species searches and recovery efforts. I search for special-status species using Department of Fish and Game and US Fish and Wildlife Service protocols. I have searched for, or otherwise worked with, California red-legged frog, arroyo southwestern toad, California tiger salamander, blunt-nosed leopard lizard, western pond turtle, giant kangaroo rat, Fresno kangaroo rat, San Joaquin kit fox, Sumatran tiger, willow flycatcher, least Bell's vireo, western burrowing owl, Swainson's hawk, Valley elderberry longhorn beetle and many other special-status species. I also help with recovery of the Fresno kangaroo rat at Lemoore Naval Air Station.

Conservation of the endangered Fresno kangaroo rat. I am performing applied research to identify the factors responsible for the decline of this endangered species at Lemoore Naval Air Station, and am implementing habitat enhancements designed to reverse the trend and to expand the area occupied by this species.

Impact of West Nile Virus on yellow-billed magpies. Since 2005 I have worked under contract to the Sacramento-Yolo Mosquito and Vector Control District to gather post-West Nile Virus epidemic data to pre-epidemic data I had gathered on multiple bird species in the Sacramento Valley in the 1990s, but particularly on yellow-billed magpie and American crow, which are particularly susceptible to WNV.

Workshops on HCPs. Assisted Dr. Michael Morrison with organizing and conducting a 2-day workshop on Habitat Conservation Plans, sponsored by Southern California Edison, and another 1-day workshop sponsored by PG&E. These Workshops were attended by academics, attorneys, and consultants with HCP experience. We guest-edited a Proceedings published in Environmental Management.

Mapping of biological resources along Highways 101, 46 and 41. I used GPS and GIS to delineate vegetation complexes and locations of special-status species along 26 miles of highway in San Luis Obispo County, 14 miles of highway and roadway in Monterey County, and in a large area north of Fresno, including within reclaimed gravel mining pits.

GPS mapping and monitoring at restoration sites and at Caltrans mitigation sites. I am monitoring the success of elderberry shrubs at one location, the success of willows at another location, and the response of wildlife to the succession of vegetation at both these sits. I am also using GPS to monitor the response of fossorial animals to yellow star-thistle eradication and natural grassland restoration efforts at Bear Valley, Colusa County, and at the decommissioned Mather Air Force Base in Sacramento County.

Mercury effects on Red-legged Frog. I assisted Dr. Michael Morrison and US Fish and Wildlife

Service in assessing the possible impacts of historical mercury mining on the federally listed California red-legged frog in Santa Clara County. I also measured habitat variables in numerous streams.

Opposition to proposed No Surprises rule. I wrote a white paper and summary letter explaining scientific grounds for opposing the incidental take permit (ITP) rules providing ITP applicants and holders with general assurances they will be free of compliance with the Endangered Species Act once they adhere to the terms of a "properly functioning HCP." I obtained 188 signatures of scientists and environmental professionals on the letter submitted to the US Fish and Wildlife Service and the National Marine Fisheries Service. The letter was also provided to all US Senators. It helped change the prevailing view of HCPs as beneficial to listed species.

Natomas Basin Habitat Conservation Plan alternative. I designed narrow channel marsh to increase the likelihood of survival and recovery in the wild of giant garter snake, Swainson's hawk and Valley Elderberry Longhorn Beetle. The design included replication and interspersion of treatments for experimental testing of critical habitat elements. I provided a report to Northern Territories, Inc.

Assessment of Environmental Technology Transfer to China, and Assessment of Agricultural Production System. I twice traveled to China and interviewed scientists, industrialists, agriculturalists, and the Directors of the Chinese Environmental Protection Agency and the Department of Agriculture to assess the need and possible pathways for environmental clean-up technologies and trade opportunities between the US and China. I spent a total of five weeks in China, including in Shandong and Linxion Provinces and in Beijing.

Yolo County Habitat Conservation Plan. I conducted the landscape ecology study of Yolo County to identify the priority land units to receive mitigation so as to most improve the ecosystem functionality within the County from the perspective of 29 special-status species of wildlife and plants. I used a hierarchically structured indicators approach to apply principles of landscape and ecosystem ecology, conservation biology, and local values in rating land units. I derived GIS maps to help guide the conservation area design, and then I developed implementation strategies.

Mountain Lion Track Count. I developed and conducted the carnivore monitoring program throughout California since 1985. Species counted include mountain lion, bobcat, black bear, coyote, red and gray fox, raccoon, striped skunk, badger, and black-tailed deer. Vegetation and land use are also monitored. The transect was established on dusty, dirt roads within randomly selected quadrats. These roads are searched for tracks of the carnivores, which routinely use the roads for travel paths.

Sumatran Tiger and other Felids. I designed and conducted track counts for seven species of wild cats in Sumatra, including the Sumatran tiger, fishing cat, and golden cat. I spent four months on Sumatra and Java, and learned Bahasa Indonesia (the official Indonesian language). I was awarded a Fulbright Research Fellowship to complete the project.

Wildlife in Agriculture. Beginning as my post-graduate research, I have studied pocket gophers and other wildlife in 40 alfalfa fields throughout the Sacramento Valley, and I surveyed for wildlife

along a 200 mile road transect for six years. The data were analyzed using GIS and methods from landscape ecology, and the results were published and presented orally to farming groups in California and elsewhere. I also conducted the first study of wildlife in cover crops used on vineyards and orchards.

Agricultural Energy Use and Tulare County Groundwater Study. I developed and analyzed a data base of energy use in California agriculture, and collaborated on a landscape (GIS) study of groundwater contamination across Tulare County, California.

Pocket Gopher Damage in Forest Clearcuts. I tested various poison baits and baiting regimes for pocket gopher control in forest plantations, and I developed gopher sampling methods. I conducted the most extensive field study of pocket gophers ever, involving thousands of gophers in 68 research plots on 55 clearcuts among 6 National Forests in northern California.

Risk Assessment of Exotic Species in North America. I developed empirical models of mammal and bird species invasions in North America, as well as a rating system for assigning priority research and control to exotic species in California, based on economic, environmental, and human health hazards.

Representative Clients

Law offices and environmental groups	Government agencies
Law Offices of Stephan C. Volker	
Law Offices of Berger & Montague	US Department of Agriculture
Law Offices of Roy Haber	US Forest Service
Law Offices of Edward MacDonald	US Fish & Wildlife Service
Law Office of John Gabrielli	US Navy
Law Office of Bill Kopper	California Energy Commission
Law Office of Donald B. Mooney	California Office of the Attorney General
Law Office of Veneruso & Moncharsh	California Department of Fish & Game
Law Office of Steven Thompson	California Department of Transportation
California Wildlife Federation	California Department of Forestry
Defenders of Wildlife	California Department of Food & Agriculture
Sierra Club	Ventura County Counsel
National Endangered Species Network	County of Yolo
Spirit of the Sage Council	Tahoe Regional Planning Agency
The Humane Society	Sustainable Agriculture Research & Education Program
Hagens Berman LLP	Sacramento-Yolo Mosquito and Vector Control District
Environmental Protection Information Center (EPIC)	East Bay Regional Park District
Goldberg, Kamin & Garvin, Attorneys at Law	County of Alameda
Californians for Renewable Energy (CARE)	
Seatuck Environmental Association	
Friends of the Columbia Gorge, Inc.	**Other organizations and Individuals**
Save Our Scenic Area	Don & LaNelle Silverstien
Alliance to Protect Nantucket Sound	Seventh Day Adventist Church
Friends of the Swainson's Hawk	Escuela de la Raza Unida
Alameda Creek Alliance	Susan Pelican and Howard Beeman
Center for Biological Diversity	Residents Against Inconsistent Development, Inc.
Businesses	Bob Sarvey
FloDesign Wind Turbine	Mike Boyd
NEXTera Energy Resources, LLC	Hillcroft Neighborhood Fund
Pacific Gas & Electric Co.	Joint Labor Management Committee, Retail Food Industry
Southern California Edison Co.	Lisa Rocca
Georgia-Pacific Timber Co.	Kevin Jackson
Northern Territories Inc.	Dawn Stover and Jay Letto
National Renewable Energy Lab	Nancy Havassy
David Magney Environmental Consulting	Catherine Portman (for Brenda Cedarblade)
Wildlife History Foundation	
Emerald Farms	
Terry Preston, Wildlife Ecology Research Center	
G3 Energy and enXco	
Comstocks Business (magazine)	
Californians for Renewable Energy	
BioResource Consultants	

Representative special-status species experience

Common name	Species name	Status[1]	Description
Field experience			
California red-legged frog	*Rana aurora draytonii*	FT, CSC	Protocol searches & detected at multiple sites
Foothill yellow-legged frog	*Rana boylii*	FSC, CSC	Research and search detections at multiple sites
Western spadefoot	*Spea hammondii*	FSC, CSC	Searches and search detections
California tiger salamander	*Ambystoma californiense*	FC, CSC	Protocol searches & detections at multiple sites
Coast range newt	*Taricha torosa torosa*	CSC	Searches and multiple detections
Blunt-nosed leopard lizard	*Gambelia sila*	FE, CE	Detected in San Luis Obispo County
California Horned Lizard	*Phrynosoma coronatum frontale*	FSC, CSC	Search and detected in San Luis Obispo Co.
Western pond turtle	*Clemmys marmorata*	FSC, CSC	Searches and detected at multiple sites
San Joaquin kit fox	*Vulpes macrotis mutica*	FE, CT	Protocol searches and detections
Sumatran tiger	*Panthera tigris*		Research in Sumatra
Mountain lion	*Puma concolor californicus*	CFP	Research and publications
Point Arena mountain beaver	*Aplodontia rufa nigra*	FE, CSC	Remote camera operation
Giant kangaroo rat	*Dipodomys ingens*	FE, CE	Detected in Cholame Valley
Fresno kangaroo rat	*Dipodomys nitratoides*	FE, CE	Research and conservation at Lemoore Naval Air Station – reports
Monterey dusky-footed woodrat	*Neotoma fuscipes luciana*	FSC, CSC	Non-target captures and mapping of dens
Salt marsh harvest mouse	*Reithrodontomys raviventris*	FE, CE	Habitat assessment, monitoring
Salinas harvest mouse	*Reithrodontomys megalotus distichlus*	G5T1S1	Captures in the Salinas area; habitat assessment
California clapper rail	*Rallus longirostris*	FE, CE	Surveys at Concord Naval Weapons Station
Golden eagle	*Aquila chrysaetos*	CSC	Research in Sacramento Valley
Swainson's hawk	*Buteo swainsoni*	CT	Research in Sacramento Valley
Northern harrier	*Circus cyaeneus*	CSC	Research and publication
White-tailed kite	*Elanus leucurus*	CFP	Research and publication
Loggerhead shrike	*Lanius ludovicianus*	FSC, CSC	Research in Sacramento Valley
Least Bell's vireo	*Vireo bellii pusillus*	FE, CE	Detected in Monterey County
Willow flycatcher	*Empidonax traillii extimus*	FE, CE	Research at Sierra Nevada breeding sites
Burrowing owl	*Athene cunicularia hypugia*	FSC, CSC	Research at multiple locations
Valley elderberry longhorn beetle	*Desmocerus californicus dimorphus*	FT	Research on mitigation site and publication

Analytical			
Arroyo southwestern toad	*Bufo microscaphus californicus*	FE, CSC	Research and report.
Giant garter snake	*Thamnophis gigas*	FT, CE	Research and publication.
Northern goshawk	*Accipiter gentilis*	FSC, CSC	Research and publication.
Northern spotted owl	*Strix occidentalis*	FT	Research and reports. Publication in progress.

[1] FE = Federal Endangered, FT = Federal threatened, FC = Federal candidate for listing, FSC = Federal species of concern, CE = California Endangered, CT = California threatened, CFP = California Fully Protected, CSC = California Species of Concern, G5T1S1 = CNDDB rating of imperiled throughout California range.

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Smallwood, K.S. 1996. Assessment of the BIOPORT model's parameter values for pocket gopher burrowing characteristics. Report to Berger & Montague, P.C. and Roy S. Haber, P.C., Philadelphia. (peer reviewed).

Smallwood, K.S. 1997. Assessment of plutonium releases from Hanford buried waste sites. Report Number 9, Consulting in the Public Interest, 53 Clinton Street, Lambertville, New Jersey, 08530.

Smallwood, K.S. 1996. Soil Bioturbation and Wind Affect Fate of Hazardous Materials that were Released at the Rocky Flats Plant, Colorado. Report to Berger & Montague, P.C., Philadelphia.

Smallwood, K.S. 1996. Second assessment of the BIOPORT model's parameter values for pocket gopher burrowing characteristics and other relevant wildlife observations. Report to Berger & Montague, P.C. and Roy S. Haber, P.C., Philadelphia.

Smallwood, K.S., and R. Leidy. 1996. Wildlife and Their Management Under the Martell SYP. Report to Georgia Pacific, Corporation, Martel, CA. 30 pp.

EIP Associates. 1995. Yolo County Habitat Conservation Plan Biological Resources Report. Yolo County Planning and Development Department, Woodland, California.

Smallwood, K.S. and S. Geng. 1995. Analysis of the 1987 California Farm Cost Survey and recommendations for future survey. Program on Workable Energy Regulation, University-wide Energy Research Group, University of California.

Smallwood, K.S., S. Geng, and W. Idzerda. 1992. Final report to PG&E: Analysis of the 1987 California Farm Cost Survey and recommendations for future survey. Pacific Gas & Electric Company, San Ramon, California. 24 pp.

Fitzhugh, E.L. and K.S. Smallwood. 1987. Methods Manual – A statewide mountain lion population index technique. California Department of Fish and Game, Sacramento.

Salmon, T.P. and K.S. Smallwood. 1989. Final Report – Evaluating exotic vertebrates as pests to California agriculture. California Department of Food and Agriculture, Sacramento.

Smallwood, K.S. and W. A. Erickson (written under supervision of W.E. Howard, R.E. Marsh, and R.J. Laacke). 1990. Environmental exposure and fate of multi-kill strychnine gopher baits. Final Report to USDA Forest Service –NAPIAP, Cooperative Agreement PSW-89-0010CA.

Fitzhugh, E.L., K.S. Smallwood, and R. Gross. 1985. Mountain lion track count, Marin County, 1985. Unpublished report on file at Wildlife Extension, University of California, Davis.

Comments on Environmental Documents

I was retained or commissioned to comment on environmental planning and review documents, including:

- Mount Signal and Calexico Solar Farm Projects DEIR (2011; 16 pp);
- City of Elk Grove Sphere of Influence EIR (2011; 28 pp);
- Comment on Sutter Landing Park Solar Photovoltaic Project MND (2011; 9 pp);
- Statement of Shawn Smallwood, Ph.D. Regarding Proposed Rabik/Gudath Project, 22611 Coleman Valley Road, Bodega Bay (CPN 10-0002) (2011; 4 pp);
- Declaration of K. Shawn Smallwood on Biological Impacts of the Ivanpah Solar Electric Generating System (ISEGS) (2011; 9 pp);
- Comments on Draft Eagle Conservation Plan Guidance (2011; 13 pp);
- Comments on Draft EIR/EA for Niles Canyon Safety Improvement Project (2011; 16 pp);
- Declaration of K. Shawn Smallwood, Ph.D., on Biological Impacts of the Route 84 Safety Improvement Project (2011; 7 pp);
- Rebuttal Testimony of Witness #22, K. Shawn Smallwood, Ph.D, on Behalf of Intervenors Friends of The Columbia Gorge and Save Our Scenic Area (2010; 6 pp);

- Prefiled Direct Testimony of Witness #22, K. Shawn Smallwood, Ph.D, on Behalf of Intervenors Friends of the Columbia Gorge and Save Our Scenic Area. Comments on Whistling Ridge Wind Energy Power Project DEIS, Skamania County, Washington (2010; 41 pp);
- Evaluation of Klickitat County's Decisions on the Windy Flats West Wind Energy Project (2010; 17 pp);
- St. John's Church Project Draft Environmental Impact Report (2010; 14 pp.);
- Initial Study/Mitigated Negative Declaration for Results Radio Zone File #2009-001 (2010; 20 pp);
- Rio del Oro Specific Plan Project Final Environmental Impact Report (2010;12 pp);
- Answers to Questions on 33% RPS Implementation Analysis Preliminary Results Report (2009: 9 pp);
- SEPA Determination of Non-significance regarding zoning adjustments for Skamania County, Washington. Second Declaration to Friends of the Columbia Gorge, Inc. and Save Our Scenic Area (Dec 2008; 17 pp);
- Comments on Draft 1A Summary Report to CAISO (2008; 10 pp);
- Categorical Exemption of Hilton Manor Project, as determined by County of Placer (2009; 9 pp);
- Protest of CARE to Amendment to the Power Purchase and Sale Agreement for Procurement of Eligible Renewable Energy Resources Between Hatchet Ridge Wind LLC and PG&E (2009; 3 pp);
- Tehachapi Renewable Transmission Project EIR/EIS (2009; 142 pp);
- Delta Shores Project EIR, south Sacramento (2009; 11 pp + addendum 2 pp);
- Declaration of Shawn Smallwood in Support of Care's Petition to Modify D.07-09-040 (2008; 3 pp);
- The Public Utility Commission's Implementation Analysis December 16 Workshop for the Governor's Executive Order S-14-08 to implement a 33% Renewable Portfolio Standard by 2020 (2008; 9 pp);
- The Public Utility Commission's Implementation Analysis Draft Work Plan for the Governor's Executive Order S-14-08 to implement a 33% Renewable Portfolio Standard by 2020 (2008; 11 pp);
- Draft 1A Summary Report to California Independent System Operator for Planning Reserve Margins (PRM) Study (2008; 7 pp.);
- SEPA Determination of Non-significance regarding zoning adjustments for Skamania County, Washington. Declaration to Friends of the Columbia Gorge, Inc. and Save Our Scenic Area (Sep 2008; 16 pp);
- California Energy Commission's Preliminary Staff Assessment of the Colusa Generating Station (2007; 24 pp);
- Rio del Oro Specific Plan Project Recirculated Draft Environmental Impact Report (2008: 66 pp);
- Replies to Response to Comments Re: Regional University Specific Plan Environmental Impact Report (2008; 20 pp);
- Regional University Specific Plan Environmental Impact Report (2008: 33 pp.);
- Clark Precast, LLC's "Sugarland" project, Negative Declaration (2008: 15 pp.);
- Cape Wind Project Draft Environmental Impact Statement (2008; 157 pp.);

- Yuba Highlands Specific Plan (or Area Plan) Environmental Impact Report (2006; 37 pp.);
- Replies to responses to comments on Mitigated Negative Declaration of the proposed Mining Permit (MIN 04-01) and Modification of Use Permit 96-02 at North Table Mountain (2006; 5 pp);
- Mitigated Negative Declaration of the proposed Mining Permit (MIN 04-01) and Modification of Use Permit 96-02 at North Table Mountain (2006; 15 pp);
- Windy Point Wind Farm Environmental Review and EIS (2006; 14 pp and 36 Powerpoint slides in reply to responses to comments);
- Shiloh I Wind Power Project EIR (2005; 18 pp);
- Buena Vista Wind Energy Project Notice of Preparation of EIR (2004; 15 pp);
- Negative Declaration of the proposed Callahan Estates Subdivision (2004; 11 pp);
- Negative Declaration of the proposed Winters Highlands Subdivision (2004; 9 pp);
- Negative Declaration of the proposed Winters Highlands Subdivision (2004; 13 pp);
- Negative Declaration of the proposed Creekside Highlands Project, Tract 7270 (2004; 21 pp);
- On the petition California Fish and Game Commission to list the Burrowing Owl as threatened or endangered (2003; 10 pp);
- Conditional Use Permit renewals from Alameda County for wind turbine operations in the Altamont Pass Wind Resource Area (2003; 41 pp);
- UC Davis Long Range Development Plan of 2003, particularly with regard to the Neighborhood Master Plan (2003; 23 pp);
- Anderson Marketplace Draft Environmental Impact Report (2003: 18 pp + 3 plates of photos);
- Negative Declaration of the proposed expansion of Temple B'nai Tikyah (2003: 6 pp);
- Antonio Mountain Ranch Specific Plan Public Draft EIR (2002: 23 pp);
- Response to testimony of experts at the East Altamont Energy Center evidentiary hearing on biological resources (2002: 9 pp);
- Revised Draft Environmental Impact Report, The Promenade (2002: 7 pp);
- Recirculated Initial Study for Calpine's proposed Pajaro Valley Energy Center (2002: 3 pp);
- UC Merced -- Declaration of Dr. Shawn Smallwood in support of petitioner's application for temporary restraining order and preliminary injunction (2002: 5 pp);
- Replies to response to comments in Final Environmental Impact Report, Atwood Ranch Unit III Subdivision (2003: 22 pp);
- Draft Environmental Impact Report, Atwood Ranch Unit III Subdivision (2002: 19 pp + 8 photos on 4 plates);
- California Energy Commission Staff Report on GWF Tracy Peaker Project (2002: 17 pp + 3 photos; follow-up report of 3 pp);
- Initial Study and Negative Declaration, Silver Bend Apartments, Placer County (2002: 13 pp);
- UC Merced Long-range Development Plan DEIR and UC Merced Community Plan DEIR (2001: 26 pp);
- Initial Study, Colusa County Power Plant (2001: 6 pp);
- Comments on Proposed Dog Park at Catlin Park, Folsom, California (2001: 5 pp + 4 photos);
- Pacific Lumber Co. (Headwaters) Habitat Conservation Plan and Environmental Impact

Report (1998: 28 pp);

- Final Environmental Impact Report/Statement for Issuance of Take authorization for listed species within the MSCP planning area in San Diego County, California (Fed. Reg. 62 (60): 14938, San Diego Multi-Species Conservation Program) (1997: 10 pp);
- Permit (PRT-823773) Amendment for the Natomas Basin Habitat Conservation Plan, Sacramento, CA (Fed. Reg. 63 (101): 29020-29021) (1998);
- Draft Recovery Plan for the Giant Garter Snake (*Thamnophis gigas*). (Fed. Reg. 64(176): 49497-49498) (1999: 8 pp);
- Review of the Draft Recovery Plan for the Arroyo Southwestern Toad (*Bufo microscaphus californicus*) (1998);
- Ballona West Bluffs Project Environmental Impact Report (1999: oral presentation);
- California Board of Forestry's proposed amended Forest Practices Rules (1999);
- Negative Declaration for the Sunset Skyranch Airport Use Permit (1999);
- Calpine and Bechtel Corporations' Biological Resources Implementation and Monitoring Program (BRMIMP) for the Metcalf Energy Center (2000: 10 pp);
- California Energy Commission's Final Staff Assessment of the proposed Metcalf Energy Center (2000);
- US Fish and Wildlife Service Section 7 consultation with the California Energy Commission regarding Calpine and Bechtel Corporations' Metcalf Energy Center (2000: 4 pp);
- California Energy Commission's Preliminary Staff Assessment of the proposed Metcalf Energy Center (2000: 11 pp);
- Site-specific management plans for the Natomas Basin Conservancy's mitigation lands, prepared by Wildlands, Inc. (2000: 7 pp);
- Affidavit of K. Shawn Smallwood in Spirit of the Sage Council, et al. (Plaintiffs) vs. Bruce Babbitt, Secretary, U.S. Department of the Interior, et al. (Defendants), Injuries caused by the No Surprises policy and final rule which codifies that policy (1999: 9 pp).

I also issued formal comments on the following documents:

- Draft Program Level EIR for Covell Village (2005; 19 pp);
- Bureau of Land Management Wind Energy Programmatic EIS Scoping document (2003: 7 pp.);
- NEPA Environmental Analysis for Biosafety Level 4 National Biocontainment Laboratory (NBL) at UC Davis (2003: 7 pp);
- Notice of Preparation of UC Merced Community and Area Plan EIR, on behalf of The Wildlife Society—Western Section (2001: 8 pp.);
- Preliminary Draft Yolo County Habitat Conservation Plan (2001; 2 letters totaling 35 pp.);
- Merced County General Plan Revision, notice of Negative Declaration (2001: 2 pp.);
- Notice of Preparation of Campus Parkway EIR/EIS (2001: 7 pp.);
- Draft Recovery Plan for the bighorn sheep in the Peninsular Range (*Ovis candensis*) (2000);
- Draft Recovery Plan for the California Red-legged Frog (*Rana aurora draytonii*), on behalf of The Wildlife Society—Western Section (2000: 10 pp.);
- Sierra Nevada Forest Plan Amendment Draft Environmental Impact Statement, on behalf of The Wildlife Society—Western Section (2000: 7 pp.);
- State Water Project Supplemental Water Purchase Program, Draft Program EIR (1997);

- Davis General Plan Update EIR (2000);
- Turn of the Century EIR (1999: 10 pp);
- Proposed termination of Critical Habitat Designation under the Endangered Species Act (Fed. Reg. 64(113): 31871-31874) (1999);
- NOA Draft Addendum to the Final Handbook for Habitat Conservation Planning and Incidental Take Permitting Process, termed the HCP 5-Point Policy Plan (Fed. Reg. 64(45): 11485 - 11490) (1999; 2 pp + attachments);
- Covell Center Project EIR and EIR Supplement (1997).

Position Statements I prepared the following position statements for the Western Section of The Wildlife Society, and one for nearly 200 scientists:

- Recommended that the California Department of Fish and Game prioritize the extermination of the introduced southern water snake in northern California. The Wildlife Society--Western Section (2001);
- Recommended that The Wildlife Society—Western Section appoint or recommend members of the independent scientific review panel for the UC Merced environmental review process (2001);
- Opposed the siting of the University of California's 10th campus on a sensitive vernal pool/grassland complex east of Merced. The Wildlife Society--Western Section (2000);
- Opposed the legalization of ferret ownership in California. The Wildlife Society--Western Section (2000);
- Opposed the Proposed "No Surprises," "Safe Harbor," and "Candidate Conservation Agreement" rules, including permit-shield protection provisions (Fed. Reg. Vol. 62, No. 103, pp. 29091-29098 and No. 113, pp. 32189-32194). This statement was signed by 188 scientists and went to the responsible federal agencies, as well as to the U.S. Senate and House of Representatives.

Printed Mass Media

Smallwood, K.S., D. Mooney, and M. McGuinness. 2003. We must stop the UCD biolab now. Op-Ed to the Davis Enterprise.

Smallwood, K.S. 2002. Spring Lake threatens Davis. Op-Ed to the Davis Enterprise.

Smallwood, K.S. Summer, 2001. Mitigation of habitation. The Flatlander, Davis, California.

Entrikan, R.K. and K.S. Smallwood. 2000. Measure O: Flawed law would lock in new taxes. Op-Ed to the Davis Enterprise.

Smallwood, K.S. 2000. Davis delegation lobbies Congress for Wildlife conservation. Op-Ed to the Davis Enterprise.

Smallwood, K.S. 1998. Davis Visions. The Flatlander, Davis, California.

Smallwood, K.S. 1997. Last grab for Yolo's land and water. The Flatlander, Davis, California.

Smallwood, K.S. 1997. The Yolo County HCP. Op-Ed to the Davis Enterprise.

Radio/Television

KXJZ Capital Public Radio -- Insight (Host Jeffrey Callison). Mountain lion attacks (with guest Professor Richard Coss). 23 April 2009;

KXJZ Capital Public Radio -- Insight (Host Jeffrey Callison). Wind farm Rio Vista Renewable Power. 4 September 2008;

KQED QUEST Episode #111. Bird collisions with wind turbines. 2007;

KDVS Speaking in Tongues (host Ron Glick), Yolo County HCP: 1 hour. December 27, 2001;

KDVS Speaking in Tongues (host Ron Glick), Yolo County HCP: 1 hour. May 3, 2001;

KDVS Speaking in Tongues (host Ron Glick), Yolo County HCP: 1 hour. February 8, 2001;

KDVS Speaking in Tongues (host Ron Glick & Shawn Smallwood), California Energy Crisis: 1 hour. Jan. 25, 2001;

KDVS Speaking in Tongues (host Ron Glick), Headwaters Forest HCP: 1 hour. 1998;

Davis Cable Channel (host Gerald Heffernon), Burrowing owls in Davis: half hour. June, 2000;

Davis Cable Channel (hosted by Davis League of Women Voters), Measure O debate: 1 hour. October, 2000;

KXTV 10, In Your Interest, The Endangered Species Act: half hour. 1997.

Posters at Professional Meetings

Smallwood, K. S. and C. G. Thelander. 2005. Lessons learned from five years of avian mortality research in the Altamont Pass WRA. AWEA conference, Denver, May 2005.

Neher, L., L. Wilder, J. Woo, L. Spiegel, D. Yen-Nakafugi, and K.S. Smallwood. 2005. Bird's eye view on California wind. AWEA conference, Denver, May 2005.

Smallwood, K. S., C. G. Thelander and L. Spiegel. 2003. Toward a predictive model of avian fatalities in the Altamont Pass Wind Resource Area. Windpower 2003 Conference and Convention, Austin, Texas.

Smallwood, K.S. and Eva Butler. 2002. Pocket Gopher Response to Yellow Star-thistle Eradication as part of Grassland Restoration at Decommissioned Mather Air Force Base, Sacramento County, California. White Mountain Research Station Open House, Barcroft Station.

Smallwood, K.S. and Michael L. Morrison. 2002. Fresno kangaroo rat (*Dipodomys nitratoides*) Conservation Research at Resources Management Area 5, Lemoore Naval Air Station. White Mountain Research Station Open House, Barcroft Station.

Smallwood, K.S. and E.L. Fitzhugh. 1989. Differentiating mountain lion and dog tracks. Third Mountain Lion Workshop, Prescott, AZ.

Smith, T. R. and K. S. Smallwood. 2000. Effects of study area size, location, season, and allometry on reported *Sorex* shrew densities. Annual Meeting of the Western Section of The Wildlife Society.

Presentations at Professional Meetings and Seminars

Comparing Wind Turbine Impacts across North America. California Energy Commission Staff Workshop: Reducing the Impacts of Energy Infrastructure on Wildlife, 20 July 2011.

Siting Repowered Wind Turbines to Minimize Raptor Collisions. California Energy Commission Staff Workshop: Reducing the Impacts of Energy Infrastructure on Wildlife, 20 July 2011.

Siting Repowered Wind Turbines to Minimize Raptor Collisions. Alameda County Scientific Review Committee meeting, 17 February 2011

Comparing Wind Turbine Impacts across North America. Conference on Wind energy and Wildlife impacts, Trondheim, Norway, 3 May 2011.

Update on Wildlife Impacts in the Altamont Pass Wind Resource Area. Raptor Symposium, The Wildlife Society—Western Section, Riverside, California, February 2011.

Siting Repowered Wind Turbines to Minimize Raptor Collisions. Raptor Symposium, The Wildlife Society—Western Section, Riverside, California, February 2011.

Wildlife mortality caused by wind turbine collisions. Ecological Society of America, Pittsburgh, Pennsylvania, 6 August 2010.

Map-based repowering and reorganization of a wind farm to minimize burrowing owl fatalities. California burrowing Owl Consortium Meeting, Livermore, California, 6 February 2010.

Environmental barriers to wind power. Getting Real About Renewables: Economic and Environmental Barriers to Biofuels and Wind Energy. A symposium sponsored by the Environmental & Energy Law & Policy Journal, University of Houston Law Center, Houston, 23 February 2007.

Lessons learned about bird collisions with wind turbines in the Altamont Pass and other US wind farms. Meeting with Japan Ministry of the Environment and Japan Ministry of the Economy, Wild Bird Society of Japan, and other NGOs Tokyo, Japan, 9 November 2006.

Lessons learned about bird collisions with wind turbines in the Altamont Pass and other US wind farms. Symposium on bird collisions with wind turbines. Wild Bird Society of Japan, Tokyo, Japan, 4 November 2006.

Responses of Fresno kangaroo rats to habitat improvements in an adaptive management framework. California Society for Ecological Restoration (SERCAL) 13th Annual Conference, UC Santa Barbara, 27 October 2006.

Fatality associations as the basis for predictive models of fatalities in the Altamont Pass Wind Resource Area. EEI/APLIC/PIER Workshop, 2006 Biologist Task Force and Avian Interaction with Electric Facilities Meeting, Pleasanton, California, 28 April 2006.

Burrowing owl burrows and wind turbine collisions in the Altamont Pass Wind Resource Area. The Wildlife Society—Western Section Annual Meeting, Sacramento, California, February 8, 2006.

Mitigation at wind farms. Workshop: Understanding and resolving bird and bat impacts. American Wind Energy Association and Audubon Society. Los Angeles, CA. January 10 and 11, 2006.

Incorporating data from the California Wildlife Habitat Relationships (CWHR) system into an impact assessment tool for birds near wind farms. Shawn Smallwood, Kevin Hunting, Marcus Yee, Linda Spiegel, Monica Parisi. Workshop: Understanding and resolving bird and bat impacts. American Wind Energy Association and Audubon Society. Los Angeles, CA. January 10 and 11, 2006.

Toward indicating threats to birds by California's new wind farms. California Energy Commission, Sacramento, May 26, 2005.

Avian collisions in the Altamont Pass. California Energy Commission, Sacramento, May 26, 2005.

Ecological solutions for avian collisions with wind turbines in the Altamont Pass Wind Resource Area. EPRI Environmental Sector Council, Monterey, California, February 17, 2005.

Ecological solutions for avian collisions with wind turbines in the Altamont Pass Wind Resource Area. The Wildlife Society—Western Section Annual Meeting, Sacramento, California, January 19, 2005.

Associations between avian fatalities and attributes of electric distribution poles in California. The Wildlife Society—Western Section Annual Meeting, Sacramento, California, January 19, 2005.

Minimizing avian mortality in the Altamont Pass Wind Resources Area. UC Davis Wind Energy Collaborative Forum, Palm Springs, California, December 14, 2004.

Selecting electric distribution poles for priority retrofitting to reduce raptor mortality. Raptor Research Foundation Meeting, Bakersfield, California, November 10, 2004.

Responses of Fresno kangaroo rats to habitat improvements in an adaptive management framework. Annual Meeting of the Society for Ecological Restoration, South Lake Tahoe, California,

October 16, 2004.

Lessons learned from five years of avian mortality research at the Altamont Pass Wind Resources Area in California. The Wildlife Society Annual Meeting, Calgary, Canada, September 2004.

The ecology and impacts of power generation at Altamont Pass. Sacramento Petroleum Association, Sacramento, California, August 18, 2004.

Burrowing owl mortality in the Altamont Pass Wind Resource Area. California Burrowing Owl Consortium meeting, Hayward, California, February 7, 2004.

Burrowing owl mortality in the Altamont Pass Wind Resource Area. California Burrowing Owl Symposium, Sacramento, November 2, 2003.

Raptor Mortality at the Altamont Pass Wind Resource Area. National Wind Coordinating Committee, Washington, D.C., November 17, 2003.

Raptor Behavior at the Altamont Pass Wind Resource Area. Annual Meeting of the Raptor Research Foundation, Anchorage, Alaska, September, 2003.

Raptor Mortality at the Altamont Pass Wind Resource Area. Annual Meeting of the Raptor Research Foundation, Anchorage, Alaska, September, 2003.

California mountain lions. Ecological & Environmental Issues Seminar, Department of Biology, California State University, Sacramento, November, 2000.

Intra- and inter-turbine string comparison of fatalities to animal burrow densities at Altamont Pass. National Wind Coordinating Committee, Carmel, California, May, 2000.

Using a Geographic Positioning System (GPS) to map wildlife and habitat. Annual Meeting of the Western Section of The Wildlife Society, Riverside, CA, January, 2000.

Suggested standards for science applied to conservation issues. Annual Meeting of the Western Section of The Wildlife Society, Riverside, CA, January, 2000.

The indicators framework applied to ecological restoration in Yolo County, California. Society for Ecological Restoration, September 25, 1999.

Ecological restoration in the context of animal social units and their habitat areas. Society for Ecological Restoration, September 24, 1999.

Relating Indicators of Ecological Health and Integrity to Assess Risks to Sustainable Agriculture and Native Biota. International Conference on Ecosystem Health, August 16, 1999.

A crosswalk from the Endangered Species Act to the HCP Handbook and real HCPs. Southern California Edison, Co. and California Energy Commission, March 4-5, 1999.

Mountain lion track counts in California: Implications for Management. Ecological & Environmental Issues Seminar, Department of Biological Sciences, California State University, Sacramento, November 4, 1998.

"No Surprises" -- Lack of science in the HCP process. California Native Plant Society Annual Conservation Conference, The Presidio, San Francisco, September 7, 1997.

In Your Interest. A half hour weekly show aired on Channel 10 Television, Sacramento. In this episode, I served on a panel of experts discussing problems with the implementation of the Endangered Species Act. Aired August 31, 1997.

Spatial scaling of pocket gopher (*Geomyidae*) density. Southwestern Association of Naturalists 44th Meeting, Fayetteville, Arkansas, April 10, 1997.

Estimating prairie dog and pocket gopher burrow volume. Southwestern Association of Naturalists 44th Meeting, Fayetteville, Arkansas, April 10, 1997.

Ten years of mountain lion track survey. Fifth Mountain Lion Workshop, San Diego, February 27, 1996.

Study and interpretive design effects on mountain lion density estimates. Fifth Mountain Lion Workshop, San Diego, February 27, 1996.

Small animal control. Session moderator and speaker at the California Farm Conference, Sacramento, California, Feb. 28, 1995.

Small animal control. Ecological Farming Conference, Asylomar, California, Jan. 28, 1995.

Habitat associations of the Swainson's Hawk in the Sacramento Valley's agricultural landscape. 1994 Raptor Research Foundation Meeting, Flagstaff, Arizona.

Alfalfa as wildlife habitat. Seed Industry Conference, Woodland, California, May 4, 1994.

Habitats and vertebrate pests: impacts and management. Managing Farmland to Bring Back Game Birds and Wildlife to the Central Valley. Yolo County Resource Conservation District, U.C. Davis, February 19, 1994.

Management of gophers and alfalfa as wildlife habitat. Orland Alfalfa Production Meeting and Sacramento Valley Alfalfa Production Meeting, February 1 and 2, 1994.

Patterns of wildlife movement in a farming landscape. Wildlife and Fisheries Biology Seminar Series: Recent Advances in Wildlife, Fish, and Conservation Biology, U.C. Davis, Dec. 6, 1993.

Alfalfa as wildlife habitat. California Alfalfa Symposium, Fresno, California, Dec. 9, 1993.

Management of pocket gophers in Sacramento Valley alfalfa. California Alfalfa Symposium, Fresno, California, Dec. 8, 1993.

Association analysis of raptors in a farming landscape. Plenary speaker at Raptor Research Foundation Meeting, Charlotte, North Carolina, Nov. 6, 1993.

Landscape strategies for biological control and IPM. Plenary speaker, International Conference on Integrated Resource Management and Sustainable Agriculture, Beijing, China, Sept. 11, 1993.

Landscape Ecology Study of Pocket Gophers in Alfalfa. Alfalfa Field Day, U.C. Davis, July 1993.

Patterns of wildlife movement in a farming landscape. Spatial Data Analysis Colloquium, U.C. Davis, August 6, 1993.

Sound stewardship of wildlife. Veterinary Medicine Seminar: Ethics of Animal Use, U.C. Davis. May 1993.

Landscape ecology study of pocket gophers in alfalfa. Five County Grower's Meeting, Tracy, California. February 1993.

Turbulence and the community organizers: The role of invading species in ordering a turbulent system, and the factors for invasion success. Ecology Graduate Student Association Colloquium, U.C. Davis. May 1990.

Evaluation of exotic vertebrate pests. Fourteenth Vertebrate Pest Conference, Sacramento, California. March 1990.

Analytical methods for predicting success of mammal introductions to North America. The Western Section of the Wildlife Society, Hilo, Hawaii. February 1988.

A state-wide mountain lion track survey. Sacramento County Dept Parks and Recreation. April 1986.

The mountain lion in California. Davis Chapter of the Audubon Society. October 1985.

Ecology Graduate Student Seminars, U.C. Davis, 1985-1990: Social behavior of the mountain lion; Mountain lion control; Political status of the mountain lion in California.

Other forms of Participation at Professional Meetings

- Workshop co-presenter at Birds & Wind Energy Specialist Group (BAWESG) Information sharing week, Bird specialist studies for proposed wind energy facilities in South Africa, Endangered Wildlife Trust, Darling, South Africa, 3-7 October 2011.

- Scientific Committee, Conference on Wind energy and Wildlife impacts, Trondheim, Norway, 2-5 May 2011.

- Chair of Animal Damage Management Session, The Wildlife Society, Annual Meeting, Reno, Nevada, September 26, 2001.

- Chair of Technical Session: Human communities and ecosystem health: Comparing perspectives and making connection. Managing for Ecosystem Health, International Congress on Ecosystem Health, Sacramento, CA August 15-20, 1999.

- Student Awards Committee, Annual Meeting of the Western Section of The Wildlife Society, Riverside, CA, January, 2000.

- Student Mentor, Annual Meeting of the Western Section of The Wildlife Society, Riverside, CA, January, 2000.

Reviews of Journal Papers (Scientific journals for whom I've provided peer review)

Journal	Journal
American Naturalist	Journal of Animal Ecology
Journal of Wildlife Management	Western North American Naturalist
Auk	Journal of Raptor Research
Biological Conservation	National Renewable Energy Lab reports
Canadian Journal of Zoology	Oikos
Ecosystem Health	The Prairie Naturalist
Environmental Conservation	Restoration Ecology
Environmental Management	Southwestern Naturalist
Functional Ecology	The Wildlife Society--Western Section Trans.
Journal of Zoology (London)	Proc. Int. Congress on Managing for Ecosystem Health
Journal of Applied Ecology	Transactions in GIS
Ecology	Tropical Ecology
Biological Control	The Condor

Committees

- Scientific Review Committee, Alameda County, Altamont Pass Wind Resource Area
- Ph.D. Thesis Committee, Steve Anderson, University of California, Davis
- MS Thesis Committee, Marcus Yee, California State University, Sacramento

Other Professional Activities or Products

Testified in Federal Court in Denver during 2005 over the fate of radio-nuclides in the soil at Rocky Flats Plant after exposure to burrowing animals. My clients won a judgment of $553,000,000. I have also testified in many other cases of litigation under CEQA, NEPA, the Warren-Alquist Act, and other environmental laws. My clients won most of the cases for which I testified.

Testified in Skamania County Hearing in 2009 on the potential impacts of zoning the County for development of wind farms and hazardous waste facilities.

Testified in deposition in 2007 in the case of O'Dell et al. vs. FPL Energy in Houston, Texas.

Testified in Klickitat County Hearing in 2006 on the potential impacts of the Windy Point Wind Farm.

Memberships in Professional Societies

The Wildlife Society
Raptor Research Foundation
American Museum of Natural History

Honors and Awards

Certificate of Appreciation, The Wildlife Society—Western Section, 2000, 2001
Fulbright Research Fellowship to Indonesia, 1987.
Northern California Athletic Association Most Valuable Cross Country Runner, 1984.
J.G. Boswell Full Academic Scholarship, 1981 (Paid expenses for undergraduate education).
American Legion Award, Corcoran High School, 1981, and John Muir Junior High, 1977.
CIF Section Champion, Cross Country in 1978 and Track & Field 2 mile run in 1981.
National Junior Record, 20 kilometer run, 1982.
National Age Group Record, 1500 meter run, 1978

Community Activities

District 64 Little League Umpire, 2003-2007
Dixon Little League Umpire, 2006-07
Davis Little League Chief Umpire and Board member, 2004-2005
Davis Little League Safety Officer, 2004-2005
Davis Little League Certified Umpire, 2002-2004
Davis Little League Scorekeeper, 2002
Davis Visioning Group member
Petitioner for Writ of Mandate under the California Environmental Quality Act against City of Woodland decision to approve the Spring Lake Specific Plan, 2002
Served on campaign committees for City Council candidates

ATTACHMENTS

Review

Biological Consequences of Ecosystem Fragmentation: A Review

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Abstract: *Research on fragmented ecosystems has focused mostly on the biogeographic consequences of the creation of habitat "islands" of different sizes, and has provided little of practical value to managers. However, ecosystem fragmentation causes large changes in the physical environment as well as biogeographic changes. Fragmentation generally results in a landscape that consists of remnant areas of native vegetation surrounded by a matrix of agricultural or other developed land. As a result, fluxes of radiation, momentum (i.e., wind), water, and nutrients across the landscape are altered significantly. These in turn can have important influences on the biota within remnant areas, especially at or near the edge between the remnant and the surrounding matrix. The isolation of remnant areas by clearing also has important consequences for the biota. These consequences vary with the time since isolation, distance from other remnants, and degree of connectivity with other remnants. The influences of physical and biogeographic changes are modified by the size, shape, and position in the landscape of individual remnants, with larger remnants being less adversely affected by the fragmentation process. The dynamics*

Resumen: *La investigación sobre los ecosistemas fragmentados se ha enfocado principalmente en las consecuencias biogeográficas de la creación de "islas" de hábitat de diferentes tamaños y ha sido de muy poco valor práctico para los manejadores del recurso. Como quiera que sea, la fragmentación de los ecosistemas causa grandes cambios en el medio ambiente físico así como en el ámbito biogeográfico. La fragmentación resulta generalmente en terrenos que consisten de áreas remanentes de vegetación nativa rodeada de una matriz de tierras agrícolas u otras formas de uso de la tierra. Como un resultado de esto, el flujo de la radiación, del momentum (ej. el viento), del agua y de los nutrientes a través de la tierra son alterados significativamente. Esto en su turno, puede influenciar e la biota dentro de las áreas remanentes, especialmente en o cerca de los límites entre los remanentes y la matriz que los rodea. El aislamiento de las áreas remanentes por la tala también tiene importantes consecuencias para la biota y estas consecuencias varian con, el tiempo desde el momento del aislamiento, la distancia hasta los otros remanentes y el grado de conección entre ellos. La influencia de los cambios físicos y biogeográficos es modificada por el tamaño, la forma y la posición en el terreno de remanentes individuales siendo los remanentes grandes los menos afectados adversamante por el proceso de fragmentación. La dinámica de las áreas remanentes son dirigidas*

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of remnant areas are predominantly driven by factors arising in the surrounding landscape. Management of, and research on, fragmented ecosystems should be directed at understanding and controlling these external influences as much as at the biota of the remnants themselves. There is a strong need to develop an integrated approach to landscape management that places conservation reserves in the context of the overall landscape.

predominantemente por factores que surgen en el terreno circundante. El manejo y la investigación de los ecosistemas fragmentados debería de dirigirse tanto al entendimiento y control de estas influencias externas como a las biotas remanentes en sí. Hay una fuerte necesidad para el desarrollo de un enfoque integrado en el manejo de tierras que coloca a las reservas para la conservación en el contexto del terreno en general.

Introduction

Since the development of agriculture, the natural vegetation cover of every continent except Antarctica has been extensively modified. A cycle of agricultural development followed by overexploitation of the land has been repeated throughout recorded history. Forman (1987) quotes Plato's (ca. 2350 BP) description of how an area of ancient Greece was stripped of its soil following clearing and grazing, leaving "the mere skeleton of the land." Overexploitation and the use of inappropriate agricultural practices have led to desert encroachment, as in the Sahel region in North Africa (Le Houérou & Gillet 1986; Ehrlich & Ehrlich 1987), and to extensive loss of soil, often with disastrous and dramatic consequences, as in the Dust Bowl of the United States (Hudson 1981).

The process of land clearing and the consequent environmental degradation is continuing rapidly in many regions such as Southeast Asia and South America, particularly in areas of tropical rain forest (Myers 1988). Australia provides an example of recent agricultural development, with vast areas being cleared over the last 100 years for cereal cropping and stock grazing (Saunders & Hobbs 1989; Hobbs & Hopkins 1990; Saunders et al. 1990). In some regions over 93% of the native vegetation has been removed and the agricultural land that has replaced it is subject to extensive wind and water erosion or soil salinization, with consequent pollution of water supplies for drinking and irrigation.

One legacy of the extensive removal of native vegetation is that the remaining vegetation is usually in fragmented patches across the landscape. These patches or remnants are situated in different positions in the landscape and on different soil types, possess different vegetation types, and vary in their size, shape, isolation, and type of ownership. Over much of the world, conservation of regional biotas depends entirely on the retention and management of these remnants. Conservation managers are therefore faced with the dual issues of whether the remnants have any practical conservation values, and if they do, of how they must be managed to retain these values (Saunders et al. 1987*a*).

In this paper we use the word *remnant* to define any patch of native vegetation around which most or all of the original vegetation has been removed (Saunders et al. 1987*a*). Remnants often have been called habitat islands and the changes that result from the isolation of these islands have been the subject of considerable debate in the literature. This debate has centered mostly on the equilibrium theory of island biogeography (MacArthur & Wilson 1963, 1967) and its applicability to conservation. In particular, the importance of size, shape, and design of single reserves and reserve systems, extinction and colonization rates, and species-area relationships have been much discussed (Wilson & Willis 1975; Diamond 1975, 1976; May 1975; Terborgh 1976; Whitcomb et al. 1976; Simberloff & Abele 1976*a*, 1982; Pickett & Thompson 1978; Game 1980; Margules et al. 1982; Boecklen & Gotelli 1984). Particular attention has been paid to the question of whether one large reserve could preserve more species than several small reserves adding up to the equivalent area of the larger reserve (the so-called SLOSS, or "single large or several small" debate; Simberloff & Abele 1976*b*, 1984; Gilpin & Diamond 1980; Higgs & Usher 1980; Järvinen 1982; Willis 1984).

These questions have been reviewed elsewhere (Simberloff 1988) and are not examined in detail here. While of theoretical interest, most of these issues are of little practical value in managing fragmented systems (Zimmerman & Bierragaard 1986; Margules 1987; Hobbs 1988; Margules & Stein 1989). The species-area equation, for example, may give a manager a rough idea of how many species will be maintained on a remnant of a given area, but will yield absolutely no information on the practical issue of which habitats contribute most to species richness or on which species are most likely to be lost from the remnant. Simberloff (1986) stated, "It is also sad that unwarranted focus on the supposed lessons of island biogeography theory has detracted from the main task of refuge planners, determining what habitats are important and how to maintain them." Margules (1986), in a discussion about two conservation evaluation exercises, notes that, "no panel members in either exercise considered the species-area relationship or the equilibrium theory of island biogeography in their evaluations; at least not explicitly." In addition, the debates about reserve design and SLOSS are of limited relevance because, with very few exceptions, managers of conser-

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vation reserves are faced with a fait accompli. Conservation considerations have rarely been taken into account during the development of areas for agriculture, mining, forestry, or other such uses. Conservation managers must work with the remnants left following these developments and virtually never have the opportunity to design a reserve network before an area is fragmented. There is an increasing need to utilize design criteria to improve conservation networks in already fragmented areas, but this requires a clear understanding of the problems created by fragmentation in the first place.

Hence we believe that research and discussion should focus on practical issues relating to the impact of fragmentation on natural ecosystems and managing remnants for conservation (Saunders et al. 1987*b*). We share the fear of Noss and Harris (1986) that conservation agencies have not realized the important biological consequences of ecosystem fragmentation and have therefore not developed policies to manage their remnants to maintain conservation values. The aim of this paper is to point out the physical effects of fragmentation, the biological consequences for natural ecosystems of these effects, and the options available for conservation research and management.

Characteristics of Fragmented Ecosystems

Fragmentation of the landscape produces a series of remnant vegetation patches surrounded by a matrix of different vegetation and/or land use. Two primary effects of this are an alteration of the *microclimate* within and surrounding the remnant and the *isolation* of each area from other remnant patches in the surrounding landscape. Thus, in a fragmented landscape there are changes in the physical environment as well as biogeographic changes. Most discussions of habitat fragmentation have concentrated on the biogeographic aspects, and the physical changes have received little attention. All remnants are exposed to these physical and biogeographic changes to a greater or lesser degree, but their effects are modified by the *size, shape,* and *position in the landscape* of individual remnants. We examine first the physical effects of fragmentation and then discuss the operation of the modifying factors.

Changes in Microclimate

Fragmentation of the landscape results in changes in the physical fluxes across the landscape. Alterations in fluxes of radiation, wind, and water can all have important effects on remnants of native vegetation.

1. RADIATION FLUXES

The energy balance of a fragmented landscape will differ markedly from one with a complete cover of native vegetation, especially where the native vegetation was dense before clearing. Removing native vegetation and replacing it with crop species with differing architecture and phenology alters the radiation balance by increasing the solar radiation reaching the ground surface during the day, changing the albedo, and increasing reradiation at night. These features vary depending on time of year; ploughing, crop growth, and harvesting produce an alternation of bare ground and varying degrees of vegetation cover (Geiger 1965; Milthorpe & Moorby 1974). In cleared areas, in general, daytime temperatures are higher and night temperatures lower than in naturally vegetated areas. This leads to greater temperature ranges both at the surface and in the upper layers of the soil, and an increased incidence of frost (Geiger 1965).

These changes in the cleared parts of the landscape impinge on the remnant native vegetation, especially at the edge between the two. Except near the equator, the orientation of the edge affects the degree to which solar radiation increases within a remnant at different times of year (Geiger 1965; Wales 1972; Ranney et al. 1981). Latitude also affects radiation input, and at high latitudes especially, where solar angles are low, a remnant edge can receive significantly more solar radiation than unfragmented areas receive (De Walle & McGuire 1973; Hutchinson & Matt 1976, 1977). Air temperatures at the edge of a forest remnant can be significantly higher than those found in either the interior of the remnant or the surrounding agricultural land (Geiger 1965; Kapos 1989).

The consequences of increasing solar radiation at the edges of remnants are not clear. The indications are, however, that a different suite of species may come to occupy this altered habitat. Lovejoy et al. (1986) report that fragmentation in tropical forests results in the rapid growth of vines and other secondary vegetation in a 10–25 m strip around the remnant edge. This may effectively seal off the remnant and maintain an environment within the remnant similar to that that existed prior to fragmentation (F. Crome, personal communication). This also occurs to some extent in temperate regions (Gysel 1951; Trimble & Tryon 1966; Ranney et al. 1981).

Shade-tolerant species may become restricted to the interior parts of the remnant, with different species requiring different distances from the edge. The composition of remnant edges may be affected by edge aspect (Wales 1972; Palik & Murphy 1990). Distinct sets of "interior" and "edge" species have been recognized in landscapes that have been fragmented for a long time, for instance in the eastern United States (Ranney et al. 1981).

Nutrient cycling processes may be affected by increased soil heating and its effect on soil microorganism

and invertebrate numbers and activity (Klein 1989; Parker 1989), on litter decomposition, and on soil moisture retention. Changes in the radiation balance also affect larger fauna both directly and indirectly through altering resource availability (via changes in plant growth and phenology). Lovejoy et al. (1986) attribute changes in butterfly community composition in tropical forest fragments partly to increased insolation within small remnants. Increased radiation load and dessication rates may lead to reduced foraging opportunities. Saunders (1982) considered that elevated temperatures in fragmented landscapes reduced the foraging time available to adult Carnaby's cockatoos (*Calyptorhynchus funereus latirostrus*) and contributed to their local extinction. Alternatively, some species dependent on temperature thresholds may be able to forage for longer periods. For instance, the strongly dominant ants of the *Iridomyrmex* genus are known to forage only when insolation and temperatures are high, and other ant species forage only when *Iridomyrmex* is absent (Greenslade & Halliday 1983; Andersen 1987). Increased insolation and ambient temperatures could then increase the foraging time available to *Iridomyrmex* but reduce it for subordinate species.

Altered temperature regimes can also have the effect of destabilizing competitive, predator-prey, and parasitic interactions. Geiger (1965) quotes the example of the timber pest *Ocneria monacha*, which lays eggs on tree trunks. Elevated springtime temperatures on trunks at the forest edge allow larvae to emerge before their parasites, which emerge from the cooler forest floor. This gives the pest a head start and results in population buildups.

2. WIND

With the removal of surrounding vegetation, the entire pattern of momentum transfer over the landscape is altered. As air flows from one vegetation type to another, the wind profile adjusts to the new roughness characteristics. When air flowing over one vegetation type comes to a boundary with a new vegetation type, the upper part of the wind profile initially retains the characteristics of the previous vegetation type, but the lower part takes on new characteristics reflecting the roughness of the new vegetation type. The wind profile does not fully equilibrate with the new vegetation for some distance. Rules of thumb for wind profile measurements give the minimum "fetch" (i.e., the minimum distance from the vegetation boundary that will ensure that the profile has taken on the characteristics of the vegetation under study) as 100–200 times the height of the vegetation under study (Monteith 1975; Grace 1983; Jones 1983). Turbulent transfer is important for the transport of atmospheric gases, and gas fluxes above vegetation are controlled by these processes. It follows, then, that these processes must be significantly modified in remnant vegetation areas, where the wind profile will not be in equilibrium with the remnant vegetation (Jarvis & McNaughton 1986). Given the fetch requirements, a woodland with 20-m-tall trees would need to be at least 2–4 km wide before wind profiles would resemble those in an unfragmented situation. The implications of this for plant gas exchange and growth have not been examined, but could be significant.

A more obvious effect of landscape fragmentation is that remnants are subjected to increased exposure to wind. This may result in damage to the vegetation, either through direct physical damage (Moen 1974; Grace 1977), or by increasing evapotranspiration with reduced humidity and increased dessication (Tranquillini 1979; Lovejoy et al. 1986). Direct physical damage can take the form of wind pruning (Caborn 1957) or windthrow of trees. Distinct edge structures have been found to develop at the edges of tree plantations (Fraser 1972), and this is likely to be the case for remnant areas also (see Ranney et al. 1981 for a discussion of edge structures). Trees near the edge of recently isolated remnants are particularly at risk of windthrow since they have matured within a closed canopy and have therefore developed in the absence of strong winds and lack the necessary support mechanisms to deal with such winds. Windthrow of dominant trees results in changes in the vegetation structure and increased availability of regeneration gaps, allowing recruitment, particularly of pioneer or light-demanding species. Increased litter fall through tree damage is likely to alter soil surface characteristics and hence the habitat of ground-dwelling fauna. Similarly, increased exposure to wind may remove loose bark and reduce the substrate available for bark-dwelling invertebrates, and hence also reduce their availability as a food resource. Increased wind turbulence due to clearing has been shown to affect the breeding success of birds by creating difficulties in landing due to wind shear and vigorous canopy movement (Brett 1989; Reville et al. 1990). In the case of tropical forests, fragmentation can result in hot, dry winds blowing into remnant areas from the surrounding cleared areas, with the probable result of increased tree mortality (Lovejoy et al. 1986) and prevention of regeneration of species whose successful establishment requires humid conditions or persistent soil moisture (Janzen 1986). This may also be important in the regeneration of species in other areas, such as those with mediterranean climates, where successful establishment requires adequate soil moisture (e.g., Gordon et al. 1989; Williams & Hobbs 1989). This effect will be lessened in cases where the edges of remnants are sealed off by rapid secondary growth.

Increased wind speeds at remnant edges have the secondary effect of increasing the transfer of material such as dust and seeds in from the surrounding matrix. Gei-

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ger (1965) gives an example where particulate matter deposition at the edge of a forest remnant increased by 40% over that in the open. Transfer of nutrients by saltation of surface soil particles is also possible, and strong gradients in soil nutrient levels have been found at the edges of remnant areas (Muir 1979; Cale & Hobbs 1991). Wind can deposit seeds of nonnative species over considerable distances into remnant areas (Hobbs & Atkins 1988). Transfer of insects and disease organisms into remnant areas may also be increased.

3. WATER FLUX

Fragmentation of the landscape results in modification of the local water regime by altering the various components of the hydrological cycle. Removal of native vegetation changes the rates of rainfall interception and evapotranspiration, and hence changes soil moisture levels (Kapos 1989). The pathways by which water penetrates the soil may also be markedly altered (Bormann & Likens 1979; Nulsen et al. 1986; Peck & Williamson 1987; Sharma et al. 1987; Bell 1988). Replacement of deep-rooted perennial species with herbaceous crop or pasture species leads to greatly reduced evapotranspiration and increased surface- and groundwater flows. The hydrological system in general becomes much less buffered with more extreme run-off events (Hornbeck 1973; Simons 1989). Increased surface water flows lead to increased erosion and transport of particulate matter (e.g., Bormann et al. 1974). Topsoil removed from high in the catchment ends up as sediment in the river system. Transport of nutrients into streams also increases (Likens et al. 1970). Rises in water tables can bring stored salts to the surface and cause secondary salinity, with considerable impacts on both remnant vegetation and the surrounding agricultural matrix (Peck 1978; Williamson et al. 1987). Movement of stored salts, nutrients, and pesticides washed from cleared land can have significant impacts on river systems (Kendrick 1976; Karr & Schlosser 1978).

The impact of these changes on an individual remnant depends greatly on its position in the landscape (Swanson et al. 1988). Remnants at the top of a catchment can be expected to be relatively little affected by changes in water flux, whereas remnants on midslopes and valley bottoms will be more affected. Remnants in run-off areas can be expected to experience more erosion, while those in run-on areas will experience more soil deposition, especially on the up-slope edge.

Further impacts on remnant areas can be expected following management operations in the surrounding matrix that alter hydrological processes. Thus irrigation, water storage, or drainage may affect remnant areas. An extreme example of this is found in the fens of eastern England, where drainage has led to peat shrinkage and a drop of 4 m in land level in 130 years. Remnant areas of natural wetland now require pumping systems to retain adequate water levels (Hutchinson 1980; Rowell 1986).

Changes in water fluxes and associated particulate and nutrient fluxes can have important influences on the biota of remnants. Altered patterns of erosion lead to changes in drainage patterns and the production of new substrates for plant colonization. Of particular importance is the deposition of nutrient-rich material in run-on areas, which can act as a focus for invasion by species requiring disturbance and/or nutrient enrichment for successful establishment (Hobbs & Atkins 1988). Changes in surface and soil moisture levels could also lead to changes in decomposition rates, altered seedbed characteristics, and changes in habitat for ground-dwelling fauna.

Isolation

Landscape fragmentation has two important consequences for the biota. First, there is a reduction in the total area of habitat available, with possible increased densities of surviving fauna in the remnants, and second, the habitat that is left is broken up into remnants that are isolated to varying degrees (Lovejoy et al. 1984, 1986; Haila & Hanski 1984; Wilcove et al. 1986). The time since isolation, the distance between adjacent remnants, and the degree of connectivity between them are all important determinants of the biotic response to fragmentation.

1. TIME SINCE ISOLATION

Upon isolation, a remnant is likely to have more species than it will be capable of maintaining, and species will be lost as the changes brought about by fragmentation take effect (Miller & Harris 1977; Miller 1978; Wilcox 1980; Harris 1984). This process of "species relaxation" is considered an inevitable consequence of area reduction and isolation, on the basis of island biogeographical predictions. However, the various mechanisms by which local extinctions occur will result from the physical changes discussed above and resulting changes in biotic interactions. The rate of species relaxation will differ among different taxa. The most rapid extinctions are likely in species that depend entirely on native vegetation, those that require large territories, and those that exist at low densities. Dispersal behavior and demography will determine the response of individual species to fragmentation (Karieva 1987).

Populations that are too small to be viable may persist for long periods simply because of the longevity of individuals. For example, in remnants in the Western Australian wheatbelt, female trapdoor spiders *Anidiops villosus* can live for at least 23 years (Main 1987), and small Australian passerines of about 25 g may live over 20 years (Australian Bird Banding Scheme records). It may take several hundred years to lose some species

such as long-lived trees, especially since adult plants are often less sensitive to changed environmental conditions than seedling and juvenile stages. Alterations in disturbance regime in remnant areas may prevent successful regeneration (Hobbs 1987; Bond et al. 1988). Presence of a species in a remnant is thus no guarantee of its continued existence there; successful reproduction and recruitment are required. Managers therefore may need to examine the age structure of species on remnants to identify vulnerable species to be targeted for special management.

Time since isolation will therefore determine how far down the "relaxation track" any given remnant has traveled. Recently isolated remnants can be expected to continue losing species; this process may continue for relatively long periods in the absence of interventive management (Soulé et al. 1988; Saunders 1989). Long-isolated remnants can be expected to have lost a proportion of the species originally present, and gained an additional component of invading species that are capable of establishing in the fragmented system. It is thus wrong to consider only species numbers and not species composition when discussing species diversity in remnant areas: species numbers can potentially increase in fragmented systems where invasive and edge species can establish, but the numbers of species originally found in the area may continue to decline (Verner 1986; Murphy 1989; Webb 1989; Harris & Scheck 1991).

It is commonly assumed that at some stage the remnant will reequilibrate with the surrounding landscape. It is, however, questionable whether a new stable equilibrium will be reached since the equilibration process is liable to be disrupted by changing fluxes from the surrounding matrix, disturbances, and influx of new invasive species. The final equilibrium can be likened to an idealized endpoint that is never likely to be reached, in much the same fashion as the climatic climax is now conceptualized in succession theory. Management of remnant areas will thus be an adaptive process directed at minimizing potential future species losses.

2. DISTANCE FROM OTHER REMNANTS

The ability of species to colonize a remnant depends to some extent on the distance of the remnant from other areas of native vegetation, be they other remnants or nearby uncleared areas. Colonizing ability is related to dispersal mode, with wind-dispersed and vagile species more likely to arrive at isolated remnants. However, whether such species become successful colonists depends on physical and biotic factors such as nutrient availability and competitive interactions (Vepsäläinen & Pisarski 1982). Animal species may have the physical ability to disperse long distances, but lack the behavioral repertoire to traverse the matrix surrounding the remnant; the matrix becomes an effective barrier to movement. Organism size is also important, and 100 m over agricultural fields may be a complete barrier to dispersal for small organisms such as invertebrates (Mader 1984) and some species of bird (Saunders & de Rebeira 1991). The persistence of such species on a remnant would then depend entirely on the retention of enough suitable habitat to maintain sufficient numbers to withstand the risks of extinction (Soulé 1987*a*; Ewens et al. 1987). Some evidence exists that fragmentation of large populations into subpopulations may decrease the risk of overall species extinction even though local extinctions may occur (Higgs 1981; Quinn & Hastings 1987). It seems likely that different species will respond differently to the creation of subpopulations and that knowledge of the details of an organism's behavior will be necessary to predict its response (Karieva 1987; Merriam 1991).

3. CONNECTIVITY

Associated with the effects of distance is the degree to which individual remnants are connected in some way to adjacent areas. The issue of connectivity and the usefulness of corridors connecting remnants has received increasing attention in the literature (MacClintock et al. 1977; Wegner & Merriam 1979; Baudry 1984; Forman & Baudry 1984; Merriam 1984; Harris 1984, 1985; Fahrig & Merriam 1985; Noss & Harris 1986; Bridgewater 1987; Simberloff & Cox 1987; Noss 1987; Soulé et al. 1988), and was the subject of a recent symposium (Hobbs et al. 1990; Saunders & Hobbs 1991*a*). Corridors are generally believed to provide benefits such as enhanced biotic movement, extra foraging areas, refuges during disturbances, and enhancement of the aesthetic appeal of the landscape. In some areas they significantly add to the area of native vegetation left following fragmentation.

Simberloff & Cox (1987) pointed out that most of the work on the value of corridors has not been sufficiently controlled to demonstrate an unequivocal role in increasing immigration and/or decreasing extinctions. An increasing number of studies, however, now indicate that corridors are of value for movement, at least for a subset of the biota (papers in Saunders & Hobbs, 1991*a*). Simberloff and Cox (1987) also discussed potential disadvantages of corridors, which include facilitation of the spread of disease, pests, and fire and other disturbances, increased predation, and high costs of maintaining linear remnants with high edge:area ratios. The relative merits of corridors and their required characteristics (i.e., width, composition, etc.) will vary from place to place and will depend on the target species. Detailed predictions of corridor value in reducing isolation of remnant areas are not possible without information on the movement of individual species across the landscape. Such information is, however, difficult

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and time-consuming to collect (Saunders & de Rebeira 1991). Nevertheless, while such data are being gathered, we need to take the approach that corridors do have value for biotic movement and attempt to retain a good corridor network wherever possible (Harris & Scheck 1991; Saunders & Hobbs 1991*b*).

4. CHANGES IN THE SURROUNDING LANDSCAPE

Removal of the vegetation from the area surrounding a remnant leads to the remnant becoming the only area of suitable habitat remaining for biota displaced by clearing. This may lead to the concentration of mobile elements of the biota in the remnants (Lovejoy et al. 1986). This concentration or crowding effect may be rapid and result in supersaturation of the remnant by some species. Crowding can alter intra- and interspecific interactions. Competition and predation, for example, can be increased, resulting in changes in fecundity and the potential ultimate collapse of the population. Resource availability is also affected by overexploitation; for instance, increased herbivory by large herbivores such as the elephant in African reserves can lead to quite dramatic changes in habitat (Spinage & Guiness 1971; Laws et al. 1975; Walker 1981).

Supersaturation results from the influx of species native to the area, but there are also potential influxes of new suites of species that have increased in abundance or established in the surrounding landscape following fragmentation. Such species include those that have been introduced in the process of agricultural development (pasture and crop plant species and livestock), other deliberate and accidental introductions, and native or migrant species that can take advantage of the new habitat conditions caused by fragmentation.

Natural communities vary in their susceptibility to invasion, although there is still debate over which characteristics render one community more invasible than another (Fox & Fox 1986; MacDonald et al. 1986; Crawley 1987; Usher 1988; Rejmánek 1989). For vegetation, establishment of nonnative species seems to be enhanced by some form of disturbance, especially if this increases the availability of a limiting resource (Hobbs 1989; Panetta & Hopkins 1991). Thus the opening of light gaps in dense forests where light was limiting could enhance invasion, whereas in nutrient-limited systems, nutrient input significantly increases the performance of nonnatives, especially in conjunction with soil disturbance (Hobbs & Atkins 1988). Invasion may be restricted to the edge of remnants if disturbance factors decline with distance from edge (Cale & Hobbs 1991; Panetta & Hopkins 1991), but species with wind- or animal-dispersed seeds can establish in suitable areas within a remnant, away from the edge. Invading species can establish, for example, from seeds carried in by, or deposited in feces of, animals that feed in the area surrounding the remnant but use the remnant for shelter. An example from Western Australia is the Wedge-tailed Eagle (*Aquila audax*), which breeds or roosts in remnants but forages on carrion in the surrounding farmland, bringing parts of sheep carcasses back to the roost to consume them. Wool from carcasses carries seed that is dropped under the roost tree. Nutrient input from eagle droppings and the disturbance caused by other scavanging animals provides a focus for the establishment of nonnative species (Saunders, personal observation). Thus, even in the absence of deliberate disturbance within remnant areas, invasions may occur.

Invasive species can have significant impacts on the plant communities within remnants; for instance, invading plant species can significantly alter the fuel structure and hence fire regime, and can inhibit the regeneration of native species (Wycherly 1984; Macdonald et al. 1989; Panetta & Hopkins 1991). Nonnative herbivores, including stock, can also dramatically change vegetation structure and prevent regeneration. Species that increase because of landscape modification can also have significant impacts on the rest of the biota. For instance, in North America increased pressure from nest predators and parasites such as the Brown-headed Cowbird (*Molothrus ater*) has affected passerine bird populations in fragmented systems (Brittingham & Temple 1983; Wilcove 1985; Andren & Angelstam 1988). Similarly, the Galah (*Cacatua roseicapilla*) has moved into all agricultural areas in Australia as a result of the development of cereal cropping and the provision of watering points for stock (Saunders et al. 1985). It now roosts in remnant woodland areas, often competing with other indigenous hole nesters (Saunders & Ingram 1987; Saunders 1990), and can damage tree foliage and bark, in extreme examples causing tree mortality.

Modifying Influences

1. REMNANT SIZE

The smaller a remnant is, the greater the influence external factors are likely to have. In small remnants, ecosystem dynamics are probably driven predominantly by external rather than internal forces. Of importance here are "edge effects" (Williamson 1975; Janzen 1983; Harris 1988; Yahner 1988). Larger remnants have a bigger core area that is unaffected by the environmental and biotic changes associated with edges. Here, we regard edge effects as mainly detrimental; this is opposite to the traditional view that edges and ecotones are beneficial to wildlife (Harris 1988). The difference is that remnant edges are created by removal of the surrounding vegetation and place the remainder in juxtaposition with a completely altered surrounding matrix.

Noss and Harris (1986) have pointed out that we do not know the minimum critical size an ecosystem needs

to be to preserve its characteristic species diversity and species composition (Lovejoy & Oren 1981). In fact the "minimum dynamic area" of Pickett and Thompson (1978) or "the smallest area with a natural disturbance regime which maintains internal recolonization sources" would probably exist only in the largest conservation parks.

Larger remnants usually contain greater habitat diversity than smaller ones. A collection of smaller reserves may, however, cover a greater array of habitats than a single large one simply because a single large reserve will not contain all of the habitats likely to occur in a region. These arguments have been discussed in detail elsewhere and will not be pursued here. It is important, however, to recognize that the process of fragmentation is generally not random (Usher 1987). Land clearance usually occurs on a selective basis, with the best soil types being cleared first. For example, in southwest Western Australia, settlers selectively cleared woodlands because they occurred on the heavier soils best suited for agriculture. As a result, woodland communities are now poorly represented in conservation reserves and most woodland remaining on farms is in a highly degraded state (Saunders & Hobbs 1989). Few reserves in the area are large enough to contain representative samples of all preexisting vegetation types. Kitchener et al. (1980*a*, *b*, 1982) found, however, that even relatively small reserves (i.e., 30 ha) could be rich in some groups of fauna, but whether these populations are viable in the long term is debatable (see Saunders 1989).

Remnant size determines the potential size of populations of component species. Clearly, the number of individuals of any particular species that a given remnant will support depends on organism size and requirements. The larger the remnant, the more likely it is that populations will be large and more likely to resist chance extinctions (Gilpin & Soulé 1986; Soulé 1987*a*). Retaining populations in the long term may require large population sizes (of the order of hundreds or very much greater; Shaffer 1987), although the actual numbers required will depend on the life history and population growth rate of the species involved. Pimm et al. (1988) confirm that over a few decades extinction risk does decrease with population size, but they found no extinctions among British island birds numbering over 18 pairs. The issue of minimum population size has been discussed extensively in the literature (see Soulé 1987*b*), but there is still no real resolution as to what constitutes a minimum viable population. There has been extensive modeling of the concept, but little experimental work.

Larger populations tend to have higher levels of heterozygosity than small isolated populations. Current thinking is that heterozygosity is beneficial. Species that have gone through genetic "bottlenecks" are likely to suffer a reduction in heterozygosity with consequent loss of ability to adapt to changing conditions. Species isolated on remnants may go through such genetic bottlenecks because of small population sizes, and deliberate transfer of individuals between populations may be required (Boecklen & Bell 1987). However, the general assumption that heterozygosity is essential for long term population viability is still open to debate.

Large reserves may have some disadvantages; in particular, the possibility of disease spreading through entire populations on a large reserve has been discussed. However, there is a wide range of species' life histories and distribution patterns in the biota, and the effects of reserve size are largely species-specific. Species that have large area requirements or that require combinations of different habitats are likely to survive only in relatively large areas, whereas organisms with small, localized populations and simple habitat requirements can survive on smaller remnants. However, all will be affected by the disruption of physical ecosystem processes that result from fragmentation and were discussed earlier.

2. SHAPE

The shape of a remnant is important only for relatively small areas; there is some size beyond which shape does not really matter. However, for small remnants, shape determines the perimeter:core (or edge:interior) ratio. Long, thin remnants have proportionally much more edge than square or round remnants (Diamond 1975; Wilson & Willis 1975), and are more open to detrimental edge effects. However, some vegetation types, such as riparian strips, are naturally thin, and corridors are by definition generally long thin remnants (although the wider they are the more useful they may be to aid movement of biota; Saunders & Hobbs 1991*b*). Long, thin remnants may also, depending on their orientation, lie along environmental gradients and thus contain more vegetation types and habitats than a square reserve of similar area. Linear features are thus part of the natural and fragmented landscape, and there is no point in trying to develop optimal design principles that do not take them into account; the most important question is how to manage the remnants, whatever shape they are, so as to minimize external effects.

3. POSITION IN LANDSCAPE

The position of a remnant in the landscape has important influences on all the features so far discussed. It affects prefragmentation patterns of geomorphology, soil, and vegetation, and hence determines the structure and vegetation composition of any given remnant area. It also significantly affects postfragmentation processes.

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For instance, there is an important distinction between remnants that are predominantly run-on versus those that are predominantly run-off. This influences not only the hydrological regime of the remnant, but also the movement of soil, nutrients, and seeds into and out of the remnant area.

Lessons for Management

Management of fragmented ecosystems has two basic components: (1) management of the natural system, or the internal dynamics of remnant areas, and (2) Management of the external influences on the natural system. For large remnant areas, the emphasis should be on managing the internal dynamics, including, for instance, the disturbance regime and population dynamics of key organisms. For small remnants, on the other hand, management should be directed primarily at controlling the external influences. Janzen (1983, 1986), however, has pointed out that external influences can be important whatever the remnant size.

Since most impacts on remnant areas originate from the surrounding landscape, there is clearly a need to depart from the traditional notions of reserve management, and look instead toward integrated landscape management. It will become increasingly difficult to maintain remnants of native vegetation if the management practices in the surrounding matrix have continuous adverse impacts on them. Traditional reserve management stops at the reserve boundary; fluxes of water, particulates, and organisms do not. Placing the conservation reserves firmly within the context of the surrounding landscape and attempting to develop complementary management strategies seems to be the only way to ensure the long term viability of remnant areas (Hobbs & Saunders 1991). This has important implications for land managers since it involves a radically new way of viewing management and requires that neighboring land uses, and hence neighboring landowners, interact in a positive way. This is difficult, but not impossible, and there are encouraging examples of attempts at this type of integrated management (e.g., Fitzgerald Biosphere Project 1989; Bradby 1991).

The landscape approach to management is also essential since several remnant areas taken together may represent a system over which components of the biota travel to meet habitat and food requirements. The loss of a single component of such a network could severely affect the capability of the remaining remnants to carry out the same functions, if for instance a particular species or habitat was lost. Such a network consists not only of the designated reserves, but also other remnant areas and linkages between them.

The goal of conservation management usually is to maintain species diversity, and the method of achieving this is to attempt to maintain representative examples of each ecosystem or community type present before fragmentation. To do this, we need to know the distributions of species and communities and then select areas that represent them. In general, there are two possible scenarios. In the first, we have a system that is about to be fragmented and we have to design the ideal set of reserves for the area. In the second, we have an already-fragmented system that we need to make the most of. Most theories in conservation biology, including virtually all the discussions of island biogeography in relation to reserves, have dealt with the first scenario, whereas it is the second scenario that we most frequently have to confront. Here we present a series of guidelines for management in this situation.

1. The initial step must be to determine the minimum subset of the existing remnants that are required to represent the diversity of a given region (Margules et al. 1988; Margules & Stein 1989). This requires that we have some knowledge of the distribution of species or ecosystem types. Clearly, it would be desirable to have all existing remnants available for this purpose, but in many cases this is not achievable, and there must be priorities for reserve retention or acquisition.

2. The system must then be managed to maintain the diversity of species or ecosystems. The question of whether management should be for individual species or whole ecosystems is largely irrelevant, because individual species require functioning ecosystems to survive. Management guidelines will be area-specific, but the need to manage external influences is universal.

3. Priorities for management must be established. Clearly there are many problems to be tackled, and usually there are limited resources available for the job. There must therefore be a clear priority ranking to ensure that resources are deployed optimally. Problems that are likely to disrupt ecosystem processes and hence threaten the viability of a remnant area should be given high priority for treatment.

4. Continuous management is needed to maintain remnant areas in their current state, due to the constant pressure of altered internal dynamics and external influences. Here again, the allocation of scarce management resources must be considered. Effort should go into maintaining some remnant areas in as near a "natural" state as possible, but it will not be feasible to do this for all remnants. There is a strong case to be made for letting some areas degrade so that they become less natural but are easier to manage and still retain some conservation value (Bridgewater 1990). This is not as radical as it may sound, since the process is ongoing in many remnant areas anyway. Once we accept that many remnants now contain "synthetic" communities that are not likely ever to return to their pristine state, management priorities become easier to set.

Research Requirements

Research to date on fragmented ecosystems has provided few answers on the issues of practical importance to management. It is just as important to set priorities for research as for management, and in the same way, research costs must be taken into account since resources for research are also limited. For instance, is it better to concentrate on single-species studies that can produce results with direct practical application but are very costly and time-consuming, or should we concentrate on the community/ecosystem approach that is cheaper but may yield more equivocal results? Clearly, balanced use of both approaches is needed. We have identified a number of priority areas that require research effort (see also Soulé & Kohm 1989).

1. A major priority is to understand the effects of external factors. Comparisons of pre- and postfragmentation systems will be particularly useful (Lovejoy et al. 1986; Margules 1987). Effects of changes in radiation and water fluxes are particularly important, as is the biotic invasion process.

2. Changes in internal processes since fragmentation also require further investigation. In particular, the interaction between internal and external processes is likely to be of critical importance.

3. Isolation factors need to be better understood. In particular, rates of genetic change in isolated populations require study, as does the question of whether reduction in genetic variability is important. We also require more and better data on the role of corridors in allowing biotic (and hence genetic) movement in fragmented landscapes.

4. While theoretical studies have their place, there is an urgent need for field experimentation in both management and restoration. While such experiments are costly to set up, it is possible to make use of many situations that offer ready-made experiments. Our understanding of succession has benefited greatly from the study of abandoned old fields, and in the same way, we can use current or past management activities as large-scale experiments; there is plenty of experimental material around (McNab 1983; Hopkins & Saunders 1987; Pimm 1986; Jordan et al. 1987; Hobbs & Hopkins 1990). Research has much to gain from a close liaison with management, especially if management operations actually can be carried out as designed experiments and the results suitably monitored.

Conclusions

Emphasis in the literature has been on the design of nature reserves, but we are usually too late to do anything except try to maintain the remnants left following fragmentation. Emphasis also has been on biogeographic explanations for the patterns of species loss after fragmentation, whereas a whole suite of physical and biotic parameters are significantly altered in the fragmented system and have significant impacts on remnant biota. In particular, the switch from predominantly internally driven to predominantly externally driven dynamics is a key factor in the fragmented system. Management and research should focus on this factor. There is a pressing need for an integrated approach that treats the landscape as a whole instead of as a collection of separate biotic and legal entities.

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SCALING SWAINSON'S HAWK POPULATION DENSITY FOR ASSESSING HABITAT USE ACROSS AN AGRICULTURAL LANDSCAPE

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ABSTRACT.—By integrating population density estimates of Swainson's hawk (*Buteo swainsoni*) from other studies, I found that the areas within study boundaries consistently support much higher densities of Swainson's hawk than do the surrounding areas, and most of the variation in density was explained by the spatial extent of study. Therefore, I designed a sampling program to express habitat use across multiple potential clusters of home ranges, thereby representing the population-level interaction with the agricultural landscape of the Sacramento Valley, CA. I mapped 162 observations of Swainson's hawks in 5 yr of surveys (110 surveys) along a 204-km road transect from a car traveling at 80–88 kph. Based on use and availability of landscape elements along the transect, Swainson's hawks "preferred" riparian habitat, grassland, alfalfa stands >2 yr old during irrigation and mowing, and annual field crops during harvest. Hawks "avoided" most other crops, tilled fields, and built-up areas.

KEY WORDS: *Agriculture*; *alfalfa*; Buteo swainsoni; *density*; *road survey*; *Sacramento Valley*; *Swainson's hawk*.

Escalamiento de la densidad poblacional de *Buteo swainsoni* para evaluar uso de hábitat a través de un paisaje agrícola

RESUMEN.—Por integración de densidades poblacionales de *Buteo swainsoni* estimadas en otros estudios, encontré que áreas de borde, en estudio, consistentemente soportaban mayores densidades de esta especie que las áreas vecinas y la mayoría de la variación en densidad era explicada por la extensión espacial del estudio. De manera que diseñe un programa de muestreo para expresar uso de hábitat a través de racimos potenciales multiples de rangos de hogar, representando asi, la interacción a nivel poblacional con el paisaje agrícola de Valle de Sacramento, California. Se mapearon 162 observaciones de *B. swainsoni* en cinco años de recorridos (110 recorridos) a lo largo de un transecto carretero de 204 km, realizado en un vehículo viajando a 80–88 kph. Basados en el uso y disponibilidad de elementos del paisaje a lo largo del trahsecto, *B. swainsoni* "prefirió" hábitat ribereños, praderas y campos de alfalfa mayores a dos años de antiguedad durante la irrigación, corte y durante la cosecha anual de los campos. *Buteo swainsoni* "evitó" otros tipos de cosechas, campos cultivados y áreas de construcción.

[Traducción de Ivan Lazo]

Knowledge of the ecological resources needed by the Swainson's hawk (*Buteo swainsoni*) is important because the species is thought to have declined radically in California (Bloom 1980), and is now listed as threatened there. This knowledge is also important because Swainson's hawk management decisions, including mitigation for development, and state and federal recovery plans, affect large investments in agriculture and construction. Swainson's hawk populations are threatened by land conversions and management decisions that leave enough ecological resources for only a minimum existence (Wilcox 1989).

Most Swainson's hawk habitat-use studies occurred within small areas immediately around nest trees or within home ranges (e.g., Gilmer and Stewart 1984, Estep 1989, Bechard et al. 1990). These intensive studies were typically constrained to small geographic areas because they were expensive and thus were required to be focused on a small number of individuals. The results of these local studies sometimes have been extrapolated to estimate habitat use in larger regions (e.g., Bloom 1980, Bednarz and Hoffman 1988), which then could be used for management decisions, without making adjustments for changes in landscape attributes nor for changes in Swainson's hawk spatial pattern.

The regional context is usually excluded from analyses during population and habitat-use studies. Such intensive studies of most species usually occur where the investigator(s) had *a priori* knowledge of high density (Schonewald and Smallwood in press).

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The home range is often viewed as the spatial requirement of a species, so habitat associations are derived from observations within the home ranges. But nesting pairs choose locations for their home ranges from among many potential locations within their historic geographic range. Studies at high-density sites might not provide all the information that is needed for management of the Swainson's hawk at a regional scale. Density estimates and habitat use at small study sites could be reliably extrapolated to the region only if Swainson's hawks and habitats (and land use) are uniformly distributed across the landscape. Distribution maps of nesting pairs suggest that Swainson's hawks in California are highly aggregated (Bloom 1980, Schlorff and Bloom 1984, Estep 1989). The clusters of nest sites are where most investigations have been conducted (Schmutz et al. 1980, Gilmer and Stewart 1984, and Estep 1989).

In this paper I first test whether Swainson's hawks are uniformly distributed across studied landscapes, which would be a necessary condition for extending the results of population and habitat-use studies to larger areas. Then I complement results of intensive studies with those of a survey along an extensive road transect in the Sacramento Valley, California. The road transect was designed to sample a geographic area that was much larger than conventional population and habitat-use study areas of the valley's largest birds and mammals, and the types of agriculture that occur in the valley (Smallwood et al. in press). By exceeding the areas of conventional habitat-use studies, I was able to critically analyze the effects of agricultural crops and practices on a Swainson's hawk population.

METHODS

Scaling Population Density. From 26 population estimates in 16 research reports of Swainson's hawk studies, I recorded every estimate of nesting density within each geographic area defined for study. I used the geometric mean for multi-annual estimates made at a site. Schmutz (1984) was not used because he sampled only 4.4% of his 74 686 km² study area. Log_{10} transformed estimates of nesting density (pairs per square kilometer) were tested for linear relationships with the spatial extent of studies with the equation:

$$\text{Log}_{10}(\text{nesting density}) = a - b \times \log_{10}(\text{area}), \quad (1)$$

where a and b are the intercept and slope coefficients to be estimated with least squares regression. Model precision was assessed by examining the coefficient of determination (R^2), the root mean square error of the residuals (RMSE), and the pattern of residuals plotted against study area. The spatial pattern of Swainson's hawks across studied landscapes is increasingly homogenous (aggregated to random to uniform) as the regression slope approaches 0 in equation (1). If the hawks' spatial pattern is found to be far from homogenous, then density estimates and habitat associations cannot be reliably extrapolated to areas that are larger than the conventional study areas.

Habitat Associations. My road transect was designed to sample wildlife populations across a large geographic area in which interactions between species and the landscape could be measured. It was designed to sample interspersed landscape elements in the Sacramento Valley, including the major types of agriculture produced (field crops, rice, orchards, and pasture), along with urban and rural areas, riparian habitat, and grassland and wetland habitats in protected areas. It was also designed to provide extensive north-to-south and east-to-west coverage. The road transect was 204 km in seven segments (to provide rest periods for the investigator) along a 320-km loop around the Sutter Buttes (described further in Smallwood et al. in press).

I surveyed for wildlife from the passenger seat of a car driven at 80–88 kph at 1 wk to 1 mo intervals. Surveys always began 0700–0930 H, and typically lasted 5 hr. For multiple bird and mammal species, I recorded the species, activity, land-use/habitat association, location to the nearest 0.16 km, and side of road where the observation occurred. I mapped the crops immediately along the transect, including tilled fields, crop residues, and agricultural activities such as harvest, irrigation, and tillage. Swainson's hawk observations from 3306 km of survey (57 surveys) along the first 58 km of the transect (Davis to Sutter National Wildlife Refuge) were related to land-use and habitat elements based on the proportional occurrence of each (after Smallwood 1993, Smallwood et al. in press).

Swainson's hawk's use of alfalfa fields was further investigated during a 2-yr (1992–94) study of pocket gopher (*Thomomys bottae*) spatial dynamics in 36 Sacramento Valley alfalfa fields (Smallwood and Geng 1993b). While mapping gopher burrows by walking along borders of irrigated fields, I recorded Swainson's hawk visits from 0630–1200 H, March to September. I compared the number of visiting Swainson's hawks with my time spent in alfalfa fields of various ages and harvest phases; i.e., mowing, raking, baling hay, collecting bales.

RESULTS

Scaling Population Density. Nesting Swainson's hawks were aggregated across studied landscapes. The regression slope was significantly different from 0 ($P < 0.0001$) and substantially different from corresponding with homogeneity (Fig. 1A). The nesting density at the smallest study area was 124 times greater than the density at the largest study area when calculated from the regression, and the real difference was 310-fold. Also, the average number of pairs per 1 km² was calculated from the regression to be 2.2, which is more than can be expected at any randomly selected site across the Swainson's hawk

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nesting range. Therefore, the Swainson's hawk studies used in the regression analysis were consistently conducted at sites where Swainson's hawk population densities were much higher than across the surrounding, unstudied areas.

All of the density estimates were made after intensive ground searches for nests, although Platt (1971) included aerial searches and Littlefield et al. (1984) searched from the road. The searches were reported to be complete or inclusive of all nests in 56% of the studies and 70% of the density estimates. However, whether or not the search was reported to be complete did not influence the residual variation that remained after density was regressed against study area (Independent samples $T = 0.59$, df = 19, $P = 0.56$). Instead, this residual variation appeared to cycle with a periodicity of about 10 yr (Fig. 1B). This possible, range-wide population cycle could not have been recognized from the existing data without removing the variation in density due to the spatial extent of study area.

Habitat Associations. I made 162 Swainson's hawk observations during the entire road survey, but only 130 were used in the habitat-use analysis from the cumulative 3306 km along the first 58 km of transect during March to October. My observations were nearly evenly distributed among months from March ($N = 24$) until October ($N = 13$). Most (82%) were of birds in flight, 11 (7%) were on trees, five (3%) were on the ground, and 7% were on artificial structures such as utility poles and fence posts. Swainson's hawks occurred more often than expected by chance in alfalfa, riparian, and grassland habitats, where they occurred throughout the breeding season (Fig. 2A). The remainder of the landscape elements were used by Swainson's hawks preferentially only during brief periods of opportunity; e.g., in tomato fields 21.7 times more often during harvest than expected by chance. The 16 Swainson's hawks I saw at tilled fields were during early spring and fall when most of the landscape was tilled or being tilled (Fig. 2B). Rice stubble left through the winter was used by Swainson's hawks during early spring, but overall rice stubble was avoided by Swainson's hawks. Safflower and some other crops were never used, not even after harvest (Fig. 2A).

Both the road survey and gopher sampling revealed that Swainson's hawks used alfalfa most often while those fields were being irrigated, and secondly during hay harvesting (Figs. 3 and 4). These preferences were greatest in alfalfa that was 3–4 yr old

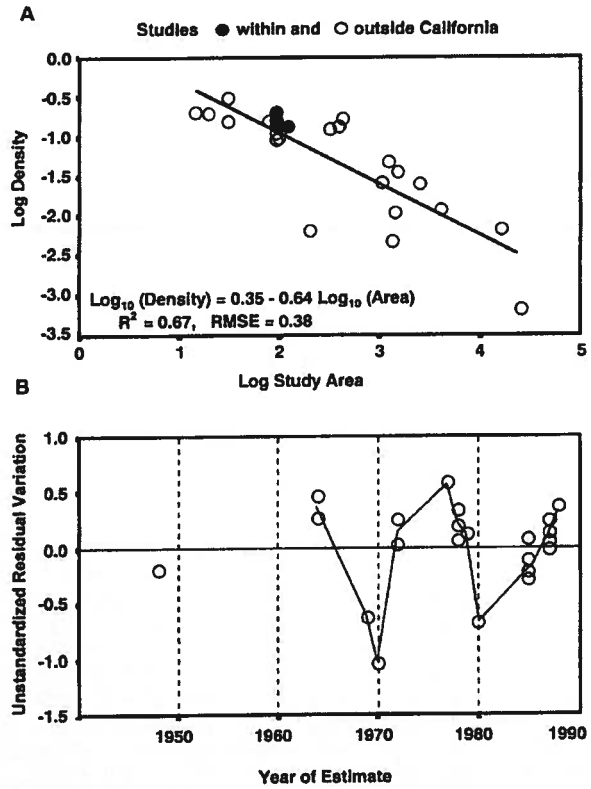

Figure 1. Log-transformed estimates of Swainson's hawk population density decrease linearly with increasing log spatial extent of study area (A), and the residuals suggest an approximately 10-yr population cycle (B) fit by lowess smoothing on 20% of the data. Estimates were from Craighead and Craighead (1956), Platt (1971), Smith and Murphy (1973), Olendorff (1975), Dunkle (1977), Fitzner (1978), Bloom (1980), Schmutz et al. (1980), Bechard (1983), Littlefield et al. (1984), Bednarz and Hoffman (1988), Gilmer and Stewart (1984), Estep (1989), Restani (1991), and Bosakowski and Ramsey (unpubl. data).

(Figs. 3 and 4B). All of the 31 Swainson's hawks seen in alfalfa fields during the road survey were at fields being irrigated, which comprised 0.02% of the transect. Thus, Swainson's hawks were 858 times more likely to occur at mowed and irrigated alfalfa fields than if they occurred randomly along the transect.

DISCUSSION

Scaling Population Density. Most of the variation in Swainson's hawk density was explained by

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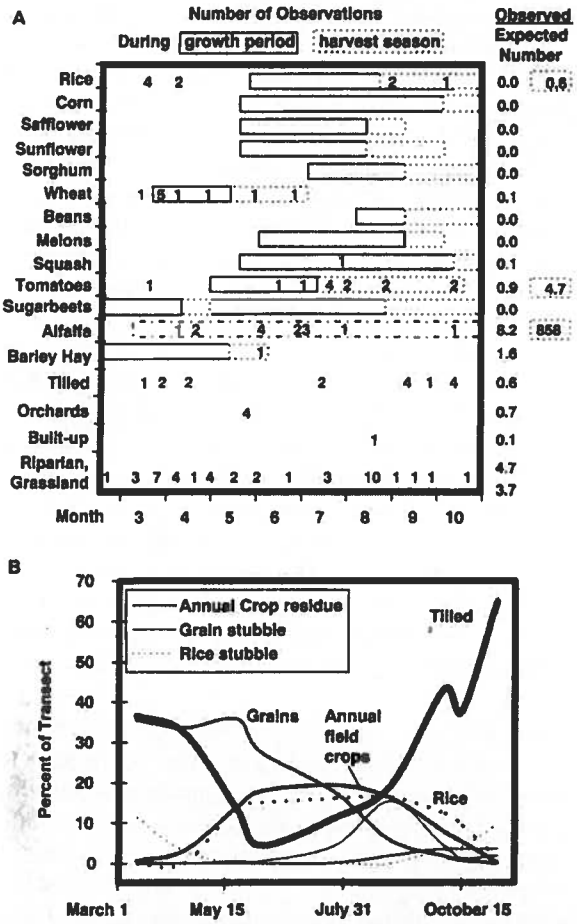

Figure 2. The Swainson's hawk distribution among habitats during the nesting seasons of 1990–94 (A) and the 1993–94 moving average of agricultural field conditions expressed as a percent of the southern 58 km of the road transect (B). Expected values are the total number of hawks observed multiplied by the proportion of each habitat in the sample.

the spatial extent of study, consistent with results for other species (Schonewald and Smallwood in press). This means that most study methods have little influence on density estimates, if the methods are rigorous. Except for Schmutz (1984), the residual variation in density estimates based on different methods plotted precisely along the lowess curve that suggests a population cycle (Fig. 1B). Clearly, results from conventional studies cannot be extrapolated to larger geographic areas without at least making analytical adjustments for the change in spatial scale.

Judging from the scientific literature, investigators were previously unaware of the magnitude to which density changes with the spatial extent of study. Bloom (1980) multiplied his density estimate in the Klamath Basin by 0.25 (25% of the then known maximum density in California) to estimate the population size across the Swainson's hawk's historical range in California, which was estimated from topographic maps, field surveys, and the literature. Bloom's minimum estimate was 4284 pairs and his maximum estimate was 17 136 pairs. Using the model in Fig. 1, I calculated a mean population 404 pairs (SD = 166) across this historic range, which falls between the estimates of 375 and 550 pairs for 1979 (Bloom 1980) and in 1988 (California Department of Fish and Game 1990), respectively, and which is much less than Bloom's historic estimates. But my calculation should not be expected to be a reliable estimate of the historic Swainson's hawk population. The regression model in Fig. 1 can provide precise estimates within the data range (high to low values of densities and study areas), but is less reliable for an estimate across the historic distribution, because we do not know whether the log-log relationship between density and area remains infinitely linear. The habitat conditions have been altered radically, so there could have been more Swainson's hawks based on habitat availability. Nevertheless, the population might not have been much larger because it was naturally aggregated despite habitat availability, and the regression model showed that study areas such as Bloom's (1980) typically have much higher densities than areas not studied.

Study areas may be fundamentally different from the surrounding areas. The average square kilometer of land does not support 2.2 pairs of Swainson's hawks as predicted by the regression model in Fig. 1. Study areas are probably dissimilar to unstudied areas in terms of habitat conditions, but habitat-use studies only occur within the boundaries of study areas. Little connection has been made between habitat conditions on study areas and those beyond the study boundaries. Therefore, different habitats on study areas are used significantly more and less than if the study boundary encompassed a much larger geographic area. My road survey was designed to complement conventional habitat-use studies by linking habitats in areas of Swainson's hawk aggregations with habitats in the surrounding landscape. Other road surveys have been conducted for Swain-

son's hawk habitat use, but the transects were arranged for a more intensive survey within the area of aggregations.

Habitat Associations. My survey design resulted in conclusions about habitat use by Swainson's hawks which differed from other reported studies. Swainson's hawk use of riparian habitat, grassland, and alfalfa were greater in my study, probably because the greater spatial extent of study provided a much lower estimate of the availability of these habitat types. In my study Swainson's hawks seemed to avoid irrigated pasture, tilled fields, annual field crops, and developed areas, probably because the availability of these habitat types was much greater across the larger landscape.

My results also show that the majority of the agricultural landscape is inhospitable to nesting Swainson's hawks most of the time (Fig. 3). Prey availability is usually greater during crop harvest when prey are exposed by the removal of the canopy that persisted during the growth period. Swainson's hawks opportunistically forage over field crops during or just following harvest or irrigation. But these opportunities occur briefly at each field. The brief foraging opportunities in alfalfa occur mostly in fields at least 2.5 yr old, after prey populations have increased to sufficient levels (Smallwood and Geng 1993a,b).

Conservation Implications. The most effective opportunities for Swainson's hawk conservation might be in the management of agricultural landscapes where nesting and foraging habitat limit population size. Swainson's hawk nesting density increased in cultivated areas where tree density (Schmutz 1984) and prey availability (Bechard 1982) were highest. Swainson's hawk conservation would benefit substantially from the protection and restoration of riparian forests with large cottonwoods and oaks, and by managing field borders, road verges, and canal banks as strip corridors of grasses and shrubs. The lack of movement corridors for small mammals in the Sacramento Valley probably decreased populations of small mammals (Smallwood 1994) which are prey of Swainson's hawks. Pocket gophers, one of the important prey species (Bechard 1982, 1983, Gilmer and Stewart 1984, Restani 1991), are controlled in many alfalfa fields because they are thought to reduce alfalfa yields. Vertebrate pest management could be altered to the benefit of Swainson's hawk by better understanding the relationship between "pests" and agricultural crops. Van Vuren and Smallwood (in press) described many alternative vertebrate pest management strategies, most of which are not currently used. Even orchards and vineyards, which are generally considered to be poor Swainson's hawk foraging areas, can provide habitat for prey when cover crops are grown. Cover crops serve as habitat and alternative food (rather than the commercial crop) for small mammals, which will disperse into habitats that are more accessible to foraging Swainson's hawks. Thus, agriculture might actually benefit Swainson's hawks so long as the critical resources are maintained and/or enhanced.

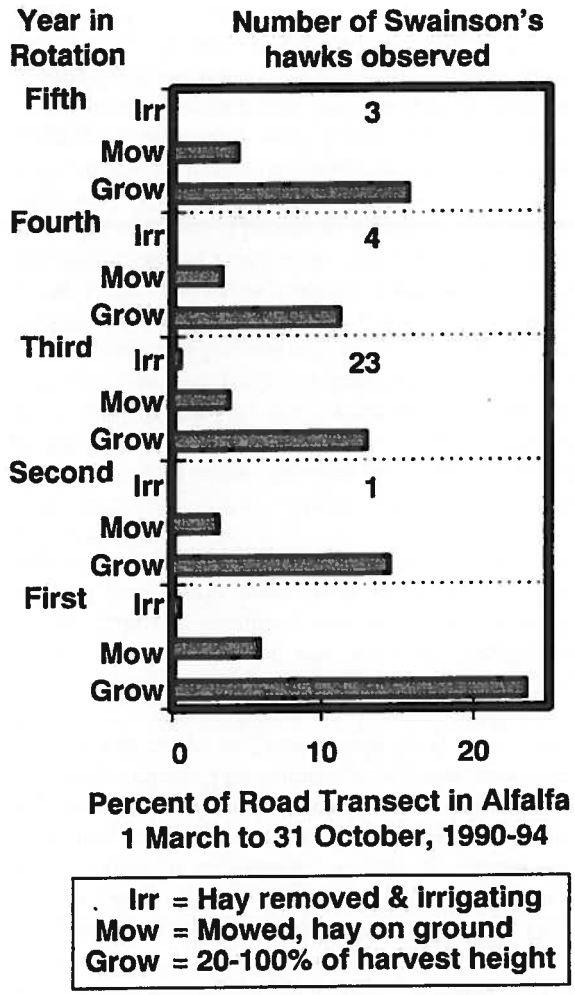

Figure 3. Swainson's hawk occurrences at alfalfa fields along the road transect.

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IMPACTS OF THE WEST NILE VIRUS EPIZOOTIC ON THE YELLOW-BILLED MAGPIE, AMERICAN CROW, AND OTHER BIRDS IN THE SACRAMENTO VALLEY, CALIFORNIA

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Abstract. After spreading across North America, West Nile virus (WNV) arrived in the Sacramento Valley of California in 2004 and began killing many corvids. To estimate the regional effect of WNV on corvids and other birds, we reinitiated a road survey along six routes totaling 203 km in the Sacramento Valley. We surveyed these transects 30 times in fall and winter from 1990 to 1995 and repeated the surveys each fall and winter from 2005 to 2008. By 2007–08, annual maximum counts of the Yellow-billed Magpie, American Crow, and Loggerhead Shrike had declined 83%, 63%, and 63%, respectively, from those of the 1990s. These species declined in riparian and rice-cultivation areas, most substantially outside Yolo County. The magpie declined 90% along our routes north of Yolo County, causing us concern for the viability of the species. After a lag, the crow began declining quickly in 2007. We recommend the Yellow-billed Magpie be given special status. Also, searches for Yellow-billed Magpies should be extended across the species' range to find locations with sizable numbers, and experimentally designed mosquito control should be considered in breeding areas, especially in areas of high densities of *Culex* mosquitoes.

Key words: *American Crow, California,* Corvus brachyrhynchos, Pica nuttalli, *West Nile virus, WNV, Yellow-billed Magpie*

Impactos del Virus del Nilo Occidental Epizoótico sobre *Pica nuttalli*, *Corvus brachyrhynchos* y Otras Aves en el Valle de Sacramento, California

Resumen. Luego de dispersarse a través de América del Norte, el Virus del Nilo Occidental (VNO) llegó al Valle de Sacramento en California en 2004 y comenzó matando a muchos córvidos. Para estimar los efectos regionales del VNO sobre los córvidos y otras aves, reiniciamos un censo a lo largo de carreteras en seis rutas totalizando 203 km en el Valle de Sacramento. Muestreamos estos transectos 30 veces en el otoño y el invierno desde 1990 a 1995 y repetimos los muestreos cada otoño e invierno desde 2005 a 2008. Para el periodo 2007–08, los conteos máximos anuales de *Pica nuttalli*, *Corvus brachyrhynchos* y *Lanius ludovicianus* habían disminuido en un 83%, 63% y 63%, respectivamente, comparados con los conteos de la década de los noventa. Estas especies disminuyeron en las áreas ribereñas y de cultivo de arroz, sobre todo en las afueras del Condado de Yolo. *P. nuttalli* disminuyó 90% a lo largo de nuestras rutas al norte del Condado de Yolo, generándonos preocupación sobre la viabilidad de esta especie. Luego de un periodo de retardo, *C. brachyrhynchos* comenzó a disminuir rápidamente en 2007. Recomendamos que se le dé estatus especial a *P. nuttalli*. También, se deberían extender las búsquedas de *P. nuttalli* en el área de distribución de la especie para encontrar localidades con números considerables de individuos y se deberían considerar diseños experimentales para el control de los mosquitos en las áreas de cría, especialmente en las áreas con altas densidades del mosquito *Culex*.

INTRODUCTION

After causing large-scale declines among some bird species—particularly members of the family Corvidae—as it spread westward across North America (Kilpatrick et al. 2007, LaDeau et al. 2007), West Nile virus (WNV) arrived in the Sacramento Valley, California, during 2004 (Reisen et al. 2006). By summer 2005 thousands of Yellow-billed Magpies (*Pica nuttallii*) and American Crows (*Corvus brachyrhynchos*) had been reported dead in cities and towns throughout the valley (Crosbie et al. 2008), and statewide declines of these and several other species had been indicated by the U.S. Geological Survey's North American Breeding Bird Survey (BBS) (Koenig et al. 2007). Concern over the effect of WNV on Yellow-billed Magpie populations increased, especially during and following the 2005 breeding season. The Sacramento Valley constitutes a substantial portion of the Yellow-billed Magpie's small geographic range, so the many deaths observed in the valley raised concern for the species' future. Although thousands of fatalities were documented among corvids in California, however, the dearth of scientific monitoring of corvid abundance before the epizootic made

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quantifying the biological effects of WNV difficult. Crosbie et al. (2008) reported post-epizootic reductions in Yellow-billed Magpie numbers of 22% on the basis of BBS data and of 42% on the basis of Christmas Bird Counts (CBC), but their sample sizes were small.

To estimate the effects of WNV on the Yellow-billed Magpie and other birds in the Sacramento Valley, in 2005 we reinitiated a road survey we had conducted during the 1990s. Our survey was designed to detect numerical trends among bird species and to estimate associations between bird species and landscape elements (Smallwood et al. 1996). Our objectives for the reinitiated surveys were to compare numbers and spatial distribution of the Yellow-billed Magpie and American Crow along our survey routes before and after the epizootic of 2004. We also compared associations with land-cover types and behaviors to test whether the magpies and crows might have altered their routines in response to the epizootic. Finally, we compared pre- and post-epizootic survey data for other species to identify which might also be affected by WNV, and we related changes in relative abundance to percentages of dead birds testing positive for WNV during dead-bird surveillance (Wheeler et al. 2009).

METHODS

Following methods summarized by Smallwood et al. (1996), Nakamoto drove an auto at 48 to 88 km hr^{-1} along six routes totaling 203 km of a 322-km loop (Fig. 1), while Smallwood surveyed for birds by scanning both sides of the road equally. From September through early March 1990–1995, we surveyed along the 203 km of transect 30 times, then we repeated the surveys 10 times in 2005–06, seven times in 2006–07, and five times in 2007–08. Survey intervals were about monthly from 1990 to 1995, every two weeks in 2005–06, every three weeks in 2006–07, and about monthly in 2007–08 and were influenced by weather and road conditions. Surveys started at 08:15 to 09:15. We recorded observations into a digital voice recorder and later transcribed them to an electronic spreadsheet. We recorded species, number of individuals in the group, location on the route in 0.16-km (0.1-mile) increments, side of the road, whether in the roadway, the road verge, or beyond the road verge, whether flying or perching, type of perch if the bird was perching, and land-cover type associated with the bird's location.

Route 1 began in Yolo County along Road 102 from Covell Blvd. in Davis (Fig. 1). It extended north to Highway 113 through Knights Landing into Sutter County, to George Washington Blvd., to O'Banion Rd., and along the eastern levee of the Sutter Bypass and Sutter National Wildlife Refuge. Route 2 began along Hughes Rd. at the east levee of the Sutter Bypass, extended west to Progress and Moroni roads, and ended at Meridian Rd. and the Sacramento River. Route 3 was Highway 45 from Meridian to Colusa in Colusa County. Route 4 was Maxwell Rd. from Highway 45 to Interstate 5 in Colusa County. Route 5 was along Norman and Princeton roads, from Interstate 5 to Highway 99 in Glenn and Butte counties. The Princeton ferry provided passage across the Sacramento River in the 1990s, but from 2005 to 2008 we had to detour the ferry and backtrack to the river from Afton. Route 6 started along Forty Mile Rd. at Highway 65 and extended south to Pleasant Grove Rd. and to Riego Rd. in Yuba and Sutter counties, from which it extended west until Power Line Rd. and turned south again into Sacramento County to Interstate 5.

Land uses along route 1 consisted mostly of annual field crops rotated with alfalfa and were typically grown for 4 or 5 years. There were a few parcels of irrigated pasture, but the rest of the route was cultivated in rice and orchards. There were homes, commercial businesses, and industry, mostly clustered along the southern section of the route. The Yolo County portion of route 1 was dominated by field crops, the Sutter County portion by rice cultivation. Route 2 was similar to route 1 but without commercial or industrial land uses. Route 3 was dominated by irrigated pasture and rice cultivation, with some field crops. Route 4 consisted of rice cultivation and marsh. Route 5 was dominated by rice cultivation, field crops, and marsh, along with some urban and rural residences and some riparian areas. Route 6 was dominated by irrigated and dry pasture, followed by rice cultivation, field crops, orchards, and rural residences. Along all six routes there were reaches of riparian forest, riverine conditions, farm houses, fallow fields, grasslands, and patches of ruderal vegetation. We mapped land uses along the routes to monitor shifts in land use through time.

During our surveys agricultural fields were managed for winter. Many fields were disked or prepared in furrows for spring planting. Rice had been harvested by late September, so most rice fields were either tilled, left in stubble, or rolled and flooded to a shallow depth. Alfalfa was dormant from November through February. Large storms heavily flooded some areas, making them inaccessible during a few surveys (we adjusted detection rates and hypothesis tests accordingly).

There were a few differences in the landscape between the 1990s and 2005–08. Residential and commercial development replaced grassland and field crops along 5 km of route 1 near Woodland. A machine yard was expanded 0.3 km on one side of route 1. Along one side of route 2, a 1.4-km stretch was graded and contoured for wetland creation in 2006; it was flooded and had attracted wetland birds by 2007. In 2006, 1.6 km of route 5 was planted in trees and shrubs for restoration of riparian forest, and another 0.8 km stretch was planted in willows in a restoration effort. An outdoor theater replaced pasture along 0.5 km of one side of route 6. Along one side of route 6, 5 km of field crops was graded in 2005 but as of 2008 still not developed. Two orchards were removed, and orchards were planted in new locations. Some valley oaks (*Quercus lobata*) were cut down in several locations, and a few homes were built in rural areas.

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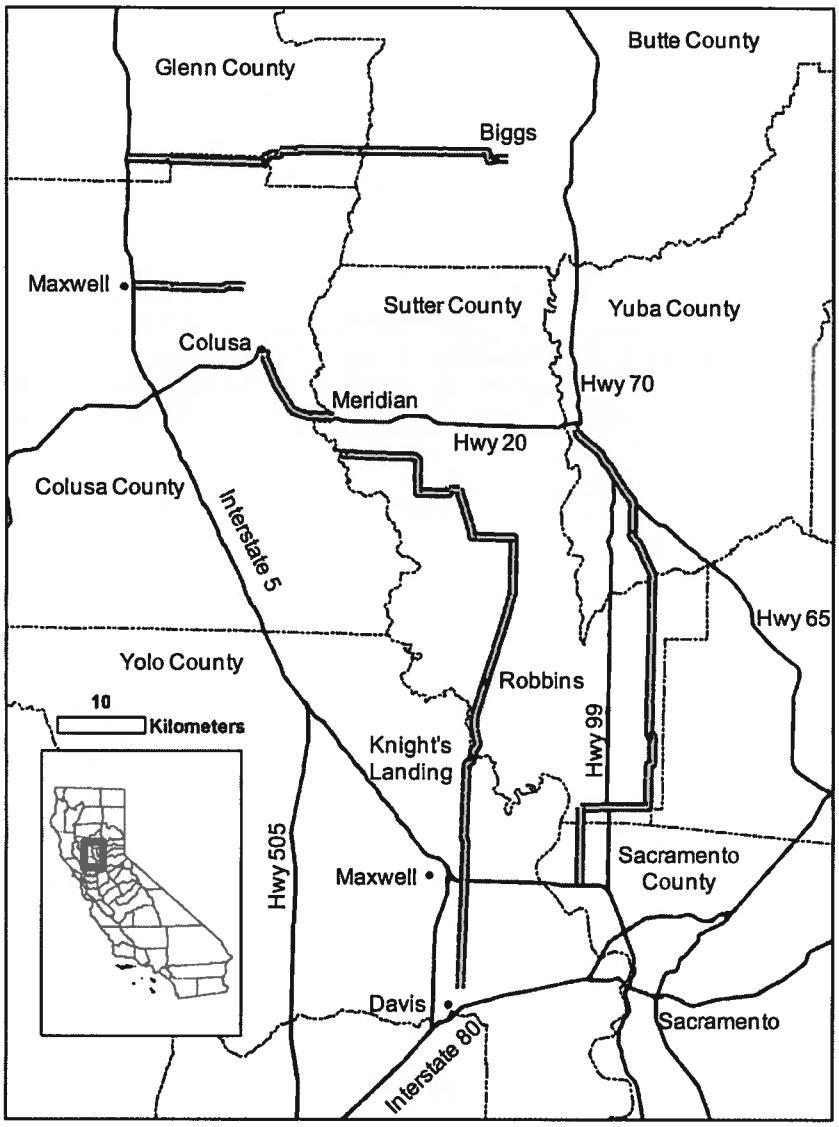

FIGURE 1. Survey routes (double lines with shade fill) for bird monitoring during the early 1990s and the winters of 2005–06 through 2007–08 within the Sacramento Valley, California. Dashed lines denote county boundaries and solid lines denote highways.

STATISTICAL ANALYSES

We compared annual maximum counts in 1990–95 with those in 2005–08 by using independent-samples *t*-test, assuming equal variances if $P > 0.05$ in Levene's test for equality of variances and assuming unequal variances otherwise. We tested hypotheses of habitat use with Pearson's chi-squared. We used two-way Pearson's correlation tests and analysis of variance to test whether changes we measured in relative abundance by species were related to WNV-risk data reported by Wheeler et al. (2009), including the percentage of dead birds testing positive for WNV and an associated risk index, percent mortality in experimental infections of live birds, host competence in experimental infections, and an overall risk score. We used statistical software developed by SPSS, Inc., for data management and hypothesis testing.

RESULTS

RELATIVE ABUNDANCE

From 1990–95 to 2005–08, on the basis of *t*-tests seven species increased and two decreased (Table 1). Notably increased were the Common Raven, White-faced Ibis, Sandhill Crane, Belted

TABLE 1. Comparisons of maximum counts per 100 km during road surveys between the four winters of 1990–1995 and the three winters of 2005–2008 by the independent-samples *t*-test, and change from 1990–95 and 2007–08 as an indicator of recent trend (no test). Under status, CT = California threatened, CFP = California fully protected, SSC2 = second-priority species of special concern (Shuford and Gardali 2008), SSC3 = third-priority species of special concern.

		t-test, 1990s to 2005–08			
Species	Status	t_6	*P*	Change (%)	Change, 1990s to 2007–08 (%)
Double-crested Cormorant, *Phalacrocorax auritus*		−1.67	0.150		+48
Great Blue Heron, *Ardea herodias*		−3.03	0.023	+39	+17
Great Egret, *Ardea alba*		−1.99	0.094	+49	−7
Snowy Egret, *Egretta thula*		−1.51[a]	0.257		+32
Black-crowned Night-Heron, *Nycticorax nycticorax*		1.76[a]	0.153		−100
White-faced Ibis, *Plegadis chihi*		−8.14	0.000	+1119	+1320
Turkey Vulture, *Cathartes aura*		−1.21	0.270		+155
White-tailed Kite, *Elanus leucurus*	CFP	1.79	0.124		−58
Northern Harrier, *Circus cyaneus*	SSC3	1.15	0.292		−58
Cooper's Hawk, *Accipiter cooperii*		−1.48	0.189		+43
Red-shouldered Hawk, *Buteo lineatus*		−1.84	0.115		+100
Red-tailed Hawk, *Buteo jamaicensis*		−1.27	0.251		+58
American Kestrel, *Falco sparverius*		1.58	0.166		−7
Prairie Falcon, *Falco mexicanus*		1.58	0.165		−100
Ring-necked Pheasant, *Phasianus colchicus*		−0.61[a]	0.604		−83
Sandhill Crane, *Grus canadensis*	CT, CFP, SSC3	−2.15	0.075	+187	+27
Killdeer, *Charadrius vociferus*		−1.21[a]	0.347		+30
Long-billed Curlew, *Numenius americanus*		−0.05	0.959		−53
Mourning Dove, *Zenaida macroura*		0.28	0.787		−55
Rock Pigeon, *Columba livia*		−6.79	0.000	+254	+301
Belted Kingfisher, *Ceryle alcyon*		−5.90	0.001	+100	+100
Northern Flicker, *Colaptes auratus*		0.46	0.665		−52
Western Scrub-Jay, *Aphelocoma californica*		0.56	0.593		−50
Yellow-billed Magpie, *Pica nuttalli*		4.77	0.003	−65	−83
American Crow, *Corvus brachyrhynchos*		−0.21	0.844		−63
Common Raven, *Corvus corax*		−5.64	0.001	+157	+131
American Robin, *Turdus migratorius*		0.46	0.664		−9
Loggerhead Shrike, *Lanius ludovicianus*	SSC2	8.34[a]	0.001	−63	−63
European Starling, *Sturnus vulgaris*		0.21	0.840		−92
Western Meadowlark, *Sturnella neglecta*		−0.66	0.537		−40

[a]Assumed unequal variances, because $P = 0.05$ in Levene's test for equality of variances.

Kingfisher, and Rock Pigeon. The species that decreased were the Yellow-billed Magpie and Loggerhead Shrike. The maximum counts in 2007–08, however, were substantially lower than those in the 1990s for the American Crow, White-tailed Kite, Northern Harrier, and nine other species.

In comparison to those of 1990–95, maximum counts of the Yellow-billed Magpie along the transects declined 48% by 2005–06, 64% by 2006–07, and 83% by 2007–08. Those of the American Crow did not decline substantially until 2007–08, in which year it was 63% lower than 1990–95. Outside Yolo County Yellow-billed Magpies declined 53% by 2005–06 and 90% by 2007–08, while within Yolo County they increased 150% by 2005–06 and 2007–08 (Fig. 2). Outside Yolo County American Crows declined 75% by 2007–08, while within Yolo County they declined 45% by 2007–08 (Fig. 2). The most substantial declines in abundance were along survey routes 5, 6, and 1 north of Yolo County for the magpie, and along routes 6 and 1 north of Yolo County for the crow (Fig. 3).

Since 1990–95, maximum counts of the Loggerhead Shrike declined 63% by 2005–06 and 2007–08 (Table 1). However, by 2007–08, they declined 75% outside Yolo County and 0% within Yolo County.

Changes in maximum counts from the 1990s to 2007–08 correlated negatively with the increasing percentage of bird carcasses testing positive for WNV ($r = -0.58$, $n = 14$, $P = 0.03$; Fig. 4). However, changes in maximum counts during our surveys did not relate significantly to any of the other variables of WNV infection or risk reported by Wheeler et al. (2009).

HABITAT USE AND BEHAVIORS

Yellow-billed Magpies shifted away from field crops, pastures, and riparian areas and into urban areas (Fig. 5). American Crows shifted away from disked and furrowed fields and into fields with crop residue and into orchards (Fig. 6).

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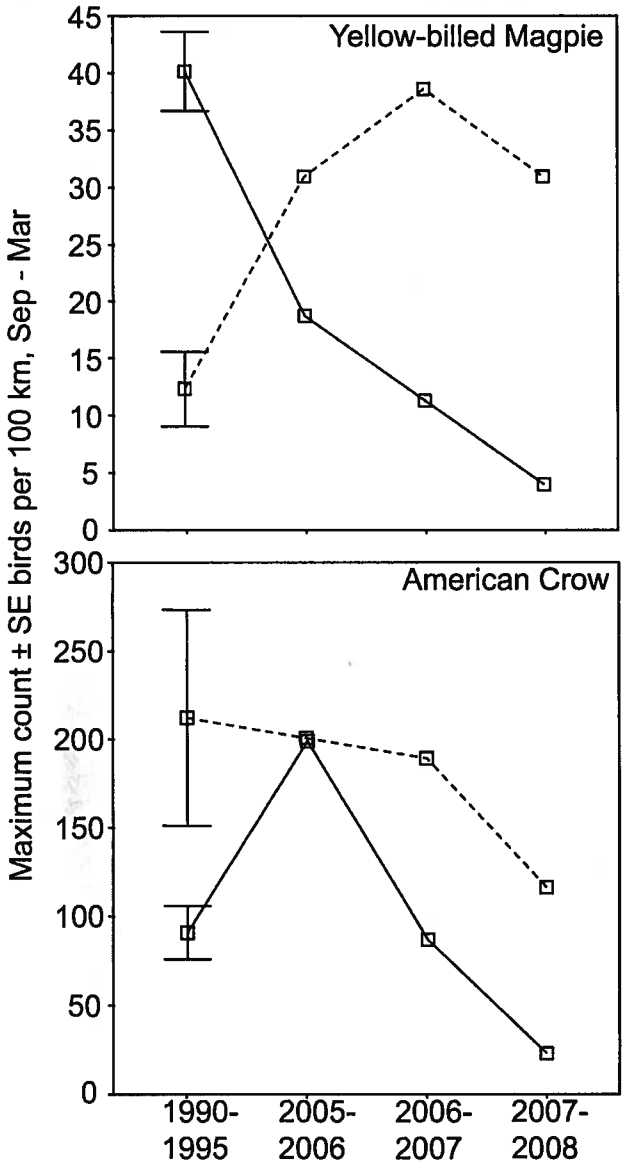

FIGURE 2. Trends in fall and winter Yellow-billed Magpie and American Crow abundance along a 203-km road transect within (25.9 km, dashed line) and outside (176.2 km, solid line) Yolo County, California, from the 1990s through 2007–08.

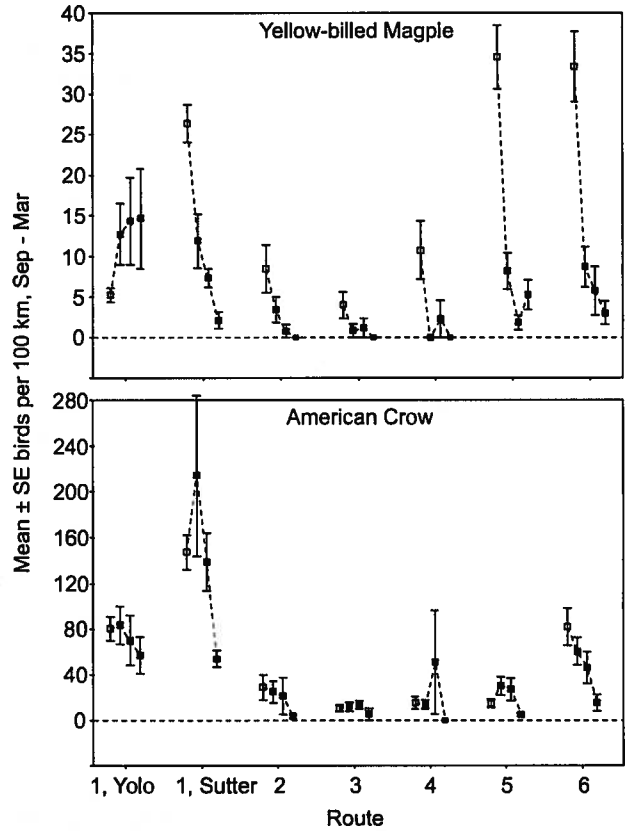

FIGURE 3. Trends in relative abundance of the Yellow-billed Magpie and American Crow by survey route in the Sacramento Valley, California from 1990–95 (unfilled squares) through 2005–06, 2006–07, and 2007–08. Route 1 was dominated by annual field crops rotated with alfalfa in Yolo County and by rice cultivation in Sutter County, route 2 was mostly field crops, route 3 was mostly irrigated pasture, route 4 was mostly rice and wetlands, route 5 was mostly rice, and route 6 was mostly rice with pastures.

From the 1990s to 2005–06, as observed from September to March, the mean group size of Yellow-billed Magpies declined 50%, with a shift to fewer groups of 7 to 30 individuals and more single individuals. By 2007–08, however, group sizes were increasing. From the 1990s to 2005–06 the American Crow also shifted from large groups to more single individuals, and its overall mean group size declined 28%. Group sizes continue to decline in 2007–08, with the largest groups no longer seen, and more crows were observed as singles or pairs. This trend in group size was similar to that observed for the Yellow-billed Magpie during the early portion of the WNV epizootic.

In 2005–06, Yellow-billed Magpies used the roadway, the road verge, and the land beyond the road verge ($\chi^2_2 = 1.91$, $P > 0.05$). They did not differ in numbers perched on the ground versus on short structures (<3 m tall), tall structures (>3 m tall), landing, taking off, or flying ($\chi^2_2 = 7.16$, $P > 0.05$). During 2005–06, however, we saw them flying, flushing, or landing 1.21 times more often other than expected ($\chi^2_2 = 4.09$, $P < 0.05$).

In 2005–06, American Crows also used the roadway, the road verge, and the area beyond the road verge in the same proportions as in the 1990s ($\chi^2_2 = 1.31$, $P > 0.05$). They did not differ in numbers perched on the ground, on short structures, on tall structures, landing, taking off, and flying ($\chi^2_2 = 0.56$, $P > 0.05$). Neither did they differ in their frequency of flying, flushing, or landing ($\chi^2_2 = 0.00$, $P > 0.05$).

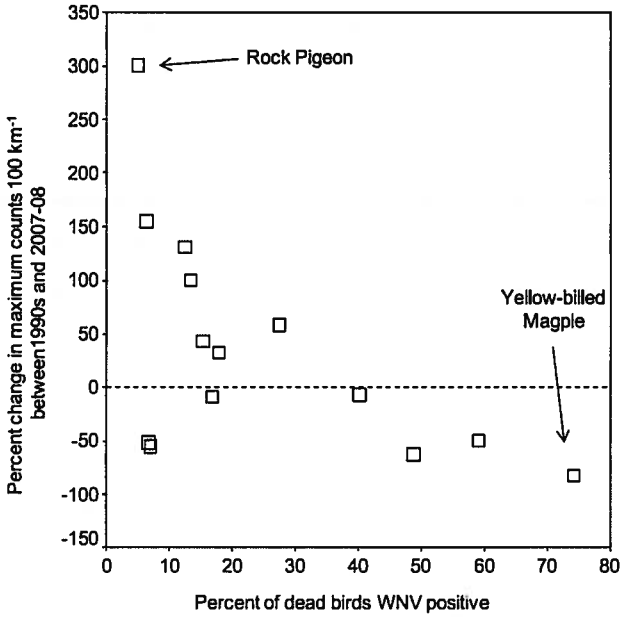

FIGURE 4. Changes from 1990–95 to 2007–08 in maximum counts of bird species during road surveys in the Sacramento Valley, California, in relation to the percentage of dead birds that tested positive for WNV among those species tested ≥25 times and testing positive at least once during dead-bird surveillance (Wheeler et al. 2009). We excluded the Black-crowned Night-Heron and European Starling because of relatively lower confidence in measured changes in abundance during the surveys.

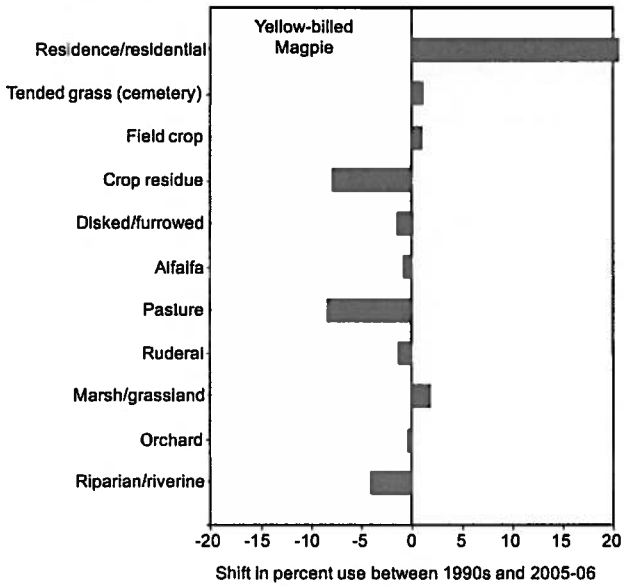

FIGURE 5. Differences between the 1990s and 2005–06 in percentage use of land-cover types by Yellow-billed Magpies along a 203-km road transect in the Sacramento Valley. Bars extending to the left indicated less use in 2005–06 than in the 1990s; bars extending to the right indicate more use.

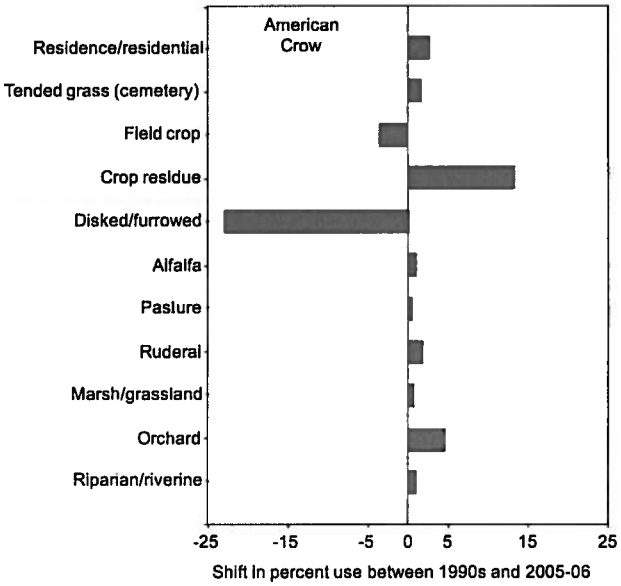

FIGURE 6. Differences between the 1990s and 2005–06 in percentage use of land-cover types by American Crows along a 203-km road transect in the Sacramento Valley. Bars extending to the left indicated less use in 2005–06 than in the 1990s; bars extending to the right indicate more use.

DISCUSSION

Along our routes, Yellow-billed Magpies declined about 83% from the 1990s to 2007–08 and have been declining since 2005. They declined 90% outside Yolo County, yet they increased 150% within Yolo County. By 2007–08, American Crows declined 63% along the entire transect and 75% outside Yolo County, exceeding the 45% decline reported nationwide by 2005 (LaDeau et al. 2007). Loggerhead Shrikes declined 63% along all our routes and 75% outside Yolo County. Declines of these magnitudes, if unabated, could threaten the continued existence of the Yellow-billed Magpie and Loggerhead Shrike and could alter the ecological role of the American Crow in the region.

Crosbie et al. (2008) reported smaller reductions in abundance of Yellow-billed Magpies counted during BBS and CBCs. The trends they reported differed from ours, perhaps because Yellow-billed Magpies did not decline throughout their range to the same degree they did in the Sacramento Valley. Another reason for the difference may be methodological. The BBS is performed in spring and early summer, when Yellow-billed Magpies are nesting in thick vegetation and so are much less detectable. Also, the numbers of BBS routes and CBC circles available to Crosbie et al. (2008) were only 9 and 12, respectively, resulting in comparisons of annual means among routes of about 26 birds for the BBS and only 2 to 5 birds for the CBC throughout the species'

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range. On the other hand, our surveys took place during the fall and winter when Yellow-billed Magpies are highly visible, and our counts from 1990 to 1995 averaged 48 (SD = 18) birds per survey.

Declines of the Yellow-billed Magpie varied spatially within the Sacramento Valley and were most pronounced in rice fields, pastures, and riparian areas. American Crows and Loggerhead Shrikes declined most in areas of rice cultivation, pervaded by standing water providing breeding habitat for *Culex* mosquitoes, the principal vectors of WNV (Reisen et al. 2006). Within Davis, Yolo County, at the southern end of our survey transect, clusters of WNV-infected dead birds (mostly American Crows and Yellow-billed Magpies) corresponded spatially and temporally with WNV-positive *Culex* mosquitoes, which were reduced by aerial spraying of a mosquito adulticide during 2006 (Nielsen et al. 2008). Within Yolo County, where we observed increases of Yellow-billed Magpies and Loggerhead Shrikes and a relatively smaller decrease of American Crows, the Sacramento-Yolo Mosquito and Vector Control District aggressively controlled WNV vectors biologically, chemically, and by advising the public to minimize standing water that could be used by breeding mosquitoes. The district reduced the odds of WNV infection in humans about sixfold in two areas of Sacramento where it applied a pesticide aerially (Carney et al. 2008), possibly also reducing transmission to birds. We suspect the other districts overlapping our survey routes controlled mosquitoes much less aggressively, as our request for information on their control efforts went largely unanswered. Therefore, we hypothesize that urban and rural residential areas harbored Yellow-billed Magpies and American Crows during the epizootic because in these areas mosquitoes were controlled more vigilantly.

In contrast to the Yellow-billed Magpie and Loggerhead Shrike, the American Crow did not decline significantly until the third year of the epizootic. By 2007–08 group sizes of American Crows had decreased considerably, and clusters were many fewer. These patterns parallel those we observed for the Yellow-billed Magpie during the first two years of the WNV epizootic. Our impression was that the effects of WNV on the American Crow lagged behind those of the other two species, but we cannot explain the lag.

Other species we monitored apparently did not decline in response to WNV (see Table 1), and the difference in response also correlated with the percentage of dead birds that tested positive for WNV (Fig. 4; Wheeler et al. 2009). These other species may be more resistant to WNV, or their exposures may be lower as a result of physical or behavior defenses or of fortuitous ecological patterns. The increases in abundance of the Common Raven, White-faced Ibis, and other species may be due to more wildlife-friendly farming practices in the Sacramento Valley. The ibis and Sandhill Crane appeared to benefit from the recent transition to rolling instead of burning stubble following rice harvest. Increases in other species could also be due to shifts in crop production, although we did not document much change in the incidence of crops along our survey routes. Expanded residential and commercial development appeared to correspond with the increase in Rock Pigeon abundance.

In April 2008 came the first confirmation of a Yellow-billed Magpie surviving WNV infection, indicating some resistance (Crosbie et al. 2008). Nevertheless, the rate of decline of the Yellow-billed Magpie has been so fast that we are concerned for the persistence of the species.

RECOMMENDATIONS

Because the Yellow-billed Magpie has a small geographic range, the recent and continuing decline may pose a threat to the continued existence of the species. We suggest that the California Fish and Game Commission consider giving special status to Yellow-billed Magpie. Steps should be taken to better understand the exposure pathways, the effects of WNV, and possible means to reduce or minimize these effects. Searches should be initiated across the species' range to locate areas additional to Yolo County where the species persists in groups larger than scattered singles and pairs, and these locations should be compared to discern patterns that may lead to the formulation of effective conservation measures. One such measure might include experimentally targeting certain areas for aggressive mosquito control so that Yellow-billed Magpies can maintain an ecological foothold while building resistance to WNV. For example, known breeding areas could be identified, delineated, and selected in an experimental design for control of WNV-bearing mosquitoes.

ACKNOWLEDGMENTS

We thank the Sacramento–Yolo Mosquito and Vector Control District for funding and David Brown and Rhonda Laffey for administrative and logistical support during the study. We also thank Lee Neher for GIS support and Douglas Bell and an anonymous reviewer for helpful comments on the manuscript. We also thank editor Michael Patten for sharing new information that improved our manuscript.

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Association Analysis of Raptors on a Farming Landscape

Shawn K. Smallwood, Brenda J. Nakamoto and Shu Geng

Abstract – We developed an extensive sampling program for a landscape study of raptors on the farming landscape of the Sacramento Valley, California. By September 1993, after 47 months and 97 surveys along a 200-km road transect, we mapped 5662 observations of 11 species of Accipitridae, 1505 of 3 species of Falconidae and 986 of turkey vulture. With each observation, we recorded activity or perch used, and association with landscape elements and other species. Pooled observations of Accipitridae and Falconidae demonstrated a strong migratory cycle and aggregation in the landscape. They preferentially selected riparian, wetland and upland vegetation, alfalfa fields, and rice stubble and other crop debris, all of which occurred rarely. They avoided human settlements, plowed fields, and most grain and row crops. Accipitridae preferred trees with snags and open views, and utility poles with multiple horizontal beams. The associations we identified will help agriculturalists develop effective strategies for increasing raptor populations on farmland. Strategies under study include farmscaping, changes in cultural practices, and landscape engineering, all of which will benefit raptor conservation, farming efficiency and the aesthetic value of the landscape.

Key words: Accipitridae; agriculture; association analysis; conservation; Falconidae; landscape ecology; perch preference; road survey; turkey vulture.

Agriculture is conducted on lands that used to support the most diverse and abundant flora and fauna in the corresponding regions (Pimentel *et al.* 1992). Cropland and grassland/pasture comprise about 100 000 000 km^2 of the earth's terrestrial surface area, and most of the cropland was added during the last 300 yr (Meyer and Turner 1992). Amidst such rapid change, many of the native species still exist on these managed lands (Banaszak 1992, Kromp and Steinberger 1992, Smallwood in press), often within riparian corridors (Naiman *et al.* 1993), nature reserves, or fragments of natural habitat. But administrative boundaries of nature reserves should not be expected to translate into real biological boundaries (Schonewald-Cox and Bayless 1986). Agriculture impairs inter-reserve movement and intra-reserve survival of native mammal species (Smallwood in press), thus reducing the food supply of raptors across most of the landscape.

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Prey-bearing habitat on the farmland of the Sacramento Valley, California, might limit raptor populations regionally, because many raptors from western North America aggregate in the Valley during one phase of their annual migration (Bloom 1985), and because raptor populations respond to their prey population dynamics (Grant *et al.* 1991). Therefore, raptor populations can be conserved, and even augmented, by increasing the availability of prey-bearing habitat in the Sacramento Valley with changes in landscape structure and cultural practices. Such changes might be made most efficiently by learning how raptors use the existing landscape, given its structure, perches and management.

Previous studies have shown that populations of bird species benefit from greater structural complexity on farms (O'Connor and Shrubb 1986) and roadside edges (Ferris 1979, van der Zande *et al.* 1980, Arnold and Weeldenburg 1990). Insectivorous birds best infiltrate corn fields that are adjacent to woodlots (Best *et al.* 1990). Existing landscape engineering efforts in the Sacramento Valley (Griggs 1993, Yolo County Farmland and Open Space Conference, May 8, 1993) are focused on increasing the spatial extent of natural vegetation, mainly as a network (*sensu* Forman 1981) of restored riparian habitat and strips of natural vegetation between agricultural fields. These 'corridors' are where the richest and most diverse assemblages of wildlife species occur in the Valley (Griggs 1993). However, the commodity type and cultural practices in agricultural fields can significantly affect the food base of raptors that would use the adjacent or nearby corridor network. Vertebrate pest control programs in some agricultural fields can seriously reduce the food supply of hawks. Certainly, raptor conservation on the farming landscape requires more than open space; it also requires a suite of crops and cultural practices (or lack thereof) that provide resources for wildlife and that are non-destructive. Our goal is to provide these types of information by combining landscape ecology with ecosystem ecology (Forman 1981, Risser 1985) and with conservation biology (Turner 1989).

We report on patterns of seasonal distribution, activity and perch use of functional/taxonomic raptor assemblages among landscape elements of the Sacramento Valley. A landscape is a spatially heterogeneous area in which its patch and corridor elements are *structured* by type, size, shape and configuration, and in which they *function* to store and channel the flow of energy, material and organisms (Foreman 1981, Turner 1989). Landscape ecology can help identify how raptors interact with landscape elements, and with landscape structure, so long as the *extent* of the study is at a spatial scale large enough to recognize structure (Turner 1989). To achieve a sufficiently large spatial scale for a landscape study of raptors, we used non-conventional, high-speed surveys, which provided large sample sizes across large areas, but also new types of error (Smallwood and Geng in press). Most other road surveys for raptors occurred only during winter in smaller areas with simple categories of landscape elements (Wilkinson and Debban 1980, Bauer 1982, Craig *et al.* 1986, Andersen and Rongstad 1989).

METHODS

We conducted wildlife surveys along 200 km of road transect, which was in 7 parts along a 320-km loop in the Sacramento Valley (Fig. 1). One person drove a car at 84 kph, while the other searched for wildlife and recorded observations into a tape-recorder. Each survey was begun between 0800 h and 1000 h and ended by 1400 h. Surveys were conducted during all weather conditions, except during the rare winter storms when visibility was severely limited. Along this transect, we mapped crops, natural vegetation, the Sacramento River (encountered 3 times), creeks, canals, roads, houses, roadside vegetation height and width, and potential perches such as trees, utility poles, transmission towers, fences, standpipes and artificial hawk perches. Landscape changes and cultural

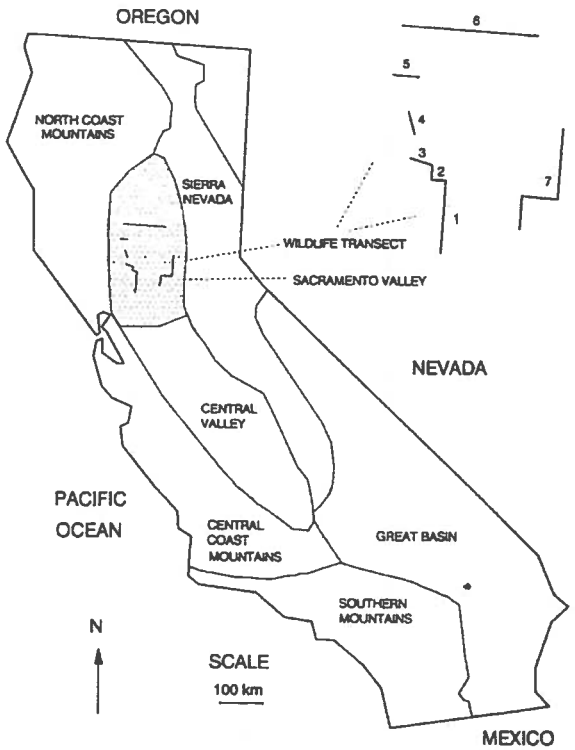

Figure 1. Locations of the 7 road transects for raptor survey in the Sacramento Valley, California. Dominant landscape elements were riparian and upland/wetland along transect 1, dry and irrigated pasture along transect 7, rice along transects 5 and 6, and field crops along transects 2 and 3. Transect 4 was a mix of pasture, riparian, field crops and rural.

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practices were monitored and mapped. For example, we recorded dates of planting, harvest, irrigation, plowing, burning of debris, and spraying of pesticides when possible. We surveyed the first 58 km of the transect 97 times no more than once per week for 47 months. We recorded the abundance, locations, and activities and types of perches of 82 vertebrate species. Locations included odometer reading to the nearest 0.16 km, side of road, distance from road, and the associated landscape element. All animal observations of questionable taxonomic identification were not recorded. Species were added to the survey as developing expertise allowed accurate identification.

Similar to Marion and Ryder (1975) and Preston (1990), we identified associations between raptors and landscape elements by comparing the incidence of the species population on a landscape element (percentage "use") with the incidence of that element on the sampled landscape during the sampled time (percentage "availability"). Association of a species with a landscape element can be expressed by the ratio:

$$M_i = \frac{r_i}{p_i} = \frac{n_i}{N * p_i} = \frac{\text{Observed}}{\text{Expected}},$$

where n_i is the number of individuals counted in the ith landscape element, N is the number of individuals counted in the entire sample, r_i is n_i/N (as used by Marion and Ryder 1975), and p_i is the incidence of the ith landscape element in the sample (Smallwood 1993). M_i interprets as the species occurrence in the ith landscape element as the multiple of that to be expected from a uniform pattern of the species on the landscape. Values <1 express avoidance of the ith landscape element, and values >1 express selection preference. Observed and expected values were also rearranged for testing the hypothesis of homogeneity:

$$\chi^2 = \sum \frac{(O - E)^2}{E},$$

where O is observed and E is expected values, and the degrees of freedom is $i - 1$ landscape elements.

RESULTS

Populations of Accipitridae, Falconidae and turkey vulture varied annually (Fig. 2), seasonally (Fig. 3) and among sites (Table 1). Accipitridae and Falconidae were most numerous in the valley during winter, although the Swainson's hawk was most numerous during summer. Vultures were most numerous during spring and summer. As these raptor populations varied, they changed their use of landscape elements and cultural practices, both of which also varied spatially and temporally (Fig. 4).

Accipitridae

Hawks were most dense along transect 2, and least dense along transect 5 (Table 1, Fig. 3). The species distribution of Accipitridae among transects was heterogeneous (groups compared: ferruginous hawk, red-tailed hawk, Swainson's hawk, rough-legged hawk, red-shouldered hawk, northern harrier, white-tailed kite, and sharp-shinned and Cooper's hawks combined, $\chi^2 = 183.1$, df = 35, $P < 0.001$). More than the expected number of ferruginous hawks and Swainson's hawks occurred on transects 2 and 3, rough-legged hawks on transects 1 and 6, northern harriers on transects 3 and 6, white-tailed kites on transect 6, and accipiters on transect 1.

Hawks preferred alfalfa and riparian, upland, and wetland vegetation throughout the year, but alfalfa was most preferred during summer (Fig. 4). Rice stubble was also preferred, but unavailable during summer. Burned and unburned rice stubble were equally preferred during fall and winter. Grain crops other than rice were preferred during fall, and annual vegetable crops were preferred during winter, when they were rare. Dry pasture, rice, plowed fields and rural areas were avoided throughout the year.

The incidence of potential perches on the landscape has not been quantified, so an association analysis of perch use could not be completed. Of the hawks observed, 30% were in flight, 29% on utility poles, 15% on telephone wires, 15% on trees, 5% on the ground, 4% on the rarely occurring transmission towers, and 2% on miscellaneous perches such as irrigation standpipes and pumps, fences, houses/buildings, tractors, street lights, signs and bridge rails. Hawks were observed on artificial hawk perches (narrow dowel on thin pole) only three times. Hawks used major types of perches/activity seasonally ($\chi^2 = 351$, df = 15, $P < 0.001$); they were observed more often than expected by chance in flight during spring and summer, on trees during winter, on utility poles during fall, and on transmission towers during summer. Of those observed in flight, more than the expected number of hawks were soaring during spring and fall, and in flutter-flight during winter and summer ($\chi^2 = 75.5$, df = 6, $P < 0.001$). Hawks preferred utility poles with multiple crossbeams or no crossbeams (Fig. 5). When possible, utility poles were used in such a way as to keep some structure above the hawk. Of the hawks observed in trees, 31% were on willows (*Salix* spp.), 30% on cottonwoods (*Populus fremontii*), 17% on oaks (*Quercus* spp.), 13% on American elm, 5% on eucalyptus (*Eucalyptus globulus*), and 4% on walnuts (*Juglans* spp.).

Falconidae

Falcons preferentially selected natural vegetation throughout the year (Fig. 4). They preferred annual vegetable crops during winter; rice stubble, annual vegetables and irrigated pasture during spring; alfalfa, fallow and plowed fields during summer; and grain fields and burned rice stubble during fall. Falcons avoided rural areas, rice, asparagus and dry pasture throughout the year.

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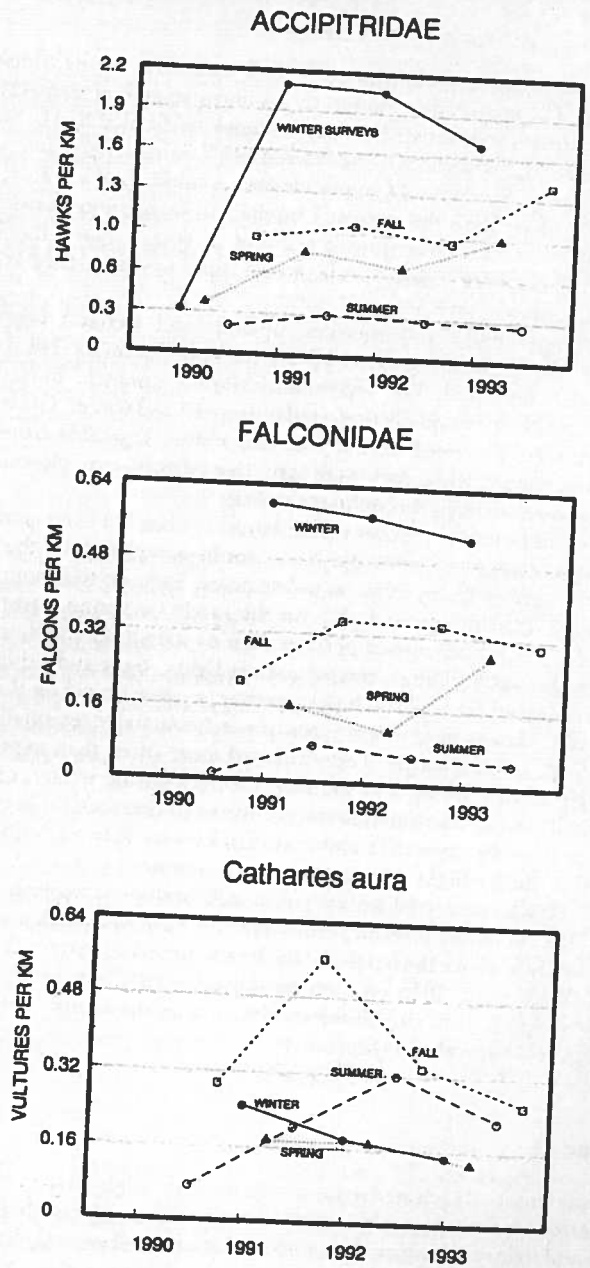

Of the falcons observed, 55% were on telephone wires, 23% were on utility poles, 14% were in flight, 4% were in trees, 1% were on the ground, and 3% were on transmission towers and miscellaneous perches. Of the falcons in flight, they tended to be in flutter-flight more often during spring and summer, and less often during fall ($\chi^2 = 7.27$, df = 3, $P = 0.064$).

Turkey Vulture

This species preferentially selected upland/wetland vegetation throughout the year (Fig. 4). It also preferred riparian vegetation and orchards during all seasons except fall, and irrigated pasture during all seasons but spring. Winter vegetables were strongly preferred, as were rice stubble and debris from summer vegetables. Dry pastures, asparagus, rice, plowed fields and rural areas were avoided throughout the year.

Of the vultures observed, 85% were in flight, of which 53% were soaring. Twelve percent were on the ground (usually at carrion), 1% were on trees, and the rest of the available perches were scarcely used.

DISCUSSION

We only analyzed seasonal variation in selection of landscape elements, but the substantial locational variation in density (Table 1) suggests the need for very large samples of raptor observations in time and space. Future analysis for raptor associations with landscape elements needs to include seasonal variation at each transect. The heterogeneity of species distribution among transects suggests that future analysis also needs to be conducted for each species separately. As sample sizes increase, and the association analysis is further split in time, space, and by species, we will learn much more about how raptors interact with landscape elements, landscape structural properties and agricultural practices.

Repeat, high-speed surveys for raptors along extensive road transects can provide the precision and heterogeneous distribution that are needed for pattern analysis (Smallwood and Geng in press). Predictions from models of distributional dynamics can be tested by surveying for raptors along extensions of the transect into nearby areas. The measure of association and related statistics are easy to use and free of the unrealistic assumptions required of surveys for

Figure 2. Population dynamics of the three species groups studied during the road surveys. Densities were calculated by summing among transects the numbers observed and distances traveled during each season of each year.

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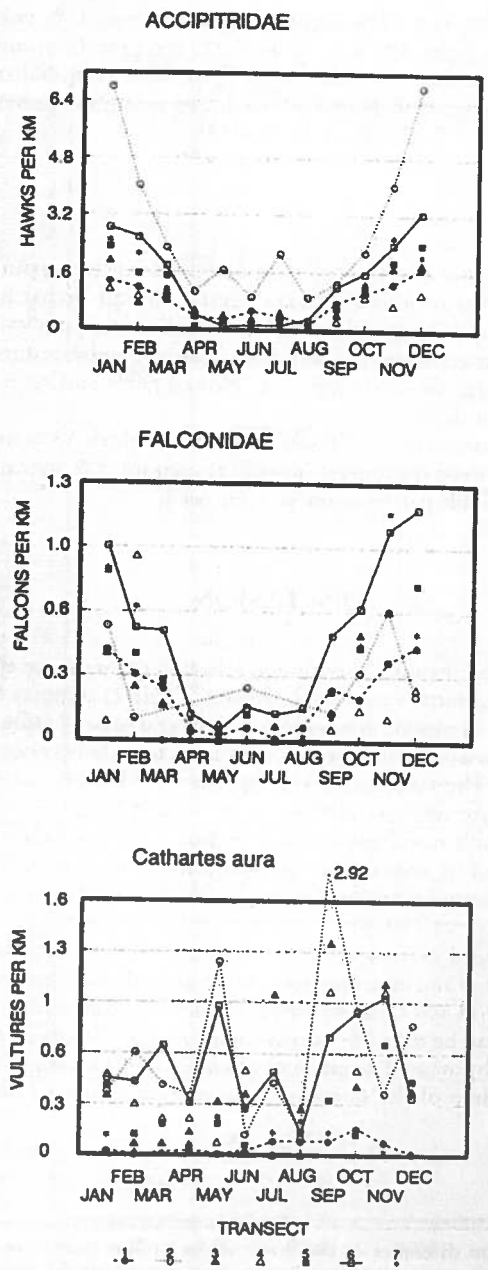

population estimation (Seber 1973, Eberhardt 1978, Burnham *et al.* 1980, Mikol 1980). However, sightability varies among species, landscape elements and season (perch use and flight patterns change seasonally), and needs to be assessed with long-term observation of individual hawks, e.g. Diesel (1989), Preston (1990), and other methods.

Riparian, upland and wetland vegetation were preferred by all raptors during most seasons, yet they comprised a minority of the landscape. A landscape engineering effort for restoring and extending riparian and strip corridors would likely increase raptor populations in the Sacramento Valley. Most raptor activity was concentrated at or nearby the Sacramento River and major streams with riparian habitat. Adjacency to riparian, upland and wetland vegetation accounted for many of the raptor associations with other landscape elements, e.g. orchards and pasture. Craighead and Craighead (1959) also observed many hawks off their preferred hunting grounds, but nearby.

Burned rice stubble attracted falcons during fall, but contributed only a short-term pulse of food. Unburned rice stubble provided a longer-lasting food source, and was preferred by raptors, especially as it grew more rare during the spring. Other crop debris, when they occurred, were also preferred by hunting raptors. Such strong preference for fields with crop debris suggests that food-bearing land is a limiting resource for wintering raptors on this farming landscape; there is little of it when it is most needed.

Plowed fields comprised a large portion of the landscape along our survey transects, but they were avoided by most raptors most of the time. Many falcons were recorded at plowed fields, but they were always near fallow strips of vegetation along canals, road verges or fence lines. We did not include these strips of vegetation in the association analysis. A widespread delay in plowing crop residue until just before the next planting would probably support substantially larger winter aggregations of raptors in the Sacramento Valley, which would translate into increased regional populations of raptors. Raptor conservation could be served by addressing this and other cultural practices. Farmers have practical and economic reasons for their farm management, but there usually are alternatives that would benefit wildlife without risking economic loss to the farmer.

Consistent avoidance of rural or developed areas by raptors demonstrated the need for preventing extensive housing and industrial development in the Sacramento Valley. Again, regional populations of raptors would be severely affected. Farming *is* less destructive to wildlife than is urban and industrial expansion. Many farmers do not wish to sell their farms to developers, but often yield to pressure from city and county governments and economic necessity.

Figure 3. Seasonal dynamics of the three species groups. Densities per month were calculated by summing among years the numbers observed and distances surveyed in each month.

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Table 1. Number of observations of raptor species during the Sacramento Valley farmland survey from January 1990 until September 1993.

Species Common names	Transect 1	2	3	4	5	6	7	Total
Cumulative one-way survey distance (km)	5148	364	835	498	610	2174	2119	11748
Accipitridae	2026	522	320	135	299	1431	929	5662
Hawks, unidentified	299	116	44	50	40	148	133	830
Red-tailed hawk	497	226	99	43	227	340	306	1738
Swainson's hawk	78	5	11	2	8	17	9	130
Red-shouldered hawk	5	7	3	1	4	9	5	34
Rough-legged hawk	4	1	0	0	0	5	0	10
Ferruginous hawk	15	0	2	0	1	1	1	20
Osprey	0	0	1	0	0	0	0	1
Accipiters, unidentified	2	0	0	0	0	2	2	6
Sharp-shinned hawk	1	1	0	0	0	0	0	2
Cooper's hawk	2	4	0	0	0	3	0	9
Kites, unidentified	12	2	0	3	4	28	8	57
Northern harrier	138	11	46	4	30	180	100	509
White-tailed kite	46	29	6	3	8	79	34	205
Golden eagle	1	0	0	0	1	1	0	3
Unidentified	423	87	24	8	24	125	37	728
Falconidae	484	33	85	21	94	494	294	1505
Falcons, unidentified	405	25	60	17	79	405	244	1235
American kestrel	71	6	22	2	13	81	44	239
Merlin	5	0	0	1	0	1	3	10
Prairie falcon	3	2	3	1	2	7	3	21
Cathartidae								
Turkey vulture	86	101	141	81	61	422	94	986

Now is the time to manage farmland for raptor conservation, because the loss of farmland is a loss to wildlife, to our food base and to the farmer's way of life. A new farming landscape, with more raptors and supporting habitat, would strengthen its aesthetic value and its prospects for protection from development and over-intense use.

Patterns of perch use in the Sacramento Valley suggest that farmscaping could successfully attract raptors to fields where prey is available. Perches were not continuously present along our survey transects. Some alfalfa fields were not bordered by trees or utility poles; these fields were visited by few falcons and hawks. Many other fields were bordered by trees that raptors did not use, or by utility poles that lacked the structure preferred by hawks. Preferred tree species could be added to field borders, or a non-utility crossbeam could be added 0.5 m beneath the utility beam on many poles. This additional lower crossbeam would not only attract hawks to field borders, but also increase the distance between hawks and the dangerous aspect of the pole. It would reduce the risk of electrocution to hawks, especially in combination with other protective measures (Olendorff 1981, Ferrer *et al.* 1991). Multiple crossbeams possibly offer perched hawks protection from aggressive approaches by other hawks.

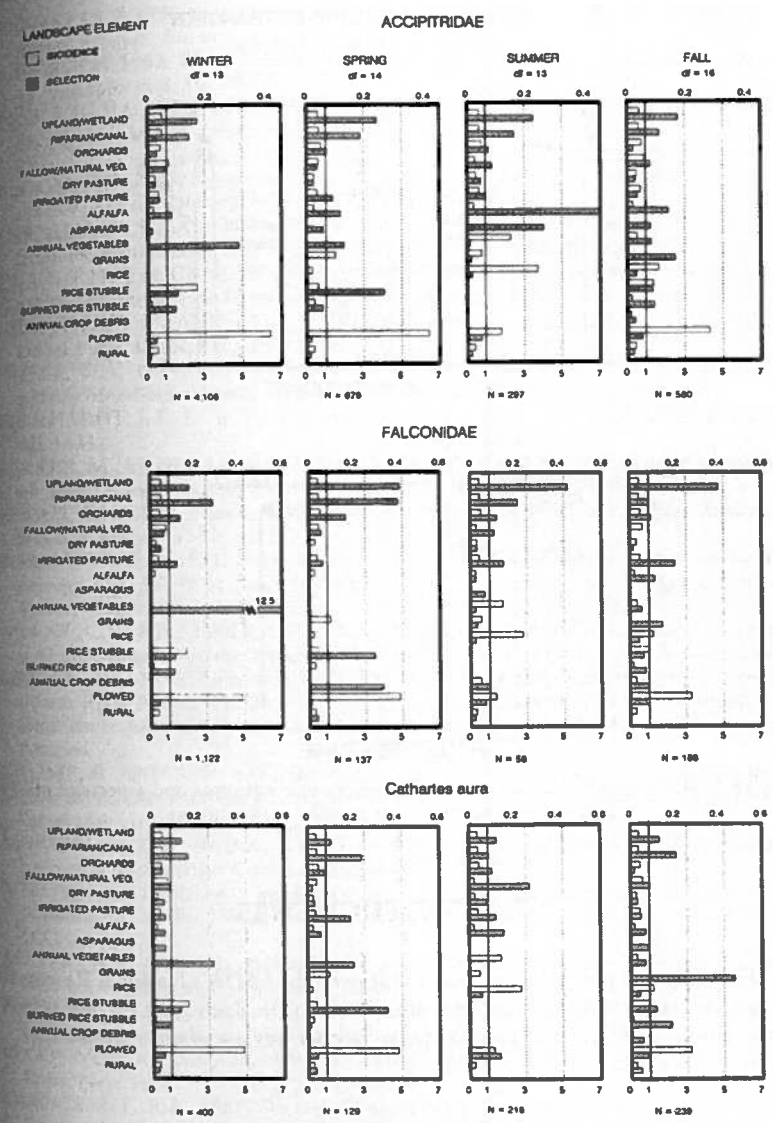

Figure 4. Seasonal variation in selection of landscape elements by species of Accipitridae, Falconidae and turkey vulture (*Cathartes aura*). The top horizontal axes correspond with incidence of landscape elements, and the lower axes correspond with the measure of ecological association, M_i, or "selection". The solid vertical lines at $M_i = 1.0$ corresponds with the selection to be expected based on chance. Use of the landscape was nonhomogeneous for all three taxonomic groups during each season ($P < 0.001$ for all χ^2 tests).

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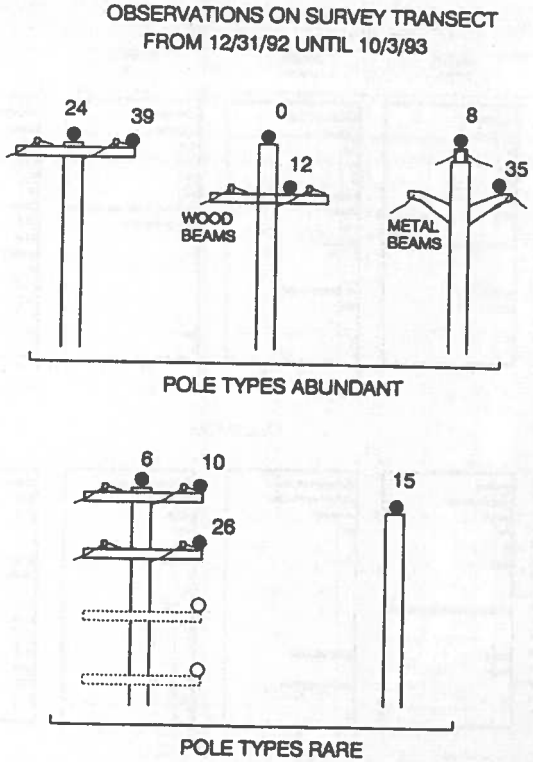

Figure 5. Occurrence frequency of Accipitridae on different types and aspects of utility poles during the latest nine months of the survey.

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Using the Best Scientific Data for Endangered Species Conservation

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ABSTRACT / The Endangered Species Act calls for the use of the best scientific data in conserving threatened or endangered species and the ecosystems upon which they depend. The language of this act and other environmental laws and relevant judicial rulings also require assessments based on modern scientific standards that are routinely applied in ecological research. Particularly for the Endangered Species Act, "take" decisions should be made only after the supporting documents provide: (1) designation of critical habitat based on use and availability methods; (2) risk assessment(s) for proposed take and other project impacts; (3) ecosystem assessment by trained ecosystem ecologists; (4) a description of an adaptive management program involving more than post hoc adjustments to problems in mitigation design; (5) a description of the proposed scientific monitoring along with thresholds for application of adaptive management; (6) uncertainty analysis along with estimates of species' abundance and project impacts; (7) nonselective, academic-quality referencing of data, methods, and theory supporting the conclusions; and (8) reviews of the assessment by independent scientists. These standards have been rarely applied to assessments of environmental take, due to lack of incentives for cooperation among academic scientists, environmental consultants, and the government regulatory agencies. Particularly important is requiring the type of independent review used by academic scientists. Such review would help ensure that take decisions are based on use of the appropriate scientific standards, thereby qualifying the supporting data as scientific and the best available, no matter how limited the data. Until these standards are applied prior to political trade-off and pragmatism, the environmental laws will continue to have little bearing on conservation.

Government and judicial chambers across the United States are rife with struggles between citizen groups, take permit applicants, and the multijurisdictional regulatory agencies responsible for implementation and enforcement of the Endangered Species Act (ESA) of 1973 [16 U.S.C. §§1531–1544 (1988)] and other environmental laws protecting biological species. The ESA is also at the center of debate over how it should be reauthorized by the US Congress. These struggles have often been complex and confusing. Implementation and enforcement of the ESA have been subjective and inconsistent (Taylor 1993, Gordon and others 1997), thereby leaving the interested parties bitter in its wake. ESA compliance issues have arisen frequently across the United States as human population and land-use changes have expanded during the last 25 years since the ESA was enacted. These latest land-use changes follow a rapid global change in land-use cover and hydrology (Meyer and Turner 1992, Dynesius and Nilsson 1994) that have disturbed ecosystems worldwide (Hannah and others 1994), leaving many biological species vulnerable to extinction where areas with high levels of endemism are under anthropogenic pressure (Karr 1995, Dobson and others 1997).

Specific applications of the ESA include listings of species as threatened or endangered, development of recovery plans, biological or environmental assessments (EAs), and habitat conservation plans (HCPs). The HCP is becoming a popular ESA application and, along with other agreements, involves issurance of permits for incidental take. Environmental impact statements (EISs) are developed to comply with the National Environmental Policy Act (NEPA), and there are similar documents required by state governments. The environmental consulting industry has developed many of the EA, EIS, and HCP documents, and the Fish and Wildlife Service and the National Marine Fisheries Service have developed some as well (hereinafter referred to as the

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Services). Although there are federal guidelines for the ESA applications (US Departments of Interior and Commerce) (USDI and USDC 1996), the confusion and inconsistency has been impressive. In a thorough review of US Fish and Wildlife Service Reports to Congress on the Endangered and Threatened Species Recovery Program, Gordon and others (1997) concluded recently that conservation under the ESA has failed to recover species due to: (1) subjective listing standards with poor use of taxonomic standards; (2) disproportionate application of funding across the United States; (3) use of unreliable in-house reporting and monitoring methods; and (4) high incidence of "data errors," which were mistakes or inapplicable listings and reporting of recovery status. Beside these problems, failed conservation could also be due to misapplications of scientific data and conservation measures.

Except for listings and funding allocations, the struggles over ESA applications have centered on the scientific rationale for making any of the following conclusions: (1) whether the proposed project will significantly reduce the likelihood of survival and recovery in the wild; (2) the extent or magnitude of the impacts; and (3) the type and extent of impact avoidance or mitigation to be implemented. The scientific rationale for these conclusions largely determines ESA effectiveness and credibility. This rationale also bears on the integrity of modern environmental science, due process under the law, and the public trust.

Pragmatism and political trade-off should follow, rather than precede, the use of the best scientific information in making take decisions. According to Gordon and others (1997), "The problems within the ESA are profound and require drastic revisions or wholesale replacement to create an endangered species program that will result in real conservation achievements." However, we suggest that the conservation failures have more to do with the Services than with the ESA. The intent of the ESA is clear enough, although its translation into modern scientific standards and enforceable statutes requires consideration by trained environmental scientists.

The purpose of our paper is to describe the modern scientific standards that are applicable and should be implemented to biological assessments prior to, and following, the issuance of take permits. These are the standards that would apply to implement the intent of the ESA using current scientific principles and methods. We specifically do not address scientific standards applicable to listings, recovery plans, or specific mitigation measures. The appropriate standards for implementing each of these aspects of the ESA should be proposed and debated in the scientific literature and then implemented by the Services. For example, the National Research Council (NRC 1995), Carroll and others (1996), Kennedy (1997), and Smallwood (1998) provided initial scientific discussions of listing standards, and the NRC (1995) and Gordon and others (1997) did so for recovery standards. The standards we present are applicable to other environmental compliance issues, although regulations vary in specific wording. No matter how politics influences the language of these environmental laws, the best scientific data should be used for assessing impacts and mitigation effectiveness (NRC 1995).

Science Applied to the ESA

The intent of the ESA was amply demonstrated in several of its phrases. For example, the direct and incidental taking of threatened and endangered species "shall not appreciably reduce the likelihood of their survival and recovery in the wild" [Sections 7(a)(2) and 10(a)(2)(B)]. Federal agencies are supposed to demonstrate that their actions and consultations are "not likely to jeopardize the continued existence of any endangered species or threatened species or result in the destruction or adverse modification of habitat of such species" [Section 7(a)(2)]. To this end, "each agency shall use the best scientific and commercial data available" [Section 7(a)(2)]. Furthermore, the take permit applicant and the Services need to assess the proposed project's "impact which will likely result from such taking" [Section 10(a)(2)(A)(i)]. The risk assessments must not be limited to the defined project area, because Section 4(a)(3)(A) of the ESA requires the designation of critical habitat, which can include all specific areas "on which are found those physical or biological features essential to the conservation of the species" at the time of listing [Section 3(5)(A)]. One purpose of the ESA is "to provide a means whereby the ecosystems upon which endangered species and threatened species depend may be conserved" [Section 2(b)]. Therefore, the intent of the ESA is to assess the likely project impact on the species by including the larger spatial and systemic context in which the species exists, and this should include a cumulative impact assessment.

ESA Sections 2(c)(1) and 7(a)(1) declared Congressional policy to be that all federal agencies use their authorities to conserve listed species. The ESA defined conservation as the use of all methods and procedures necessary to recover listed species, including use of "scientific resources management such as research, census . . . " [Section 3(3)]. Science was put at the core

of the ESA statutory scheme. Science is a structured process by which humans gain understanding of nature (Popper 1969, Kuhn 1970). It includes testing hypotheses in an attempt to refute conjectures generated by previous experience and theory, and it includes a methodology for dealing with uncertainty. Given the structure of science, scientific assessments of impacts and risks due to proposed take also require scientific monitoring plans integrated with adaptive management strategies.

Implementing the ESA's intent of using the best scientific data requires several other standards, as well as a basic understanding and use of the scientific method. Scientific data are meaningless without proper use and interpretation by scientists. The data need scientific evaluation of their limitations and uncertainties, and their interpretation requires existing theory and method. Congress certainly did not intend that ESA decisions should use bad science to interpret data. Therefore, the best scientific data are those codified into scientific theory and based on use of the best scientific methods.

Scientific Standards for ESA Compliance

To meet the intended use of science in the ESA, take decisions should be made only after designating critical habitat, assessing risks for populations and their supporting ecosystems, detailing a scientifically founded adaptive management plan with an integrated monitoring program, conducting uncertainty analyses, properly referencing source data and analytical methods, and undergoing independent scientific review. The NRC (1995) also recommended risk assessment and uncertainty analysis, but their recommendations differed from ours in several ways. For example, they recommended designation of "survival habitat" as a stop-gap measure to designating critical habitat; they did not explicitly recommend adaptive management and did not consider source referencing and independent scientific review as qualifiers for using the best scientific data. In the following section, we will describe our eight recommended standards.

Identify and Designate Critical Habitat

Habitats are defined by the species' use of the environment, and therefore use and availability of environmental resources must be considered (Smallwood 1993, Morrison and others 1998). Vegetation and soil types are not habitat unless they can be directly identified as resources required by a particular species (Hall and others 1997). Resource patch structure varies among spatial scales of observation (Kotlier and Wiens 1990, Levin 1992), so spatial scale of observation can influence interpretation of habitat, because as the scale of observation changes, our measures of availability and use likely also change (Smallwood 1995, Riitters and others 1997). Therefore, multiple spatial and temporal scales need consideration for identifying and designating critical habitat.

Critical habitat was not defined explicitly in the ESA, although examples were provided (also see USDI and USDC 1996). Bogert (1994) interpreted ESA's critical habitat as the geographic area occupied by a species at the time of its listing, as well as areas outside the range that are essential to the conservation of the species. However, this critical habitat definition erroneously assumes species are statically distributed only at places where their populations can persist. The NRC (1995) corrected this misinterpretation of critical habitat, but they misused the terms "habitat" and "critical habitat" as consisting of particular vegetation types. Hall and others (1997) clarified the situation by defining critical habitat as areas that can provide resources for population persistence, consistent with the concept of high-quality habitat. Therefore, not only does a species' preference for available environmental elements require quantification, but reproductive success also needs to be linked to the preferred environmental elements before they are designated critical habitat. Most listed species lack scientifically founded critical habitat designations (US NRC 1995, Gordon and others 1997).

Knowledge of habitat for legally rare species is usually limited to primarily qualitative natural history observations. Such observations are indeed important, but inadequate for reducing the uncertainty about which condition is preferable among those claimed by multiple naturalists. The strongest scientific foundation for designating critical habitat is the scientific field experiment. Such experiments can be mensurative or manipulative (sensu Hurlbert 1984). Mensurative experiments involve counts of species' individuals or their signs along with each environmental resource thought to possibly comprise habitat. These counts are then related to the availability of environmental elements that might be habitat. Manipulative experiments involve replication and interspersion of multiple sets of environmental conditions that possibly serve as habitat. Such experiments can help reduce the uncertainty in critical habitat designations.

Smallwood and Morrison (1997) synthesized opinions from multiple naturalists to design an experiment for the giant garter snake (*Thamnophis gigas*), which is listed by the US Fish and Wildlife Service as threatened and which is proposed to be taken incidentally due to

the development of the Natomas Basin, near Sacramento, California (US Fish and Wildlife Service 1997a). Nearly all natural history observations of the giant garter snake were made along the water edge, usually along narrow channels (ditches) and the banks of sloughs. However, these observations varied in bank slope, vegetative cover and composition along banks, flow rates, and water depth. In our experiment, we proposed that water channels be arranged hierarchically for water depth management and in parallel for replicating and interspersing treatments representing the range of habitat conditions believed by naturalists to be important for the snake. This and other types of appropriately and rigorously designed experiments can be used by the Services as one tool to develop and implement recovery plans or mitigation designs that need to reduce high uncertainty of success, as per the adaptive management approach to be described later.

Attempting to demonstrate rigor in habitat designation, many geographic information system (GIS) maps of vegetation types and other environmental variables have been presented to the public in support of HCPs. These maps usually look impressive but are very often flawed with inappropriate categorization (e.g., "habitat types" rather than vegetation complexes), data aggregation at scales too coarse for the intended analysis, inaccuracy, and inappropriately hard ecological boundaries (Rejesky 1993). It is also important not to carelessly replace the terms "vegetation" and "vegetation type" with "habitat" or "habitat type," because such replacement is inappropriate (Hall and others 1997), and the wording has ramifications for land-use decisions and policy (Rejesky 1993). Thus, the "habitat" depicted in a GIS map may not be the critical habitat that still needs to be identified and designated for ESA compliance.

Conduct Risk Assessment

Population viability analysis (PVA) is a relevant risk assessment method for environmental documents such as EISs and HCPs. PVA is a flexible approach to estimating time to extinction, probability of extinction by a given date or period of time, probability of persistence, and minimum viable population size for persistence (Boyce 1992). All of these estimates have corresponding error rates or uncertainty ranges, because their parameter values are founded on assumptions with implicit uncertainty. The negative version of PVA is population vulnerability analysis, which is more appropriate for assessing whether or not mitigation will comply with the ESA recovery standard. Until 1992, PVA had been applied to only 35 species (Boyce 1992); it has been applied numerous times since then. It is growing in acceptance among ecologists and conservation biologists and is intended for use with rare, vulnerable species. Connell and Sousa (1983) recommended that the minimum area for population or community persistence be estimated, and Schonewald-Cox and Buechner (1991) furthered this recommendation by providing methodology to do so. Soulé (1991) recommended a viability analysis be performed for nature reserves. Gilpin (1996) recommended georeferencing the population data used in PVA. All these recommended variations of PVA would provide useful risk assessments, so long as the appropriate high-quality data are collected and used to build the models.

Environmental documents rarely make use of the necessary data for PVA, including estimates of abundance and abundance patterns through time and space, reproductive rates, survival rates, dispersal distances, and in some cases, genetic variability. Even quantitative impact assessments are rarely provided. Without use of these data, however, scientifically defensible PVAs are impossible, so the risk to survival and recovery of species due to project impacts would not be assessed using all the methods available to the Services, as per ESA Sections 2(c)(1) and 7(a)(1).

The PVA parameter values are especially relevant to assessing extinction risk in the face of declining habitat space for the listed species (Shaffer 1981). Based on the theoretical foundations of ecology and the tenets of conservation biology (MacArthur and Wilson 1967, Soulé and Wilcox 1980, Verner and others 1986), ecological space is one of the most important resources for all listed species. Habitat fragmentation, which is the physical restructuring of the landscape producing habitat patches of smaller average size and greater average separation (Wilcox and Murphy 1985), is the principal threat to species conservation. Without a full-scale PVA, to conclude that listed species are not in jeopardy of extinction due to the level of take proposed in many HCPs is to ignore scientific knowledge. Such conclusions are unscientific when made with no empirical evidence to support them and give the impression they were driven by some process other than environmental science. The existing uncertainty in the parameter values used for PVA will be exacerbated as ecological space and spatial contiguity are lost due to project take and cumulative impacts. Space and contiguity of habitat influence many aspects of species' natural history, population dynamics, genetics, as well as the impacts of environmental stochasticity (Wilcox and Murphy 1985, Morrison and others 1998).

Reduced habitat area due to project take can translate to reductions in species distributions and abundance within the planning area. Wide geographic distri-

bution appears to be critical for the persistence of rare species (Goodman 1987), so reduced geographic ranges of rare species may contribute significantly to cumulative impacts. Without careful analysis of the nature of the reduction in habitat area, the planners would be prudent to assume, as a starting point, at least a proportional reduction in distribution and abundance along with reduction in habitat area. Time to extinction decreases with smaller spatial areas on which the population can occur (Schoener and Schoener 1983, Pimm and others 1988). That smaller populations are more vulnerable to extinction is fundamental to population viability analysis (Boyce 1992).

For PVA, estimating distribution and abundance of legally rare species must involve multiple spatial and temporal scales, the minimum spatial scale being the area encompassing a persistent, natural population or community, and the minimum temporal scale, typically spanning at least six years (Cyr 1997). Smaller spatial scales are unlikely to reveal spatial requirements. The largest scale considered should include the species' recent and current geographic range of distribution, so as to assess cumulative impacts and collateral take (losses). Estimates of population size and project impact due to foreseeable take must represent at least several generations of each species (for estimates of variance) and must account for dynamic spatial and temporal patterns (Hunsaker and others 1990). Populations are typically clustered in space (den Boer 1981, Greig-Smith 1983, Hanski 1994), and these clusters tend to shift locations through time (Taylor and Taylor 1979). Furthermore, population density estimates decline with increasing spatial extent of study area, thereby requiring the relation of density with spatial scale (Blackburn and Gaston 1996, Smallwood and Schonewald 1996). Extrapolating local population density estimates to larger geographic areas is inappropriate without adjusting the estimate down to include the inevitable space that is devoid of the species. When lacking data from sufficiently large spatial and temporal scales, PVA parameter values should be very conservative.

In developing data for an ESA take decision, it is important to consider the cumulative impacts on the species due to other land conversion and water diversion projects, both those in the planning stages and those likely to arise as a normal outgrowth of economic development. To this end, an assessment must be made of projected land conversions in the species' range. Projections should be made of growth in population and development, as well as relevant demographic shifts. Specific plans of industry and government need also be addressed, and long-range transportation and energy plans should be given high priority. Assessing cumulative impacts for ESA take decisions should be done much more rigorously and defensibly than is typical of its use in many National Environmental Policy Act applications (McCold and Holman 1995).

At a minimum, the cumulative impact assessment should extend over the amortized life of the project or any permit duration. An assessment should also be made of how long facilities of the type under consideration generally last. In the case of a housing development, the projected lifetime is likely to be indefinite. Thus, in such a case, a cumulative impact assessment should extend to such a time that all unprotected land is converted due to development or resource extraction.

Among the 19 HCPs we have examined, we have not yet seen a risk assessment for any of the species to be permitted for incidental take. Except for the San Bruno Mountain Area HCP (Thomas Reid Associates 1982, Palo Alto, California), population estimates with error ranges and other population parameters relevant to a risk assessment have not been provided in the HCPs we examined. Once the methodological steps are routinely applied, PVAs should escape the common perception of the Services that PVAs unfairly delay or stop projects (US Fish and Wildlife Service 1997b).

Conduct Ecosystem Assessment

If the Services are to conserve the ecosystem upon which listed species depend, then they must describe and assess ecosystems for project impacts. Drawing from multiple ecosystem definitions (O'Neill and others 1986, Blew 1996, Fauth 1997), we consider an ecosystem to be an open system with inputs, outputs, and recycling of energy and material resources through hierarchically organized biological interactions. Such a conceived system need not have geographic boundaries, but research and management goals often require them. The interactions between organisms and their environment that are key to any definition of an ecosystem require landscape structures that facilitate the movement of both raw and embodied energy and material resources through environmental media such as soil, water, and the atmosphere (Turner 1989). Conservation of an ecosystem requires protection of the landscape structure, its natural disturbance regime, the endemic biological community, and the levels of resource inputs that maintain its functionality (Ricklefs and others 1984, Holling 1986). Its conservation also requires an effort to avoid disruption of its interactions and reductions of its resource assimilation efficiencies due to intrusion by invasive species, chemical pollutants, and physical barriers placed on streams and terrestrial landscapes (Rapport and others 1985).

According to Karr (1994), ecosystem integrity is jeopardized by reduced capacity of the landscape to support biological communities with a species composition and organization similar to the region under natural hydrologic processes. As terrestrial landscapes are altered by the expansion of human activities, some native species lose their capacity to move across the landscape and interact, which is critical for maintaining ecosystem integrity (Karr 1994). Fragmented habitats also fragment species' distribution patterns, and in combination with the resources provided by human activities, fragmentation provides opportunities for exotic species to invade (Smallwood 1994). Exotic species interact with local species and possibly dilute their resource assimilation rates. ESA documents such as HCPs will have made no contribution to conserving ecosystems upon which listed species depend without addressing habitat fragmentation and the intrusive effects of invasive species.

Conserving ecosystems is possible when ESA documents such as HCPs include assessments of the principal environmental media in which raw and embodied resources flow, are stored, and cycle. These principal media are water and soil (Ricklefs and others 1984). The character of soil depends fundamentally on the regional geology, topography, and the past and current hydrology influencing inundation and sediment deposition patterns. The spatial patterns of these media and their associated biota determine terrestrial landscape structure, its change, and its function (Turner 1989). Through time, assemblages of biological species have adapted to the character and structure of these media on the landscape, such as riparian forests along major streams, vernal pools in seasonally inundated patches of clay soils, and grasslands on loam and sandy soils lacking seasonal inundation. Complex symbiotic relationships have developed among species that enhance the chemical characteristics of water and soil media so as to increase assimilation efficiencies and productivity (Maser and others 1978, Ricklefs and others 1984). Conserving ecosystems requires the conservation of their functional landscape structures and healthy water and soil conditions, especially those most often associated with rarity and listed species. Ecosystem conservation can be guided by known system stability principles (Watt and Craig 1986).

By requiring conservation of the supporting ecosystem of listed species, the intent of the ESA was clearly to leave the Services with no room for developing narrowly defined statutes to justify actions that would in any way jeopardize the goal of recovery. Like critical habitat designation, ecosystem assessments must be made at multiple scales because ecosystems are conceptually organized hierarchically (Klijn and Udo de Haes 1994) and are best examined from the top-down of the hierarchy (O'Neill and others 1986, Bedford and Preston 1988). Ecosystems also are not predisposed to convenient description within project boundaries, even though they are arbitrary assignments of the environmental elements into conceptual compartments. Assessments of project impact on ecosystem function will likely differ according to whether they are done at the scale of the project area or the region.

The EIP Associates' (1996) ecosystem assessment for the Yolo County HCP consisted of a brief reference to Yolo County's "functioning ecosystem" (p. 6-1). However, although the term ecosystem was frequently used in the Yolo County and Natomas Basin HCPs (EIP Associates 1996, US Fish and Wildlife Service 1997a), neither HCP was based on any form of ecosystem assessment. Neither HCP assessed the influences of stream barriers, agricultural diversions, stream channelization, riparian vegetation removal from both within and outside the channels, and loading of agricultural chemicals and nutrients. Furthermore, of the 22 animal species to be permitted for take under the Yolo County HCP, and of the 18 to be permitted for take under the Natomas Basin HCP, 10 each rely on burrowing rodents as prey resources or on their burrows as habitat. These rodents, principally pocket gophers (*Thomomys bottae*) and ground squirrels (*Spermophilus beecheyi*), are now restricted to remnant patches of soils suitable for their burrowing, which are loams and sands lacking seasonal inundation and at the thin margins of agriculture. Despite knowing these relationships, and despite the availability of spatially referenced soils data, this part of the ecosystem was not assessed in any way (EIP Associates 1996, US Fish and Wildlife Service 1997a).

A trend among HCPs has been to represent the status of multiple species and their habitats by a single "umbrella," "indicator," "flagship," or "keystone" species (the latter two representations being more implicit). For example, the status and take levels of 29 rare species were represented by the status of Swainson's hawk (*Buteo swainsoni*) foraging habitat in the Yolo County HCP (EIP Associates 1996). The status and take levels of 32 species were represented by the status of the giant garter snake in the Natomas Basin HCP (US Fish and Wildlife Service (1997a). The status and take levels of 85 species were represented by the status of the coastal California gnatcatcher (*Polioptila californica californica*) in the San Diego Multi-species Conservation Program (Fed Reg. 62[60]:14938-41). Scientific foundation is lacking for these and many other representations of multiple species and their habitats by a single species or a portion of its habitat (Morrison and others 1998,

Simberloff 1998). Such scientifically unfounded representations are contrary to using the best scientific data, pursuant to the ESA.

Assessments of ecosystem condition and likely project impacts require scientists who are trained in ecological theory and method with an emphasis on ecosystems. Assessments cannot be made without carefully integrating and aggregating the detail in many environmental elements comprising the ecosystem. Ecosystems are more reliably assessed using indicators of landscape structures influencing biological and physical transport and storage of material and energy (O'Neill and others 1986, Bedford and Preston 1988). Ecosystem assessments can and should be made using carefully chosen and designed ecological indicators (Cairns and McCormick 1992, O'Neill and others 1994) based on known relationships between anthropogenic pressures and their impacts (Karr and others 1986).

Modern risk assessments of ecosystem function require use of indicators expressing sensitivity, vulnerability, and impact (Rapport and others 1985, USDA 1994). Sensitivity is the predisposition of the system to degrade due to changes in the conditions. Vulnerability is the likelihood of degradation when particular anthropogenic activities pressure the sensitive parts of the system. Impact is the consequence of the pressure to the system. Assessments of the risk of project impacts on ecosystem function are now possible, at least in part, using GIS and landscape ecology (Turner 1989, Graham and others 1991, Battaglin and Goolsby 1995), and the ecosystem indicators approach (Bedford and Preston 1988, Cairns and McCormick 1992, Rotmans and others 1994, Schulze and others 1994). Using this approach, sensitive and vulnerable parts of the ecosystem can be identified and mapped along with the pressures (Smallwood and others 1998), and these maps can be compared to maps of realized impacts for validation (Karr and others 1986, Zhang and others 1998). These modern assessment methods should be used to conserve the ecosystems upon which the listed and other species depend. Just stating that the ecosystem will be conserved by reserve establishment or other types of mitigation is inadequate for decision makers.

Conduct Adaptive Management

Adaptive resource management (ARM) is an approach to management that acknowledges uncertainty and the need to learn (Holling 1978, Walters 1986). The term "adaptive" refers to managers learning about systems as they attempt to manage them. Recently, Lancia and others (1996) described the core failures of managers to properly implement ARM. They noted that managers typically base their decisions on intuition and experience and contend that enough is known to proceed with management. To make matters worse, when the need for quick action is perceived, solutions may be implemented in ways that make it difficult to evaluate what was done (e.g., no or inadequate replication and controls). ARM offers a potential solution to these dilemmas by encouraging research and management to be conducted simultaneously as one coordinated effort. ARM is not equivalent, however, to trial-and-error approaches that recognize error and then apply some post hoc remedial action. ARM requires that sound management experiments are planned prior to implementation of a plan. ARM then permits administrators and managers to hedge their bets because they can consider several different models simultaneously. Costly problems, unforeseen when management is initiated, may be discovered. Thus, higher short-term costs should be recouped over the long term.

Adaptive management incorporates the ecological indicators approach, described earlier under ecosystem assessments, as one of multiple steps towards achieving a range of alternative objectives (Holling 1978, Walters 1986). The first step involves the formulation of a clear set of alternative objectives, and step 2 involves designing effective policies to achieve them. Adaptive management then involves the generation of relevant indicators for decision-making; evaluation of each policy in terms of the spatiotemporal behavior of the indicators; synthesis of indicator information for screening of the most important policies; and communication among the staff, decision-makers, and citizens for policy formulation. According to Haney and Power (1996), the essential steps in any project developed around adaptive resources management are to: (1) compile all existing data, (2) develop project goals, (3) develop working hypotheses, (4) implement the prescriptions, (5) monitor results, (6) evaluate and test monitoring data, and (7) return to step #3. Either way, adaptive management is a structured process designed to incorporate learning about the managed resources through management actions that enable hypothesis testing, much like the description provided in the HCP Guidelines (USDI and USDC 1996).

Halbert (1993, p. 262) noted that the original intent of ARM was to apply "experimentation to the design and implementation of natural resource and environmental management policy." ARM is not an excuse to follow a trial-and-error or wait-and-see approach. It requires a rigorous, biologically and statistically valid approach. McLain and Lee (1996) noted that an essential element of ARM was development of a model to simulate key relationships among components of the system being managed. This model is used to test a

range of hypotheses and identify those policy options likely to achieve management objectives.

Adaptive management was proposed for the Natomas Basin HCP in a manner recently defended by the US Fish and Wildlife Service as "typical" (W. Lehman, personal communication, 16 October 1997). According to the US Fish and Wildlife Service (1997a), "adaptive management is a process that allows conservation programs and land use decisions under a given plan to be adopted through time." This statement shows that the Service is violating the most basic tenet of the adaptive management concept. As reviewed above, adaptive management is not a trial-and-error process that, in the words of the Service, can simply be adopted through time. The Natomas Basin HCP did not describe an operating model of ecosystem functioning. It did not develop testable hypotheses or describe specific tests, experiments, or other designed evaluations of the proposed mitigation. It also did not describe a quantitative monitoring plan. The only description of how the HCP could be modified states that the controlling authorities (i.e., the Service) can submit proposed changes, and the "affected permittees" may review the changes. This is a post hoc, trial-and-error process that uses no conceptual model and tests no hypotheses. The Natomas Basin HCP describes a single mitigation strategy developed around rice fields and "managed marsh." The HCP notes that, "Apparently, giant garter snakes can survive in this artificial ecosystem." The HCP goes on to state, "Although it is unproven, there is good reason to believe that constructed marshes and their supporting delivery canal and ditch/drain infrastructure can support large populations." No alternative hypotheses were proposed for testing in case this supposition was false. The failure to provide alternatives for testing is both scientifically unsound and in violation of adaptive management tenets.

Following stake-holder meetings, adaptive management should proceed with the design of replicated and interspersed treatments, including controls, at a meaningful, large scale (Lee 1991, Simberloff 1998). As hypotheses are tested, the results are supposed to be transmitted to the involved policy-makers and other stake-holders so that the most appropriate of multiple objectives can be targeted for new management prescriptions. However, even the best-known attempts at implementing adaptive management have suffered fundamental shortfalls (McLain and Lee 1996). The regulatory agencies have been unable to respond to new information produced by scientific hypothesis testing, sometimes due to: (1) poor coordination between the agencies and stake-holders, (2) lack of consistent funding or personnel involvement throughout the adaptive management process, (3) aversion of agency staff to risking political consequences of failed experiments, and (4) greater agency focus on scientific analysis than on differing viewpoints on how the ecosystem ought to be managed (McLain and Lee 1996). Adaptive management is encouraging in its use of experimentation and monitoring to reduce uncertainty in system behavior under management (Haney and Power 1996, Lancia and others 1996), but the approach requires careful application and changes in how regulatory agencies are involved in the process.

Conduct Monitoring for Impacts

Monitoring for rare species is difficult and requires a detailed, rigorous design. Sampling to detect trends in rare animal species requires special sampling designs and analytical techniques (Gerrodette 1987, Green and Young 1993). Nevertheless, these methods are now well published and available in scientifically reviewed books (Heyer and others 1993, Sutherland 1996, Wilson and others 1996, Morrison and others 1998).

A broad range of conceivable take, mitigation, and conservation impacts need to be considered, particularly for applicants seeking take of multiple listed species. However, the conceivable impacts do not always match the realized impacts. Therefore, adequate, scientific monitoring needs to be implemented along with an adaptive management strategy that details adaptive management practices to be implemented when monitoring reveals particular impacts. Monitoring of legally rare species and functionally important ecosystem conditions (indicators) needs to be conducted at a spatial scale large enough to detect meaningful patterns of change through time. Meaningful patterns of change will be those informing of likely impact. The monitoring also should be adequate for conducting power analysis (Gerrodette 1987, Morrison and others 1998). Monitoring for impacts should rely more on preventing type II errors than type I errors (Shrader-Frechette and McCoy 1992). Type I errors can lead to unnecessary, but harmless, management actions, whereas type II errors can result in no action to halt the decline of a species or its habitat. Concluding lack of statistical significance based on, for example, a >5% chance of committing a type I error, does not translate into lack of impact.

We have yet to see an adequate monitoring program in any of the HCPs we have examined, even though monitoring measures were fairly well described in the HCP Guidelines (USDI and USDC 1996). Monitoring for mitigation effectiveness typically involves monitoring of the habitat area developed relative to the habitat area conserved, thereby meeting the so-called minimum statutory requirements. Habitat area is an inad-

equate representation of species population status, although it is important. Scientific monitoring for impacts due to implementation of HCPs and agreements should be described in the planning and take authorization documents. Appropriate goals and standards should be detailed for implementation of adaptive resources management practices.

Conduct Uncertainty Analyses

To be scientific, data must contain an assessment of their uncertainty. If one uses data to develop a PVA or other quantitative combination of data, uncertainties should be propagated through to the final calculation of interest. Uncertainty distributions can be assigned to each parameter and the resulting output distribution computed. Monte Carlo techniques can be useful for this purpose (US EPA 1996). When data in the literature on a parameter are limited, risk analysts normally fit the data to an uncertainty distribution with long tails, such as a log-normal distribution, to avoid excluding low and high values from the analysis.

Sometimes professional judgment is necessary to fill data gaps or extrapolate data to the current situation. It is inadequate to hide professional judgment in phrases such as, "it is believed that." These terms reflect an implicit, subjective probability assessment on the part of the analysts. Analysts should quantify the confidence and uncertainty range to be attached to these subjective probabilities. The use of expert judgments and subjective probability has been studied at length in human risk assessment (Cooke 1991, Morgan and Henrion 1990, US EPA 1996) and in developing clinical trials in medicine (Berry and Stangl 1996). Both the methodology and lessons learned from these fields should be applied to ESA analyses. Some of these lessons are: (1) Expert assessments can suffer from clustering and poor calibration; (2) an elicitation from a set of experts is to be preferred to the judgment of an individual; (3) expert views should be used to develop a broad subjective probability distribution for uncertain parameters, rather than be used as point data; (4) experts tend to be overconfident in predicting events at low probability; and (5) policy pressures can influence the judgment of experts or lead to their assessments being ignored (Cooke 1991).

If the standards for ESA analysis are to be raised as we recommend, then it is likely, based on analogy with the development of the field of human risk assessment (NRC 1995), that quantitative uncertainty analysis will one day become standard in the record for ESA decisions. Such a development will present decision makers with a new question, namely how confident should they be in the scientific data before reaching a conclusion under the ESA. Should they be protecting species with 10%, 50%, 95%, or 99% confidence? The ESA gives no guidance on this issue. Agency staff will have to use their own judgment until such time as the courts, Congress, or environmental scientists give some definitive guidance.

The confidence limit should depend on the reversibility of the take decision. If many opportunities exist for adaptive management, then it seems reasonable to tolerate a lower confidence level. Confidence levels beyond 95% are not likely to be reliable based on experience in calibrating among experts (Cooke 1991). Thus, it seems reasonable to take 95% as the decision break-point. Unless a species can be protected at a 95% confidence level, a take permit or other request under the ESA should be denied. Such a standard would doom 1 in 20 species to extinction, so should only be implemented in cases where adaptive management is a realistic possibility.

For tort litigation regarding toxins in the United States, uncertainty analysis is required for the admissibility of scientific expert testimony, which also cannot consist of unsubstantiated speculation (William Daubert and others, Petitioners v. Merrell Dow Pharmaceuticals, Inc., No. 92-102, Supreme Court of the United States). Although it remains to be seen whether the Daubert decision applies to ESA compliance issues, its requirements are consistent with the ESA intent of using the best scientific data. Scientific testimony in ESA documentation needs to be founded on the best scientific principles and methods, as described earlier, and sources and magnitudes of uncertainty need clear description.

Uncertainty analysis should be routinely applied to critical habitat designation, to PVA for assessing risks to survival and recovery, to ecosystem assessments, and to monitoring results for use in adaptive resources management. In assessing habitat and ecosystem conditions, the spatial data in GIS maps need to be analyzed for error rates at least in part by conducting ground-truth surveys (verification analysis) and iterative reassignment of derived values per land unit (sensitivity analysis). Using modern research methods, an accuracy assessment with error rates can be applied to predicted species' ranges based on habitat designations and vegetation and landform maps, thereby meeting ESA requirements, biological reality, and US court standards. Uncertainty in the estimates of project and cumulative impacts can then be characterized and reduced using simulations.

Error rates should accompany PVAs, as well as the parameter value estimates such as population abundance, reproductive rates, and dispersal distances. These

error rates must be attributed to sources such as variability in the data (uncertainty analysis) and measurement error. The same is needed of the indicators used in ecosystem risk assessments, and it has already been demonstrated using the index of biotic integrity for assessing stream resources (Fore and others 1994). An honest description of all the sources of uncertainty and model limitations must be represented (Rejesky 1993). Uncertainty ranges will sometimes require expert guesses, but when done this way, the rationale should be provided for the ranges provided. Using modern scientific standards, a PVA can be accomplished to satisfy the level of assessment rigor needed to qualify it as the best scientific data, pursuant to the ESA and justified by the stakes at issue.

Improve Referencing

To comply with the ESA's intent of using the best scientific data, referencing the sources of scientifically based conclusions must always be included in planning and take-authorization documents, whether these documents were prepared by environmental consultants or the Service's Section 10 support staff biologists. Document writers are not being scientific when they use phrases such as "it is believed that." without any reference to the source of such belief. It is believable only when the source of the belief is provided along with an uncertainty range or confidence interval. Referencing will be more scientifically defensible and useful when the following standards are met: (1) preference is given to empirically based reports, reviews of empirical reports, and scientific principles; (2) balanced or comprehensive use of data analyses, scientific ideas, and anecdotal evidence supporting different sides of an argument, rather than tactical, selective referencing; and (3) accurate representation of referenced scientific research reports or published opinions. Standard protocols for referencing in scientific document preparation are described in numerous books, papers, and scientific journal guidelines to authors.

As an example of improper referencing, the US Fish and Wildlife Service (1997a) recently claimed land cultivated for rice also serves as important habitat for the giant garter snake. In their Natomas Basin HCP, they proposed mitigating for development of 7088 ha of habitat by conserving 3544 ha with 75% maintained in rice production and 25% constructed into open water marsh (US Fish and Wildlife Service 1997a). However, the HCP contained no references to data or previous research demonstrating that rice serves as habitat for the giant garter snake. When asked to supply their annotated bibliography of source documents that led to designating rice as important habitat of the giant garter snake, the Service produced a bibliography of nine reports. However, three of the referenced reports were focused on taxonomy, and five of the remaining six did not identify rice as giant garter snake habitat in any way. One unpublished report speculated that rice may be important for newborn snakes, but snake observations in rice were not reported. Not only did the Service lack quantitative evidence in designating rice as habitat for the giant garter snake, but their supporting bibliography was inappropriate.

Until proper referencing has been recognized to qualify scientific and commercial data as the best available, we think that planning and mitigation for take of legally rare species will be unlikely to comply with the intent of the ESA.

Conduct Independent Scientific Review

Scientific research results are usually subjected to peer review. If not, then they are published in what scientists refer to as the "gray literature." Scientists find value in gray literature where expedience in publication is useful or where the author is targeting a select audience. However, scientists usually prefer to rely on peer-reviewed research results for building theory. Some scientific journals require reference only to peer-reviewed research results. Peer review is an important quality of scientific research that keeps the process credible (Woolf 1981, Heath 1989) and effective.

Because the ESA requires use of the best scientific data in biological assessments and HCPs, independent scientific review should be a standard step preceding the issuance of any take permit. Public review periods do not constitute independent scientific review, just as scientists do not obtain independent peer review by making their draft manuscripts available to the public. Rather, scientists solicit peer review, and usually the process is administered by professional editors. Without independent review, modern science cannot work. If this academic peer review process is slower than pragmatism will tolerate, then independent scientific review can be obtained in other ways. For example, although not yet in existence, professional editors of environmental assessment documents could designate reviewers in advance of the assessments and their documentation. Using this approach, the consultants or the Services support staff biologists would also know in advance that their work is going to be reviewed, which by itself would ensure better quality work.

Independent scientific review would greatly improve the public's confidence in assessments and HCPs developed by environmental consultants, who usually are

hired by the take-permit applicant. The environmental consultants have a vested interest in pleasing the take-permit applicant, so these consultants are vulnerable to bias. The Services and local government agency biologists should not serve as independent scientific reviewers, because they must issue the permits and oversee the plan's implementation—they are not independent from the projects under consideration, and could conceivably be biased. By implementing independent scientific review, the process would become more open and consistent with scientific and democratic ideals.

The need for independent scientific review was made all too clear by the reviews of the Yolo County HCP (EIP Associates 1996), which were solicited from scientists at the University of California at Davis, and summarized in a paper published in the journal *Science* (Shilling 1997). Just as the HCP appeared close to approval by all the city governments in the county, Shilling asked some of his colleagues at UC Davis to review the scientific foundations of the Final Draft Yolo County HCP document. All 12 of these scientists concluded that the science was flawed and the HCP should not be approved.

Independent scientific review should be standard and mandatory of HCPs and other biological assessments used to justify issuance of take-permits. With so much at stake in the government's issuance of take permits, the supporting science is in greater need of independent review than is academic science. Not only are biodiversity and ecosystem functionality at stake, but also legal integrity, allocation of public funds, the public trust, and the integrity of the environmental sciences. Environmental consultants and the Services' support staff biologists should not only be required to obtain independent scientific review, but they also should be expected to eventually publish their assessments in professional, scientist-reviewed outlets (NRC 1986). Making such reviewed publications routine would help prevent errors and scientific fraud in its several forms (Woolf 1981, Chubin 1985). Sufficient detail of the research should be published to facilitate replication of the research (Chubin 1985), and raw data should be kept available for independent scientific review. Perhaps a clearinghouse of HCPs and supporting data would provide the openness needed for the process to work properly. Such a clearinghouse and the cost of the reviews should be funded by the take-permit applicants, much as scientists fund their own professional journals. These reviews and their availability in a clearinghouse would: (1) promote economic efficiency by serving as templates for future assessments, and (2) help establish a track record for the consultants.

Why are Scientific Standards Missing from ESA Take Decisions?

Environmental consultants often lack incentives to apply scientific standards to their biological assessments of project impacts. Their employers are often the developers who want to reduce or obviate the regulatory requirements of the ESA. The scientific standards required for ESA compliance are the project barriers that take permit applicants want their environmental consultants to overcome. Therefore, take-permit applicants are more likely to seek repeat business with environmental consultants who bring low scientific standards to their biological assessments or who have particular biases that suit developers or the resources-extraction industries. Additionally, independent scientific review is not required by the Services or by other government agencies, even though the ESA requires use of the best scientific information.

By raising the standards for everyone in the environmental consulting industry to the appropriate levels described herein, this industry will probably get the job done properly and at a profit. The cost to the developers will appear higher at first, but the increased certainty in assessing project impacts and mitigation effectiveness will, in the long run, save everyone time and money. Projects that have a weak scientific base will likely be terminated early, but that is indeed the intention of the ESA.

Academic scientists are usually not engaged in ESA compliance projects or evaluations of agency policies because such activities are unlikely to provide funding or research results needed by academics for publication and career advancement. In our experience, when academics are involved in biological assessments, they are usually invited only to lend post-facto or pseudocredibility to the assessments, and they are not the lead on the contract. They are rarely involved in overall assessments of the project or its environmental documentation. Academic scientists are too busy conducting the scientific investigations that form the basis for decision-making. However, some of these scientists are unaware of the standards to which environmental consultants and the Services are held. They are also unaware of the uses that these consultants often make of scientific research results in addressing ESA compliance.

Conclusion

A recent review of the ESA has found it severely wanting in its ability to protect species and has called for a major overhaul (Gordon and others 1997). Perhaps a

first, less drastic, step is for agency personnel to adhere to the intent of the ESA and raise the standards under which data are collected and interpreted. A major reason for the limitations of the ESA is failure to live up to the language in the statute to rely on "the best scientific data." In this paper, we describe standards that should be applied to habitat conservation plans and environmental impact statements affecting endangered species, if the scientific standards adhered to at universities and research laboratories are to be met. It is difficult to see how anything less could allow decisions to be made based on the "best scientific data." We suggest that the best scientific data should be used prior to the pragmatism and political trade-off that are sought in making take decisions.

Based on the historical success of the scientific method, the implementation of explicit scientific standards should help solve some of the problems facing ESA compliance in the development of HCPs and EAs. The ESA provided no internal statutory guidance as to what are the best available scientific and commercial data (Bogert 1994), so it is up to environmental scientists to decide on them. Applying explicit scientific standards will require greater involvement from academic and research scientists in the development and approval of the environmental documents. Many scientific investigations have provided strong theory and method in identifying critical habitat designations, ecosystem assessments, risk assessments, environmental monitoring and adaptive resources management. Decision-makers must also know of the uncertainties when choosing among HCP and other ESA agreement alternatives, and they and the public should have access to independent review comments, the data, and the scientific reports used to make conclusions. The stakes are too high to justify issuing take permits without having used the best scientific data.

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Research Article

Burrowing Owl Mortality in the Altamont Pass Wind Resource Area

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ABSTRACT We estimated wind turbines in the Altamont Pass Wind Resource Area (APWRA), California, USA, kill >100 burrowing owls (*Athene cunicularia hypugaea*) annually, or about the same number likely nesting in the APWRA. Turbine-caused mortality was up to 12 times greater in areas of rodent control, where flights close to the rotor plane were disproportionately more common and fatalities twice as frequent as expected. Mortality was highest during January through March. Burrowing owls flew within 50 m of turbines about 10 times longer than expected, and they flew close to wind turbines disproportionately longer within the sparsest turbine fields, by turbines on tubular towers, at the edges of gaps in the turbine row, in canyons, and at lower elevations. They perched, flew close to operating turbine blades, and collided disproportionately more often at turbines with the most cattle dung within 20 m, with the highest densities of ground squirrel (*Spermophilus beecheyi*) burrow systems within 15 m, and with burrowing owl burrows located within 90 m of turbines. A model of relative collision threat predicted 29% of the 4,074 turbines in our sample to be more dangerous, and these killed 71% of the burrowing owls in our sample. This model can help select the most dangerous turbines for shutdown or relocation. All turbines in the APWRA could be shut down and blades locked during winter, when 35% of the burrowing owls were killed but only 14% of the annual electricity was generated. Terminating rodent control and installing flight diverters at the ends of turbine rows might also reduce burrowing owl mortality, as might replacing turbines with new-generation turbines mounted on taller towers. (JOURNAL OF WILDLIFE MANAGEMENT 71(5):1513–1524; 2007)

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KEY WORDS Altamont Pass, *Athene cunicularia hypugaea*, behavior, burrowing owl, fatalities, mitigation, mortality, nest density, wind turbines.

The western burrowing owl (*Athene cunicularia hypugaea*; hereafter owl) in California, USA, has declined in number and spatial distribution (DeSante et al. 1996, Klute et al. 2003). Nesting pairs occur individually or in small groups scattered among remnant habitat patches across their former geographic range, and previously known populations were extirpated in recent years (e.g., Johnson 1997). Owls residing in the Altamont Pass were omitted from the last statewide assessment of burrowing owls (DeSante et al. 1996). Researchers studying avian collisions with wind turbines observed many burrowing owls in the Altamont Pass Wind Resource Area (APWRA), as well as numerous owl carcasses under wind turbines (Rugge 2001; Thelander et al. 2003; Smallwood and Thelander 2004, 2005). Owls appeared so numerous in the APWRA that we concluded the population there must be regionally significant, and there appeared to be sufficiently high mortality to wonder whether the APWRA functions as an ecological sink.

Recent data suggested owls collide with wind turbines more often where owl burrows are more numerous near turbines (Smallwood et al. 2001). Smallwood et al. (2001) found the number of owl burrows (i.e., all burrows showing fresh signs of use, such as whitewash, pellets, decorations, or flushed owls) increased with the number of ground squirrel (*Spermophilus beecheyi*) burrow systems within 55 m of turbines. Owl nest sites close to wind turbines may expose owls to a greater threat of collision with wind turbines. Therefore, wind turbines located on the landscape away from owl burrows may reduce turbine-caused owl mortality.

Our research objectives in the APWRA, as they related to burrowing owl, were to 1) compare human-caused mortality to the predicted habitat capacity of owls in the APWRA, 2) identify key patterns of owl mortality and behavior in the APWRA, and 3) relate management practices to owl behavior and mortality patterns, and suggest mitigation measures to reduce turbine-caused owl fatalities in the APWRA.

STUDY AREA

The APWRA was in central California's eastern Alameda and southeastern Contra Costa counties, including about 16,450 ha of annual grassland. Our study area ranged from 78 m to 470 m above mean sea level, was composed of hills, ridges, and valleys, and included stock ponds, small seasonal ponds, and marshes. Most ridges were oriented northwest to southeast and were bisected by seasonal streams.

Vegetation was predominantly nonnative annual grassland, including soft chess (*Bromus hordeaceus*), rip-gut brome (*Bromus diandrus*), foxtail barley (*Hordeum murinum leporinum*), Italian rye grass (*Lolium multiflorum*), and wild oats (*Avena fatua*). Common forbs included black mustard (*Brassica nigra*), fiddle-neck (*Amsinckia menziesii intermedia*), chick lupine (*Lupinus microcarpus* var. *densiflorus*), bush lupine (*Lupinus albifrons*), and wally baskets (*Triteleia laxa*). Grasses and forbs grew during the rainy months of January through March, then died or went dormant by early June. Physiographic elements of the APWRA included annual

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grassland, alkali meadow, emergent marsh, riparian woodland and scrub, creeks and drainages, stock ponds, cultivated land, and rock outcrops.

Landowners in the APWRA principally grazed livestock but also leased land to wind turbine owners. When our study began, the APWRA included about 5,400 wind turbines of various models with a total rated capacity of about 580 MW. These wind turbines were mounted on various types of tower and at heights ranging from 4 m to 43 m aboveground. Many were on ridge crests or on ridgelines that descend into ravines from the ridge crests. About 11% of the wind turbines were within large drainage basins we referred to as canyons, which included gullies, ridges, and some ridge crests occurring at lower elevations than the canyon boundary. Other turbines were on hill slopes away from ridges and drainages. Smallwood and Thelander (2004, 2005) provided additional detail on land uses in the APWRA, wind turbine attributes, and other aspects of the study area.

METHODS

Habitat Capacity of the APWRA

We obtained owl population density estimates and study area sizes used to estimate the density estimates from Coulombe (1971), Thomsen (1971), Martin (1973), Butts (1976), Gleason and Johnson (1985), Haug and Oliphant (1990), Rodriguez-Estrella and Ortega-Rubio (1993*a*, *b*), Trulio (1993), Leptich (1994), Desmond and Savidge (1996), Botelho and Arrowood (1998), and Wiley (1998). Following the methods of Smallwood (1995, 1998) and Smallwood and Schonewald (1996), we regressed $\log_{10}$ density on $\log_{10}$ study area size using linear regression analysis because most of the variation in intraspecific density estimates can be explained by study area size due to mathematical artifact of the predictor variable appearing as the denominator of the density estimate. We relied on the root mean-square error in the regression model to estimate the uncertainty range applied to the nesting pair density estimate to be applied to the spatial area of the APWRA. We multiplied the estimate of owl nesting pair density for the APWRA by the area of the APWRA to arrive at an abundance estimate in lieu of directed field research. To this number we added the number of fledglings/pair averaged from Thomsen (1971), Martin (1973), Haug and Oliphant (1990), Johnson (1997), Botelho and Arrowood (1998), Rosenberg and Haley (2004), Lantz (2005), Lutz and Plumpton (1997), and Teaschner (2005), and the number of floaters averaged from Thomsen (1971) and Botelho and Arrowood (1998).

Owl Fatalities

From March 1998 through September 2002, we searched for bird carcasses within 50 m of 1,526 wind turbines, hereafter set 1. We periodically added groups of wind turbines as we obtained access. By September 2002, set 1 included 182 rows of mostly regularly spaced wind turbines, which were all the wind turbines available to us. From November 2002 until May 2003, we added 2,548 turbines arranged in 380 rows, hereafter set 2. We systematically selected the set 2 turbine strings to ensure full representation of the north–south and east–west extents of the APWRA. In total, we sampled about 75% of the wind turbines in the APWRA. Fatality search intervals varied interannually and among groups of wind turbines, averaging 53 ± 11.6 days among set 1 wind turbines and >90 days for set 2 turbines. Search intervals were longer for set 2 because we gained access to them late in our study, and we decided to reduce search frequency per turbine in order to minimally sample more wind turbines in the APWRA.

Two people explored the ground around each wind turbine row, maintaining a zigzag pattern about 4 m between each turn. Previous studies reported about 77% of all bird carcasses were found ≤40 m from the wind turbines (Orloff and Flannery 1992, Munsters et al. 1996, Howell 1997), so we decided to use 50 m as our search radius.

We examined all carcasses or body parts found, such as groups of flight feathers, head, wings, tarsi, and tail feathers, to determine species, age, sex, and probable cause of death. We determined cause of death by evidence of injuries, when available, such as burn marks or singed feathers typical of electrocution, and cut or twisted torsos, dismemberment, and other forms of blunt force trauma typical of collisions with wind turbine blades. Otherwise we relied on proximity of the carcass to the likely cause of death. We estimated days since death by analyzing carcass condition (e.g., fresh, weathered, dry, bleached bones) and decomposition level (e.g., flesh color, presence of maggots, odor). We used time-since-death estimate in which season the fatality occurred and to decide whether to use the fatality in our estimation of mortality.

We expressed wind turbine–caused mortality as the number of fatalities per megawatt (MW) per year, where MW was the sum of the rated power output of all wind turbines composing a row of turbines, and the number of years or fractions of a year were the time spans over which we performed searches at that wind turbine row. We derived our mortality estimates only from wind turbine–caused fatalities ≤90 days before the search. We added 0.25 (3 months) to the number of years we used in each mortality calculation to represent the time period when fresh carcasses could have accumulated prior to our first search. We assumed we would have found the same number of fatalities during a given year regardless of whether we performed 12 searches or 8 searches, but it is likely that the reduced search frequency at set 2 wind turbines yielded lower carcass detection rates.

We multiplied our raw mortality calculation by 1.164 to account for carcasses we did not find beyond our search radius only because we did not see them. While searching ≤50 m from turbines, we found 16.4% of the owl carcasses >50 m from turbines, and we assumed we missed as many of the carcasses as we found outside the search radius. We relied on other studies for searcher detection and scavenging removal rates. Orloff and Flannery (1992) estimated searcher detection of 85% of raptor carcasses in the APWRA, so we

conservatively used this value for owls and divided mortality by 0.85. We regarded the mortality estimate adjusted for search detection rates as the low end of an uncertainty range. The high end of the uncertainty range included an adjustment for rate of carcass removal by scavengers.

Erickson et al. (2003) estimated that after 40 days scavengers removed 58.6% of carcasses of large-bodied species and 80.2% of carcasses of small-bodied species. We considered burrowing owl a small-bodied species. Also, our average search interval was 53 days for set 1 wind turbines, and 90 days for set 2 wind turbines, so we adopted the carcass removal rate of Erickson et al. (2003) for set 1, assuming scavenger removal rates were similar between 40 days in their study and 53 days in ours, and we added 10% to these rates for set 2, assuming a 90.2% rate of carcass removal. To adjust our mortality estimates to include the carcasses removed by scavengers and undetected by us, we divided our raw mortality estimates by twice the proportion of carcasses detected by Erickson et al. (2003) after 40 days, which effectively halved their scavenger removal rate. Based on our experience observing raptor carcasses in the APWRA, we halved the scavenging rate of Erickson et al. We divided owl mortality in set 1 and set 2 wind turbines by 0.396 and 0.196, respectively, to adjust the estimates for carcasses we did not detect due to scavenger removal. We examined only unadjusted mortality estimates interannually because we assumed scavenger removal rates and searcher detection error did not vary interannually.

We related owl fatalities to the spatial distributions of mammal and owl burrows. We mapped burrows using a Trimble Pro-XR Global Positioning System within 90 m of 571 wind turbines composing 70 rows. We selected turbine rows representing a wide range of raptor mortality recorded during our fatality searches, as well as a variety of physiographic conditions and levels of rodent control ongoing in the APWRA (we did not participate in the rodent control program). Levels of rodent control were none, intermittent, and intense, where intense control effectively eliminated ground squirrels from the treated areas. We used a pacing method to separate burrow systems when continuity of sign rendered inter-burrow system distinctions difficult (Smallwood and Erickson 1995). We walked transects 0 m, 15 m, 30 m, 45 m, 60 m, 75 m, and 90 m away from the turbine string, thus covering increasingly larger areas around the turbine strings.

Owl Behavior

Two biologists collected bird behavior data within 28 study plots during 1,958 behavior-observation sessions (979 hr) from 26 March 1998 through 18 April 2000. The study plot boundaries encompassed wind turbines easily visible to the observers from a fixed observation point, resulting in a mosaic of irregularly shaped, nonoverlapping plots, each about 3 km^2. The plots contained 1,165 turbines, with 10–67 turbines per plot, representing the majority of the turbines accessible to us at the time. Each observer carried plot maps to identify each turbine by its number designation and to link it to recorded bird activities. A single observer performed circular visual scans (360°) to 300 m using 8 × 40 binoculars. After the 30-minute observation session, the observer moved to another sampling plot to begin another 30-minute session.

We sampled all 28 plots at least once per week stratified by morning and afternoon sessions. Morning sessions spanned 0700 hours to 1200 hours, and afternoon sessions spanned 1201 hours to dusk. We observed behaviors throughout the year in nearly every weather condition, unless rain or fog reduced observer visibility to <60%, which was too poor to track bird activity accurately. We completed 2 sessions simultaneously, averaging 6–8 sessions per field day. We conducted all simultaneous 30-minute sessions on non-adjacent plots to improve our degree of independence among sessions.

We continuously followed a bird until it left the plot. For each sighting, we recorded the species, number of birds in a group, the times when the bird was detected and last seen, predominant flight behavior, flight direction, distance to the nearest wind turbine, type of wind turbine, number of flights through a turbine string, and flight height relative to the rotor zone, which is the height aboveground from the lowest to the highest reaches of the turbine blades and extending laterally to 50 m from the rotor.

Behavior and Fatality Association Analysis

We tested measured variables for association with owl fatalities and with behaviors using chi-square analysis (Smallwood 1993, 2002). Observed values were either the number of minutes of activity of a particular behavior or the number of fatalities, and observed values were related to expected values for both statistical hypothesis testing and for deriving a measure of effect. We calculated the measure of effect as the observed divided by the expected values, and we measured the number of times greater or fewer each observed value deviated from the corresponding expected value. We calculated expected values as a product of the total sample size of the dependent variable and the incidence, or relative frequency of occurrence expressed as a proportion, of the *i*th condition of the association variable, where we also factored sampling effort into the incidence of the *i*th condition of the association variable. We caution, however, that the behavior observations are not independent events, so chi-square tests based on minutes of observation are prone to Type I error. For these reasons, we highlighted only the behavior associations with large measures of effect and significant test results. See Smallwood and Thelander (2004, 2005) for additional detail of the analytical methods.

Predictive Model

We developed a simple predictive model of each wind turbine's relative threat to owls:

$$\text{Accountable mortality} = (\text{obs} - \text{exp})/\text{total fatalities} \times 100\%.$$

Positive values expressed the percentage of total fatalities likely killed at wind turbines due to the attribute associated

with the value, and negative values expressed the percentage of total expected to have been killed but not killed. Thus, accountable mortality ranged from −100% to 100% and expressed the percentage of the fatalities attributable to a particular category of an association variable.

We calculated accountable mortality only for variables whose chi-square tests for association with fatalities were significant with most expected cell values >5. These variables also were either categorical (e.g., tower type) or graded in value with accountable mortality. For those variables included in the model, we summed accountable mortality values across the variables to arrive at a score:

$$\text{Predicted impact} = \sum \text{accountable mortality.}$$

Predicted impact values >0 represented wind turbines more likely to kill owls, whereas values ≤0 represented wind turbines less likely to kill owls. Predicted impacts were additional to impacts we could not account for based on the data we collected, which probably included a baseline level of impact simply because all wind turbines pose an inherent danger to birds because turbines are tall structures with moving parts into which birds can collide.

We compared model predictions of impact to the number of fatalities we recorded at the particular wind turbine. We assessed model effectiveness by the percent correct classification of the wind turbines that killed owls. We also assessed the model based on the percent of wind turbines whose predicted impact was >0 but at which we found no fatalities. These wind turbines will more likely kill birds, even though we did not find them yet, and this percentage represents the level of effort needed to modify wind turbines and range management practices to substantially reduce owl collisions.

Lastly, we examined the percentage of fatalities corresponding with wind turbines correctly classified as more likely to kill owls. This percentage represented the degree to which mortality could be reduced by modifying conditions expressed by the variables composing the model, assuming no interaction effects between predictor variables.

RESULTS

Turbine-Caused Mortality and Habitat Capacity in the APWRA

According to our model of owl density regressed on study area size, the APWRA should support about 35–75 nesting pairs of owl (Fig. 1). If 35–75 pairs produced on average 3.08 fledglings per pair per year (the average reported from 10 studies across the western United States and Canada), and if the number of floaters average 43 per 100 nesting adults (the average reported from 2 studies in California and New Mexico, USA), then about 208–446 owls would be present as the breeding season ended. We estimated APWRA wind turbines kill 99–380 owls per year, or between 22% and 183% of the APWRA's estimated population.

Wind turbine–caused, unadjusted mortality estimates based on fatalities found May 1998 through September

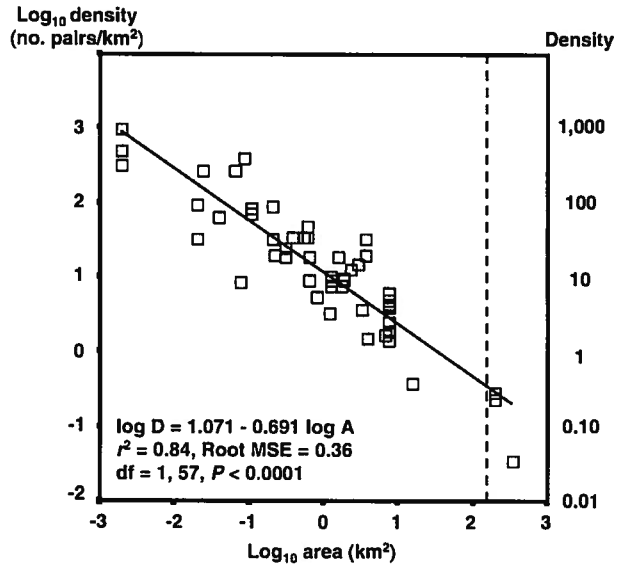

Figure 1. Nesting density estimates of burrowing owl related to study area size as an inverse power function among studies published 1971–1998 from throughout the species' geographic range. The vertical dashed line represents the geographic area of the Altamont Pass Wind Resource Area, California, USA. The abbreviation MSE stands for mean square error, expressing the percent error in the raw data.

2002 were 0.014 fatalities/MW, 0.163 fatalities/MW, and 0.087 fatalities/MW per year, respectively, among 118.02 MW, 65.33 MW, and 206.30 MW of rated capacity in areas of no rodent control (120 turbine rows), intermittent control (87 rows), and intense control (240 rows). These estimates differed (analysis of variance [ANOVA]: $F = 4.45$, df = 2, 445, $P = 0.012$). Mortality estimates adjusted by searcher detection and scavenger removal rates were 0.019–0.047 in areas of no rodent control, 0.224–0.564 in areas of intermittent rodent control, and 0.119–0.301 in areas of intense control.

Owl mortality increased from the first through third years of the study, according to the comparison including all turbine rows searched ≥1 year (ANOVA: $F = 3.20$, df = 3, 639, $P = 0.023$; Fig. 2), but it did not change among turbine rows searched all 4 years and where rodent control was applied all 4 years (ANOVA: $F = 1.24$, df = 3, 247, $P = 0.296$). At 10 turbine rows searched only during the first and second years in an area of intermittent rodent control, unadjusted owl mortality increased from 0 collisions/MW to 0.43 collisions/MW (ANOVA: $F = 5.05$, df = 1, 19, $P = 0.005$). Unadjusted owl mortality decreased between the third and fourth years in turbine fields where intense rodent control had been applied during the fourth year, from 0.42 fatalities/MW to 0.05 fatalities/MW (ANOVA: $F = 4.44$, df = 1, 75, $P = 0.039$).

Owl Fatalities and Behavior

Of the owl carcasses found during fatality searches in the APWRA, we attributed the cause of death of 79% (60 carcasses) to wind turbine collision, 13% (10 carcasses) to unknown causes we later assumed to be wind turbine

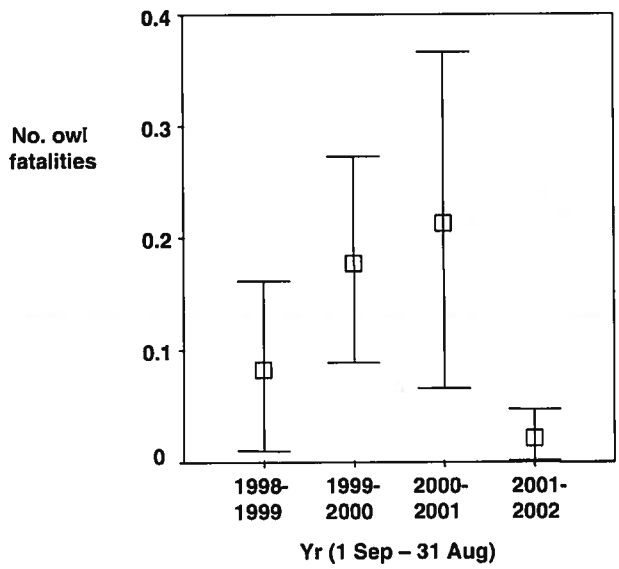

Figure 2. Burrowing owl mortality (no. fatalities/MW of wind turbines in turbine row; $\bar{x}$ and 95% CI) during 1998–2003 among 160 turbine strings searched ≥1 year in Altamont Pass Wind Resource Area, California, USA.

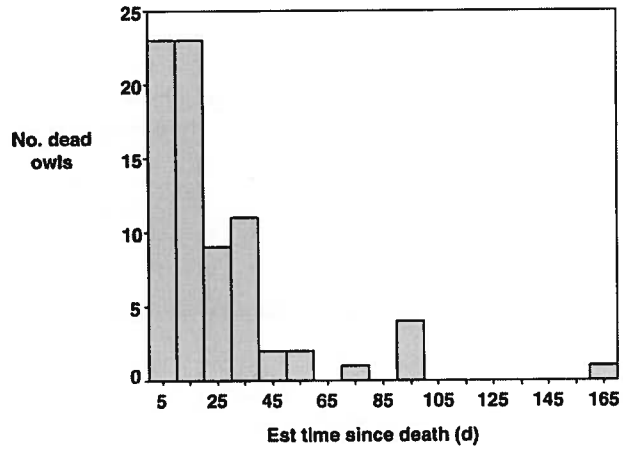

Figure 3. Number wind turbine–caused burrowing owl fatalities by the estimated number of days since death in the Altamont Pass Wind Resource Area, California, USA, 1998–2003.

collisions based on carcass locations, and 5% (4 carcasses) to predation. One owl collided with an automobile on an access road, and another collided with an electric distribution line. Field biologists searching for fatalities did not report the type of injury of most owl fatalities, but nearly half of the injury reports described broken or severed wings (Table 1). Most (76%) of the owl carcasses had been extensively scavenged, even though all but 2 appeared to have died ≤90 days before (Fig. 3).

Dead owls included 20 adults, 3 immature birds, and 53 of unknown age. Wind turbines killed 18 adults, 2 immature owls, and 50 of undetermined age. Most wind turbine–killed owls died September through December (Table 2). Owl mortality relative to seasonal APWRA power output was highest during January, February, and March (Fig. 4), which is when blades often move fast enough to kill birds but not fast enough to generate electric power. Generally, wind turbine–caused owl fatalities increased with energy generation ($\chi^2 = 0.51$, df = 1, 8, $P < 0.05$) after holding from the analysis fatalities in December, January, and March (Fig. 5). Wind turbine–caused owl fatalities associated with month of the year differently than did perch time or near-turbine flight time (Fig. 6).

Vertical axis turbines (i.e., Flowind turbines) killed disproportionately more owls, as did turbines on tubular towers (Table 3). Owls also flew close by and perched disproportionately more often near turbines on tubular towers. Turbines on lattice towers killed only half the owls expected.

Wind turbines with slower-moving blades killed 1.6–1.8 times more owls than expected, and turbines with faster-moving blades killed fewer than half the expected number ($\chi^2 = 42.26$, df = 2, $P < 0.005$). Similarly, wind turbines with the least rotor plane (in m^2) swept/second killed 1.7–1.8 times the owls expected ($\chi^2 = 24.83$, df = 3, $P < 0.005$). Wind turbines with blades reaching as low as 4.0–5.1 m

Table 1. Number of wind turbine–caused burrowing owl fatalities and levels of scavenging by types of injury reported during 1998–2003 in the Altamont Pass Wind Resource Area, California, USA.

Type of injury	Burrowing owl fatalities (n = 70)	Reported scavenging (n = 54)		
		No evidence	Some	Extensive
Not reported	38	0	2	30
None apparent	2	1	0	0
Head	3	1	0	1
Neck	2	1	0	0
Decapitated	5	1	1	2
Torso cut or twisted	4	3	0	0
Torso cut in half	1	0	0	0
Broken wing	5	0	1	2
Severed wing	4	1	1	1
Dismembered	6	0	0	5

Table 2. Percentage of annual power output, burrowing owl fatalities (n = 70), and fatalities per age group by month of the year during 1998–2003 in the Altamont Pass Wind Resource Area, California, USA.

Month	% of annual power output	Turbine-caused deaths	Age of bird at death		
			Ad	Immature	Unknown
Jan	1.9	8	0	0	8
Feb	1.8	2	0	1[a]	1
Mar	1.7	3	1	0	2
Apr	2.2	1	0	0	1
May	4.6	0	0	0	0
Jun	9.4	2	1	0	1
Jul	17.7	10	2	0	8
Aug	15.8	6	1	1	4
Sep	16.5	14	6	0	8
Oct	15.5	4	0	0	4
Nov	8.9	8	4	0	4
Dec	3.8	12	3	0	9

[a] Assignment of the month of the fatality is uncertain because we estimated the carcass as 3 months old when we found it in May. Given its state of decomposition, we might have misclassified the bird as immature or as having been killed in Feb.

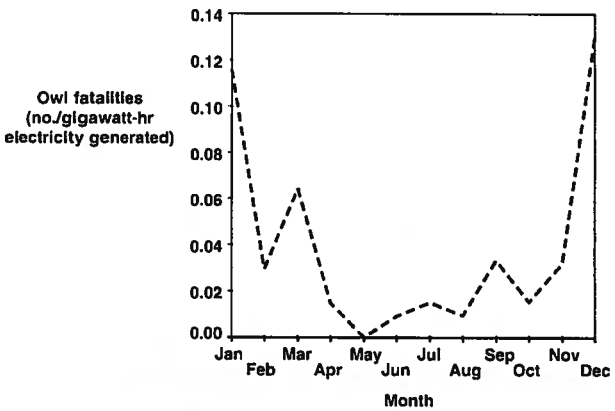

Figure 4. Number of wind turbine–caused burrowing owl fatalities (no./1,000 searches) per gigawatt-hour of electricity generated in 1999 in Altamont Pass Wind Resource Area, California, USA. Note that owl fatalities per gigawatt-hour peaks during winter and March.

aboveground killed 2.2 times the number of owls expected, and turbines whose low reach of blade was 11.1–14.9 m aboveground killed 1.5 times the number of owls expected ($\chi^2 = 22.01$, df = 4, $P < 0.005$).

Whereas owls flew within 50 m and perched nearby turbines at the edges of gaps in turbine rows nearly 1.7 times longer than expected, they collided with these turbines about as often as expected (Table 3). End-of-row turbines killed owls 2.1 times more often than expected, and interior turbines killed them disproportionately less often.

During the 1,958 behavior-observation sessions, we reported 100 owl sightings totaling 1,622 minutes, of which owls flew 193 minutes and perched 1,438 minutes. Owls averaged 117 m to the nearest wind turbine and we never saw them flying through turbine rows. However, we saw them flying within the rotor zone 31 times.

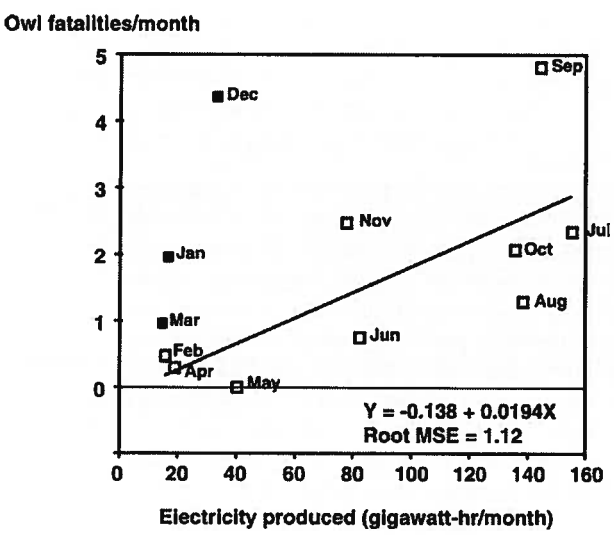

Figure 5. The number of burrowing owl deaths (no./1,000 searches) per month as a function of power output in 1999 in the Altamont Pass Wind Resource Area, California, USA. The filled squares represent outliers we held out of the analysis. The abbreviation MSE stands for mean square error, expressing the percent error in the raw data.

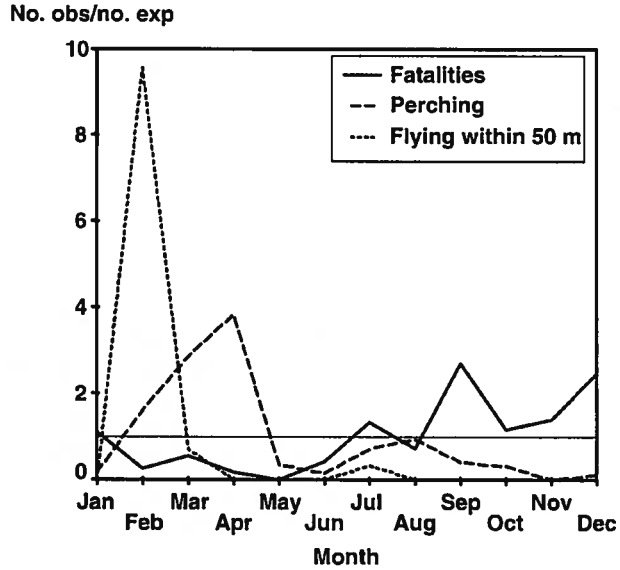

Figure 6. Number observed/number expected burrowing owl fatalities caused by wind turbines, owls perching on turbines, and owls flying within 50 m of wind turbines versus month of the year at Altamont Pass Wind Resource Area, California, USA, 1998–2003.

We observed owls flying ≤50 m from wind turbines about 10 times more often than expected ($\chi^2 = 1{,}358.15$, df = 2, $P < 0.005$), whereas we saw them perched 50–100 m from turbines >4 times longer than expected ($\chi^2 = 2{,}454.02$, df = 2, $P < 0.005$; Fig. 7). To wind turbines most sparsely distributed in the APWRA, owls flew ≤50 m from wind turbines ($\chi^2 = 711.56$, df = 3, $P < 0.005$) and perched ($\chi^2 = 278.77$, df = 3, $P < 0.005$) 6 times longer than expected (Fig. 8). However, owl collisions with turbines did not associate significantly with the number of turbines within 300 m ($\chi^2 = 6.04$, df = 3, $P > 0.05$).

Nearly all owls killed by wind turbines were outside wind walls (wind walls are turbines mounted on lattice towers of 2 heights to achieve a greater height domain of wind capture within a single row of turbines), as were all observations of owls flying close by and perching nearest wind turbines (Table 3).

Most owls were killed outside canyons, but they were killed in canyons 1.4 times more often than expected (Table 3). In canyons they also flew within 50 m of turbines and perched nearest turbines 2.6 times and 1.9 times more than expected, respectively. At the APWRA's lowest elevations, 85–235 m above mean sea level, owls collided with wind turbines 1.6–2.5 times more than expected (Table 3). We observed disproportionately longer close-by flights and perching between 135 m and 185 m elevation. Owls collided with turbines uniformly among landscape features, even though they flew close by wind turbines and perched 2.5 times longer than expected on ridge crests (Table 3).

Disproportionately more owls were killed by wind turbines with the most cattle dung within 20 m, which was also where we observed owls perching and flying close to turbines 3.3 times longer than expected (Table 3).

Owls collided with wind turbines nearly twice as often as expected in areas of intermittent rodent control, which were also where we saw them for disproportionately longer periods flying within 50 m of turbines and perching (Table 3). Disproportionately fewer collisions occurred in areas of intense rodent control. Owl mortality was greater at wind turbines with higher densities of burrow systems of fossorial mammals within 90 m (Table 4). Mortality was disproportionately greater at wind turbines with intermediate densities of ground squirrel and desert cottontail (*Sylvilagus auduboni*) burrow systems within 90 m, and it tended to be greater at the highest densities of ground squirrel burrow systems within 15 m (Table 4). Owl mortality was also significantly greater at wind turbines with owl burrows within 90 m, and the occurrence of these burrows could account for 23% of the owl fatalities in our sample (Table 4).

Predictive Model of Turbine Threat

Various wind turbine attributes contributed to model predictions of threat posed to owls by wind turbines (Table 5). We did not use some variables that related significantly to owl fatalities to construct the predictive model because they were limited in scope and we could not measure them at all wind turbines in our sample.

The model correctly predicted wind turbines to be greater collision threats where 71% of the owl fatalities actually occurred (Fig. 9). It predicted 1,215 (30%) of the wind turbines to be more dangerous, including 70% of the turbines we documented as having killed owls. The more dangerous wind turbines were distributed mostly along a low-elevation band across the wind farm, but also between the Patterson Pass and the Highway 205 corridor.

DISCUSSION

Our results suggest APWRA wind turbines annually kill somewhere between one-fifth and nearly twice the number of estimated owls in the available habitat area. We do not know the population-level impact of wind turbine–caused mortality on owls in the Altamont Pass, but it is potentially substantial. Future research in the APWRA is needed to test the following 4 alternative hypotheses stemming from our uncertain impact estimates and from the potentially paradoxical result of equal or greater adults killed compared to the number nesting in the APWRA.

Hypothesis 1: The APWRA Is an Ecological Sink for Owls

Mortality might equal or exceed production in the APWRA because owls dispersing from natal populations outside the APWRA quickly replace wind turbine–killed owls. Generally, population densities can be relatively high in ecological sinks even though mortality is high, which is one reason density is considered a poor indicator of habitat quality (Lidicker 1975, Van Horne 1983, Smallwood 2002). Although local numbers of owls might not decline in the face of wind turbine–caused mortality, other populations lose recruitment from the owls dispersing to and never leaving the APWRA.

Hypothesis 2: Many Turbine-Killed Owls Are Migrants

Many of the adults killed by APWRA wind turbines might be migrants moving through but not nesting in the APWRA. The Altamont Pass is a migration route for multiple species of raptor, and might be a route for owls because it is the low spot in the hills between the Central Valley and San Francisco Bay area populations. Most of the collisions occurred during fall and early winter when migration movements would be expected.

Hypothesis 3: We Underestimated Local Population Abundance

Our regression model (Fig. 1) might have underestimated owl abundance in the APWRA, but if it did, then spatial patterns of owl in the APWRA differ from those at study sites used to generate the published density estimates. Either the higher densities typical of smaller study areas extend to a larger portion of the APWRA than observed in similar-sized areas elsewhere, or the APWRA includes multiple high-density clusters of owls. Based on our incidental observations of owls in the APWRA, we suspect our model underestimated the number of nesting pairs, but focused research will be needed to test our suspicion.

Hypothesis 4: We Overestimated Turbine-Caused Mortality

Our mortality estimate might be too high, but if it is, then our searcher detection rates must be greater than those used by Erickson et al. (2003) or the scavenger removal rate must be lower. Mounting evidence (K. S. Smallwood, unpublished data) indicates we may have underestimated the scavenger removal rate of owls, which means we likely underestimated owl mortality. On the other hand, if we erroneously attributed a substantial portion of the owl fatalities to wind turbine collision, then we would have overestimated owl mortality. In our experience performing field work around owls in environments lacking wind turbines, however, we have not found nearly the number of owl carcasses as we found around APWRA wind turbines.

Fatality Associations

Wind turbine–caused owl fatalities were more numerous during fall and early winter, the latter season corresponding with the APWRA's reduced energy output. K. S. Smallwood and L. Spiegel (California Energy Commission, unpublished data) estimated shutting down wind turbines November through February should reduce annual owl fatalities 35% while giving up only 14% of annual electricity generation in the APWRA.

Wind turbines with lowest reach of blades $\leq$15 m aboveground killed disproportionately more owls. Replacing the older wind turbines with new-generation turbines mounted on much taller towers might reduce the collision rate by raising the rotor blades above most owl flights.

Owl perception of the turbine field might affect collision rate. Owls appeared to favor areas of lesser wind turbine presence and operations, flying and perching 6 times more than expected among turbines most sparsely distributed.

Table 3. Number of burrowing owl fatalities and observed number/expected number of fatalities, flight observations within 50 m of turbines, and observations of perching by wind turbine model, tower type, the turbine's position in the row, whether the turbine was in a wind wall, whether in a canyon, by elevation, landscape feature, level of rodent control, and abundance of cattle pats within 20 m of turbines during 1998–2003 in the Altamont Pass Wind Resource Area, California, USA.

Association variable	Turbine-caused deaths	Obs/exp: Collisions	Obs/exp: Flight time ≤50 m from turbines	Obs/exp: Perch time
Wind turbine model[a]				
Micon	8	1.63		
Bonus	31	1.60	2.13	2.16
Danwin	0	0.00	0.00	0.00
Flowind	10	3.54	0.00	0.00
Windmatic	0	0.00		
Enertech	6	1.67		
KCS-56 and Vestas	14	0.40	0.04	0.00
KVS-33	0	0.00	0.00	0.00
Howden	0	0.00		
Nordtank	0	0.00		
W.E.G.	0	0.00		
χ^2 test result		$P < 0.05$	$P < 0.05$	$P < 0.05$
Tower type				
Vertical axis	10	3.54	0.10	0.26
Tubular	39	1.49	1.77	1.53
Lattice	20	0.50	0.00	0.61
χ^2 test result		$P < 0.05$	$P < 0.05$	$P < 0.05$
Turbine position in row				
End of row	32	2.12	0.05	0.00
Gap	7	1.15	1.66	1.69
Interior	29	0.62	0.00	0.00
χ^2 test result		$P < 0.05$	$P < 0.05$	$P < 0.05$
Wind wall				
Not in wind wall	68	1.15	1.13	1.13
In wind wall	1	0.10	0.00	0.00
χ^2 test result		$P < 0.05$	$P < 0.05$	$P < 0.05$
Whether in canyon				
Not in canyon	54	0.92	0.10	0.47
In canyon	15	1.43	2.61	1.94
χ^2 test result		$P < 0.10$	$P < 0.05$	$P < 0.05$
Elevation (m above mean sea level)				
85–134	17	1.65	0.00	0.00
135–184	24	1.65	6.74	4.08
185–234	23	2.48	0.00	0.00
235–284	2	0.46	0.22	0.00
285–334	0	0.00	0.00	0.00
335–384	3	0.38	0.00	0.00
385–534	0	0.00	0.00	0.00
χ^2 test result		$P < 0.05$	$P < 0.05$	$P < 0.05$
Landscape feature				
Peak	0	0.00	0.00	0.00
Plateau	5	1.06	0.00	0.00
Ridge crest	22	1.01	2.49	2.52
Ridgeline	8	0.58	0.00	0.00
Slope	29	1.26	0.03	0.00
Swale	3	1.00	0.00	0.00
Ravine	1	1.96	0.00	0.00
χ^2 test result		ns[b]	$P < 0.05$	$P < 0.05$
Rodent control				
Unknown	2	2.40		
None	13	0.82	0.00	0.00
Intermittent	35	1.90	1.83	1.12
Intense	19	0.56	0.08	0.99
χ^2 test result		$P < 0.05$	$P < 0.05$	$P < 0.05$
No. of cattle pats ≤20 m from turbines				
0–2	4	0.47	0.00	0.00

Table 3. Continued.

Association variable	Turbine-caused deaths	Obs/exp: Collisions	Obs/exp: Flight time ≤50 m from turbines	Obs/exp: Perch time
3–9	15	0.68	0.05	0.00
10–25	25	1.18	0.00	0.00
>25	21	1.59	3.27	3.32
χ^2 test result		$P < 0.05$	$P < 0.05$	$P < 0.05$

[a] Manufacturers: Micon = Moerup Manfacturing Co., Randers, Denmark; Bonus = Bonus Wind Turbines, Inc., Brande, Denmark; Danwin = Danwin A/S, Helsingør, Denmark; Flowind = FloWind Corp., San Rafael, CA; Windmatic = Windmatic, Herring, Denmark; Enertech = Enertech Corporation, Norwich, VT; KCS-56 and KVS-33 = Kenetech Windpower Inc., Livermore, CA; Vestas = Vestas Wind Systems A/S, Randers, Denmark; Howden = James Howden and Company, Renfrew, Scotland; Nordtank = Nordtank Energy Group, Balle, Denmark; W.E.G. = Wind Energy Group, Ltd., Southall, Middlesex, England.

[b] ns = not significant.

Flights, perching, and collisions occurred primarily among wind turbines on tubular and vertical axis towers, secondarily among lattice towers, and least among wind walls, corresponding with a declining gradient of visibility through to the other side of a wind turbine row. Owls perched and flew more often in the rotor zone of turbines with slower-moving blades. Furthermore, owls perched on turbines or their towers only while the turbines did not operate, indicating the owls' awareness of turbine operations. Our findings indicate owls avoid areas they perceive as busy with fast-moving turbines, and they instead fly through areas of sparsely distributed turbines with slower-moving blades mounted on tubular towers they can more readily see around. Owls may perceive these turbine fields as safer, making them more dangerous.

Compared to expected frequencies, owls flew more often through gaps in turbine rows and were killed more often by end-of-row turbines. Owls may have approached closer and died more often at turbines in canyons because they use canyons for flight pathways or because turbines in canyons are often at row's end and their blades obscured by hills. Placing flight diverters at the ends of turbine rows, especially those extending into canyons, might encourage owls to fly farther from operating turbines while maneuvering around turbine rows. Smallwood and Thelander (2004, 2005) proposed flight diverters as tall poles erected in parallel beyond the rotor planes of the end-of-row turbines.

Despite owls staying well away from wind turbines most of the time, they still flew into the rotor zone 10 times more than expected. Flights into the rotor zone and collisions were disproportionately more common among wind turbines with the most cattle dung within 20 m. We noticed cattle congregate at the wind turbines (see photos in Smallwood and Thelander 2004, 2005) and spend more time close to the wind turbines than in the grasslands between the turbine rows. As a result, most turbine rows have shorter grass and more cattle dung. Shorter grass has often been associated with owl habitat selection, and the cattle dung fuels a food web utilized by owls, such as large

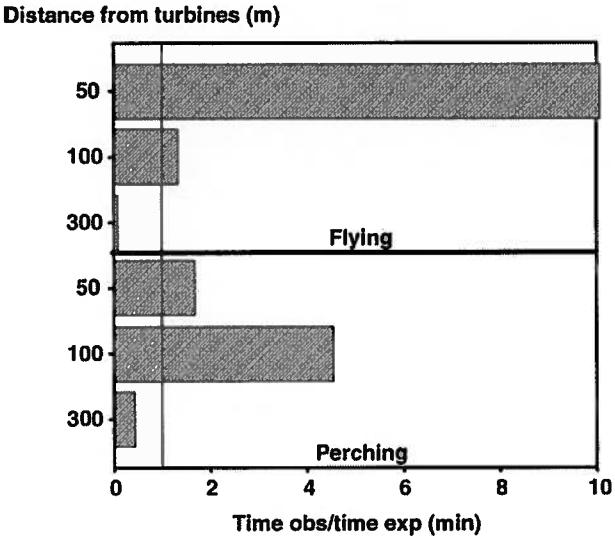

Figure 7. We observed burrowing owls longer than expected flying within 50 m and perching 100–300 m from turbines in the Altamont Pass Wind Resource Area, California, USA, 1998–2003.

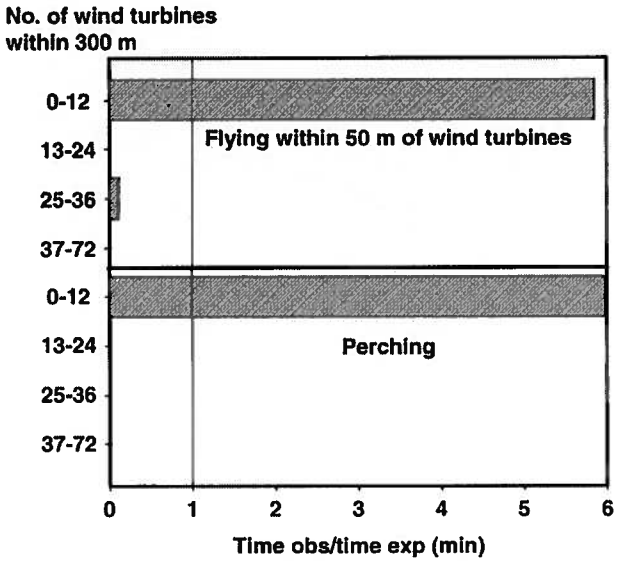

Figure 8. We observed burrowing owls longer than expected flying within 50 m of turbines and perching in areas of lower turbine density in the Altamont Pass Wind Resource Area, California, USA, 1998–2003.

Table 4. Observed number, expected number, and observed number/expected number of collision-caused fatalities of burrowing owls by ranges of density and degree of clustering of fossorial mammals and burrowing owl burrows among 27 rows of turbines in the Altamont Pass Wind Resource Area, California, USA, 1998–2003.

Variable and attribute[a]	Obs collisions	Exp collisions	Obs/exp collisions
Burrow systems/ha of all species to 90 m*			
0–5	4	10.75	0.37
5–10	15	9.77	1.54
10–22.5	8	6.49	1.23
Ground squirrel burrow systems/ha to 90 m**			
0–2	5	12.65	0.40
3–7	17	8.91	1.91
7–19.2	5	5.44	0.92
Desert cottontail burrows/ha to 90 m***			
0	9	8.75	1.03
0.2–0.7	15	10.10	1.49
0.8–1.7	3	8.16	0.37
Ground squirrel burrow systems/ha to 15 m from turbines***			
0	2	4.81	0.42
0.3–5.2	14	15.88	0.88
6.6–26.6	11	6.30	1.75
Obs/exp no. of ground squirrel burrow systems/ha ≤15 m from turbines*			
0	2	4.65	0.43
0.3–1.0	13	16.76	0.78
1.1–5.2	12	5.43	2.21
Burrowing owl burrows/ha to 90 m*			
0	12	18.16	0.66
0.02–0.88	15	8.84	1.70

* $P < 0.05$, ** $P < 0.005$, *** $0.05 < P < 0.10$.

numbers of grasshoppers (Acrididae) covering the cattle dung and lizards (*Uta stansburiana* and *Sceloporus occidentalis*) that feed on the grasshoppers. Owls may visit wind turbine rows to prey upon grasshoppers and lizards, and to

Table 5. Magnitude (%) of increase or decrease in burrowing owl mortality associated with attributes of independent variables measured during 1998–2003 in Altamont Pass Wind Resource Area, California, USA.

Variable	Magnitude of increase in mortality
Sec/rotor sweep at blade tip	30% at turbines with longer time per rotor sweep at blade tip
Tower type	19% at tubular towers, 10% at vertical axis towers
Tower ht	16% at towers of medium height
Whether in wind wall	13% at turbines not in wind walls
Position in turbine row	24% at the end of turbine row
Whether in canyon	6% in canyon
Elevation	44% at lowest elevation
Rodent control	24% in areas with intermittent control
Cattle dung at wind turbines	18% at turbines with more cattle dung

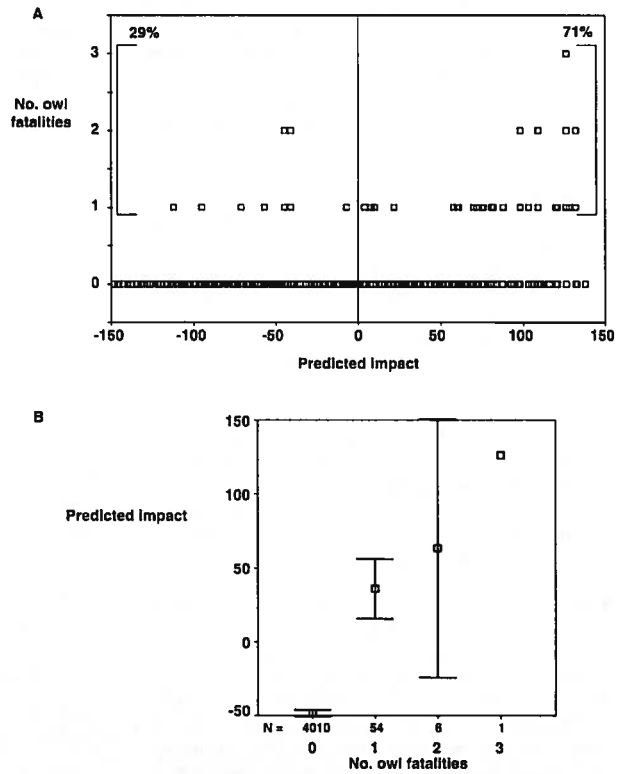

Figure 9. Using our empirical model, we predicted 71% of the wind turbines known to have killed burrowing owls were more likely to kill owls, that is, (A) predicted impact >0, and (B) our predicted impacts ($\bar{x}$ and 95% CI) increased with the actual number of owls killed by the wind turbine in the Altamont Pass Wind Resource Area, California, USA, 1998–2003.

collect cattle dung for display around their burrow entrances as dung beetle lures (Levey et al. 2004) or to mask scent from mammalian carnivores (Green and Anthony 1989), though Smith (2004) supported the former hypothesis but not the latter. We hypothesize that encouraging cattle to congregate other than around the bases of wind turbines would reduce owl flights in the rotor zone, and collisions.

Owl fatalities at wind turbines positively associated with densities of ground squirrel burrow systems and presence of owl burrows within 90 m. We found owl mortality decreased the year rodent control was implemented but eventually increased after it was implemented intermittently for >1 year. Repetitive, intense control would likely eliminate this pattern, however, because vacant squirrel burrows eventually collapse and become unavailable to owls. In fact, we did not find evidence of active owl burrows within the areas of intense control. Intense rodent control might reduce owl collisions, but results in habitat loss not only for the owl, but also for California red-legged frog (*Rana aurora draytonii*), California tiger salamander (*Ambystoma californiense*), and San Joaquin kit fox (*Vulpes macrotis mutica*), which are threatened and endangered species under the federal Endangered Species Act. Ceasing intermittent rodent control might reduce turbine-caused mortality, and ceasing intensive control might increase the habitat capacity of the APWRA.

Our model predicted 29% of the 4,074 sampled wind turbines pose greater collision threat. This 29% of the turbines killed 71% of the turbine-killed owls we found. These turbines occurred in a low-elevation band along the east side of the wind farm, where we saw disproportionately more owls flying within the rotor zone. This model can be used along with other scientific information to select a relatively small set of wind turbines for shutdown, relocation, installation of flight diverters, or other mitigation measures. We hypothesize that a small set of turbines selected in this manner could reduce owl mortality while only minimally reducing APWRA power generation.

MANAGEMENT IMPLICATIONS

In the APWRA, and to the extent managers feel comfortable extending our results to other wind farms, our results can guide the selection of wind turbine design, where to locate wind turbines in the project area, when not to operate wind turbines, and how to manage other resources to minimize owl collisions with wind turbines. To minimize collisions in the APWRA, new wind turbines should be mounted on taller towers as close together as feasible, and outside canyons, ravines, and valleys, and where rodent and owl burrows are relatively scarce. Grazing practices should be modified to prevent accumulations of dung around wind turbines. Understanding biological impacts through additional research can provide the basis of equitable compensatory mitigation for unavoidable impacts.

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SUGGESTED STANDARDS FOR SCIENCE APPLIED TO CONSERVATION ISSUES

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ABSTRACT: The Conservation Committee of The Wildlife Society (TWS)-Western Section (WS) commenced activities during the summer of 1999, and quickly encountered a profusion of conservation issues in the Western Section, reviewing environmental documents, determinations, decisions, and claims made by government agencies, political bodies, news media, and citizen groups. The Committee recognized that it could address only a fraction of these issues. In our experience, recognizing and debating each issue through both the Conservation Committee and the Executive Board will often require more time than allowed by government comment periods and the period during which the news media remain interested. We believe that it will be more effective to establish and re-affirm the standards of professional and scientific conduct that should generally found the issues. This way, TWS-WS members who are more familiar with the issues can use these standards as a collective benchmark to judge the adequacy of professional and scientific foundation underlying documents, determinations, decisions, and claims related to each issue.

We recommended to the Executive Board that we develop standards and present them at the Annual Meeting in January, 2000. On October 15th, 1999, the Executive Board moved to have our Committee act on its recommendation. This paper summarizes the preliminary standards developed by members of the Conservation Committee. These standards presented herein are preliminary, and have not been sanctioned by the Executive Board. We expect that this document is just the beginning of a debate on standards that are acceptable to TWS-WS for using scientific and other information when making conclusions that affect wildlife. We invite feedback on the standards presented herein.

Key Words: Conservation, environmental documents, science, standards, The Wildlife Society.

2000 TRANSACTIONS OF THE WESTERN SECTION OF THE WILDLIFE SOCIETY 36:40-49

Conservation issues have proliferated in the western U.S. as population and economic demands have increased the pressures and impacts on natural resources, including wildlife. Members of TWS-WS participate in these issues, oftentimes struggling against each other over a particular issue. Debates over decisions, conclusions and claims often have been contentious and fractious amongst wildlife professionals. Whether a conclusion or opinion is justified biologically is too often secondary to socio-economics and political expediency (Wilkinson 1998). These realities point not just to the diminished value given natural resources by decision-makers despite overwhelming public support to do otherwise, but also demonstrate our inability to convey our message consistently. Different backgrounds, disciplines, and philosophies can lead one to different interpretations of the data, and subsequently, to different conclusions. Disagreement amongst professionals is reasonable and not unexpected. Where we fail and consequently lose credibility as a profession is in our inconsistency to adequately support and justify our conclusions, and in the errant advocacy of wildlife biology from a non-biological inclination.

Environmental documents, decisions, determinations, and claims involving wildlife usually pertain to some *action* (or lack of action) and an *impact* to the wildlife due to that action. The action may encompass management,

"take" of species, mitigation, or some combination of all these. The impact may be positive or negative, and it may be specific to one or more species of wildlife involving one of several demographic units such as individuals, family groups, populations, or metapopulations. The impact also can be specific to some other part of the environment (including humans) as a result of changed regulatory or real-world status of the particular species of wildlife. The impacts are direct, indirect, and cumulative. All of these actions, impacts, and the related conclusions drawn by different sectors of our society bear on the interests of wildlife biologists.

Wildlife biologists have rendered conclusions (or opinions) in countless environmental documents that have justified projects and management actions affecting wildlife. Many of these projects have resulted in net losses of habitat areas, degradation of habitat, "takings," and ineffective mitigation. The majority of Habitat Conservation Plans (HCPs) result in incidental, and increasingly, direct take of listed species, net loss of habitat areas, and involve conclusions about project impacts and mitigation effectiveness that are often poorly founded in science (Kareiva et al. 1999, Smallwood et al. 1999, Smallwood 2000*a*). Natural Community Conservation Plans, (NCCPs), are California's version of HCPs, and also result in takings and net losses in habitat areas. California Environmental Quality Act (CEQA) documents often justify projects in the form of "negative declarations" or determinations of "no significant effect" due to project actions. These CEQA documents have preceded and made legal the destruction of many thousands of acres of wildlife habitat. Virtually all of the large-scale conversions of wildlife habitat require assessments and conclusions from wildlife biologists, including projects such as housing developments, construction of industrial sites, construction of hazardous waste storage and treatment sites, dredging of shipping channels in coastal bays, construction of new roads, and the clear-cutting of large tracts of late seral Redwood forests.

The conclusions of wildlife biologists affect policies, management decisions, and management prescriptions in federal and state agencies responsible for wildlife, native plants, water resources, forestry, and transportation. Decisions by these agencies affect many thousands of hectares of wildlife habitat, including livestock stocking rates, predator control and other types of animal damage management, timber harvest rates and practices, water conveyance and storage systems, pesticide usage, the locations and design of roads, and game harvest seasons and quotas. These agencies also affect wildlife habitat by listing species as threatened or endangered, designating critical habitat, and preparing and implementing recovery plans. Many additional examples could be used to support our argument that wildlife biologists profoundly influence wildlife conservation issues by contributing to, or rendering, conclusions. Not necessarily the fault of wildlife biologists (see Wilkinson 1998), many of their conclusions conflict with the objectives of TWS by leading to the degradation of wildlife and wildlife habitat and by being rendered without sound scientific foundation.

That these issues bear on the interests of TWS is clear enough in the Bylaws of TWS, as well as in the program for certification of professional wildlife biologists. The principal objectives of TWS "are:

(1) to develop and promote sound stewardship of wildlife resources and of the environments upon which wildlife and humans depend;
(2) to undertake an active role in preventing human-induced environmental degradation;
(3) to increase awareness and appreciation of wildlife values; and
(4) to seek the highest standards in all activities of the wildlife profession."

The other TWS objectives might follow if objective (4) is met, so long as we can agree about what are the highest standards. Additionally, the Bylaws describe a Code of Ethics, which asks that each member "pledges to:

(1) Subscribe to the *highest standards* of integrity and conduct;
(2) Recognize *research and scientific management* of wildlife and their environments as primary goals; ...
(5) *Promote competence* in the field of wildlife management by supporting high standards of education, employment and performance;
(6) Encourage the use of *sound biological information* in management decisions ..." (*emphasis* added).

The program for certification of professional wildlife biologists re-emphasizes these same objectives and code of ethics. Also, we point out that the TWS objectives do not pertain to only endangered species of wildlife, but to all species of wildlife. The objectives of TWS are likely shared by most professional wildlife biologists, including non-members of TWS.

Obviously, many conclusions of wildlife biologists or of their supervisors conflict with TWS objectives, as the actions that followed have resulted in many takings, widespread losses and fragmentation of habitat, habitat degradation, and declines of many species of birds, mammals, reptiles and amphibians. Given the numerous conclusions affecting wildlife deleteriously, and the many that seem to be poorly founded in science, there may be different opinions about what qualifies as sound stewardship, high standards, research and scientific management, and sound biological information. The purpose of this paper is to begin a dialogue amongst biologists as to

what they should expect, at a minimum, of themselves and others in the wildlife profession. The TWS-WS Executive Board established this dialogue as an action item for the Conservation Affairs Committee in its meeting of 15 October, 1999, but we present these preliminary standards as individuals, rather than as a Committee action.

STANDARDS

Our goals for establishing standards were:

1) To identify the standards by which to gauge the reliability of our own and others' premises and conclusions;
2) To improve the consistency in the use of our key terms and reporting methods;
3) To identify which conclusions are scientific and which are not;
4) To decide whether the conclusions are consistent with the TWS objective of conserving wildlife; and,
5) To encourage more people to involve themselves with conservation issues.

To meet these goals, we prepared a draft worksheet (Table 1) to assist preparation or review of environmental documents. Table 1 is divided into several sections, each of which follows from one of the key phrases in the objectives of the TWS Bylaws, and is discussed below. Table 1 is proposed to stimulate discussion on how best to achieve our goals. Perhaps the final analysis, including the stated goals and objectives, will take a much different form than what we have proposed here. We will, however, continue to refine our thinking through thoughtful input from wildlife biologists, in hopes of furthering the credibility and effectiveness of our profession.

Consequences of action based on conclusion(s)

The TWS Bylaws require members to steward wildlife and to prevent their degradation, meaning that wildlife biologists are expected to protect or conserve wildlife. We are expected to promote the persistence of healthy wildlife populations and their habitats for the long term. Given this stewardship role, our standards should first assist the reviewer in putting the conclusion(s) at issue into perspective. In judging the importance of a conclusion, wildlife biologists first need to clearly identify what is at stake in terms of our stewardship role. The magnitude of the likely consequences to wildlife should determine how closely wildlife biologists follow our proposed standards when rendering conclusions.

For example, one could use Table 1 to check off whether the proposed action would restore habitat for a net gain, or whether it would degrade or remove habitat. The former consequence would lessen the reviewer's level of concern over standards not being met. However, the degradation or removal of habitat for a net loss to wildlife ought to heighten the vigilance of those preparing or reviewing the environmental document(s). Similarly, one could use Table 1 to check off whether the project is likely to have no consequence for the survival or behavior of individuals, or whether the project would displace or kill all the individuals composing a population or metapopulation. The former consequence probably warrants little concern over the soundness of the supporting documents, but the latter demands the use of the highest standards of our profession.

The consequences of an action based on a conclusion has two aspects related to health and integrity: one involving habitat and the other involving demographic units. To restore habitat for a net gain or to have no impact on the health of individual animals would qualify proposed actions as achieving the highest standards relative to the conservation goals of TWS, whereas the net loss of habitat or the loss of one or more metapopulations would qualify proposed actions as achieving the lowest standards. Lower standards for these aspects of a conclusion warrant a closer examination of the scientific foundation and the soundness of the biological information leading to the conclusion.

Scientific foundation of conclusion

By expecting wildlife biologists to recognize research and scientific management as primary goals, the TWS Bylaws attach great importance to using the scientific method to understand more about wildlife and habitat, founding management decisions, and integrating them into management prescriptions. Management decisions can be founded in the scientific method by basing them on data collected as part of a scientific research program. Such data might come from a monitoring program that scientists designed or used for testing hypotheses, or they might be from scientific reports, and collected using methods that are widely accepted by scientists. Habitat determinations can be an example of scientifically derived data pulled from published reports. So long as the hypotheses in the report are consistent with the management context, the use of data from published reports can contribute to scientific management.

Adaptive management is an example of integrating science into management prescriptions (Holling 1978, Lancia et al. 1996). Hypotheses are described prior to the management implementation, and are the bases for the monitoring program. Hypotheses that are tested while management is implemented determine future management prescriptions. Whether basing management decisions on scientific data or integrating scientific methods into them, TWS prefers conclusions that are scientifically founded. Environmental documents should be clear

Table 1. Worksheet for identifying the standards applied to conclusions that have consequences for wildlife conservation. Each conclusion can be composed of 19 aspects organized under 3 key phrases in the TWS Bylaws. Each aspect of a conclusion can then be assigned a standard, which is represented by a phrase. When only *one* phrase can characterize an aspect of a conclusion, the highest standard is that phrase at the top of the list, and the lowest standard is at the bottom of the list. When *all* phrases can characterize an aspect of a conclusion, the highest standard applies when all the phrases can be checked off. The highest standards are denoted by brackets encompassing the check space: [____].

Consequences of action based on conclusion(s)

1. Conclusion can lead to action that would (check *one* applicable phrase):

Restore habitat for a net gain [___]
Enhance habitat for a net gain [___]
Protect all existing habitat at issue [___]
Protect a portion of the habitat at issue to mitigate for take
Replace habitat to mitigate for take
Pay into a conservation bank as mitigation for take
Degrade habitat
Remove habitat, or compensate financially for habitat loss

2. Conclusion can lead to action that, through habitat loss or otherwise (including a sanctioned game harvest), would likely or certainly kill or remove (check *one* applicable phrase):

No individuals, and it would not affect their behaviors or physical health [___]
No individuals, but it would affect behaviors or sicken one or more individuals ___
No individuals, but it would affect behaviors or sicken all of a population ___
No individuals, but it would affect behaviors or sicken individuals across a region ___
Individuals ___
One or more reproductive groups (i.e., mated pair) ___
A population ___
One or more metapopulations ___

Scientific foundation of conclusion

1. Uncertainty in the conclusion was (check *one* applicable phrase):

Specified using a quantitative method [___]
Specified using a qualitative method
Specified as a list of alternative outcomes
Not specified

2. Presence and condition of the species were based on (check *one* applicable phrase):

Scientific study involving an area that is larger than the project area [___]
Scientific study involving the entire jurisdiction or project area
Scientific study involving a small portion of the jurisdiction or project area
Presence of habitat, which was described elsewhere using scientific methods
Non-scientific data, such as NDDB or cursory walk-over site visits
No study or data indicated

3. Conclusion was based on (check *one* applicable phrase):

Quantitative data collected from the site and species at issue [___]
Quantitative data collected from offsite or for another species
Qualitative data collected from the site and species at issue
Qualitative data collected from offsite or for another species
No data collected

Table 1 (continued)

4. Conclusion was based on methods, in which (check all phrases that apply):
Temporal scale of data collection was specified
Spatial scale of data collection was specified
The hypotheses being tested or the assessment's objectives were clearly described
Experimental or research design was specified and described
Assumptions were identified and discussed
The conditions of the study site were described relative to the full range of conditions experienced or likely to occur at the site

5. Conclusion was reported in a document that described (check all phrases that apply)
All methods used to collect data
All methods used to aggregate data
All methods used to analyze the data
The time periods during which observations were made or data collected

6. Conclusion was based on statistical tests upon which (check all phrases that apply)
The test was appropriate for the data and the hypothesis
The assumptions of the test were met
Type II error was established, if warranted

7. Conclusion was based on research design that included (check all phrases that apply):
A control treatment, if manipulation of the study units was involved
Replicates
Interspersion of treatments, whether they be mensurative or manipulative

Soundness of biological information leading to conclusion
1. Referenced source information consisted of (check *one* applicable phrase)
Published reports subjected to independent scientific review
Published reports that were not peer-reviewed
Personal communications, opinions, and anecdotes
No referencing of source

2. Personal communications and opinions were (check *all* phrases that apply):
Supported by contact information of the individual(s) cited
Accompanied by a statement of uncertainty

3. Referencing of source information was (check *all* phrases that apply):
Comprehensive
Balanced according to the competing arguments

4. For each reference, check off whether it was (check *all* phrases that apply):
Accurate
Relevant
Fully described
Readily accessible in a library or other location

5. Document quality (check *all* phrases that apply):
All species names are spelled correctly and scientific names are current
All important terms, such as ecosystem, habitat, population, community, corridor, and net benefits were either defined or a definition referenced
All important terms were accurately used
The qualifications of the analyst or assessor were described (if not peer-reviewed)

Table 1 (continued)

6. Conclusion invoked population study including (check *all* phrases that apply):
Numbers (density) [ ]
Demography [ ]
Gender ratio [ ]
Genetics [ ]
Condition of food resources [ ]
Condition of habitat [ ]

7. Conclusion invoked habitat study (check *all* phrases that apply):
At the scale of the population or larger [ ]
Spanning at least one generation of the species [ ]
Based on use and availability analysis [ ]
At a scale smaller than the population
Spanning <1 generation of the species
Based on presence of only "optimal" or "preferred" habitat

8. Conclusion of impacts due to management was based on (check *one* applicable phrase)
Quantitative, empirical evidence from multiple examples [ ]
Quantitative, empirical evidence from one example
Qualitative, empirical evidence from multiple examples
Qualitative, empirical evidence from one example
No empirical evidence

9. Management impacts in conclusion were specific to (check *one* applicable phrase):
Each species or species' habitat [ ]
Taxonomically or functionally related species or their habitats
Umbrella species, umbrella habitat, or some other indicator of the species
Not specified

10. Management impacts in a conclusion followed consideration of (check *all* phrases that apply):
A full range of project and mitigation alternatives, including 'no project' alternative [ ]
The benefits and disadvantages of each project and mitigation alternative [ ]
Spatial requirements of the species [ ]
PVA [ ]
Appropriately designed monitoring program [ ]
Impacts on ecosystem processes that affect the species (indirect effects) [ ]
Cumulative impacts on the species [ ]

about the extent to which science was part of the conclusion or management decision. Table 1 is intended to promote this clarity.

Scientific methods are designed to reduce human uncertainty in natural phenomena (Popper 1969, Kuhn 1970). Statements of uncertainty are therefore critical to scientists, because they help maintain an honest account of scientific progress. Scientists prefer uncertainty statements that are quantitative, consisting of confidence intervals or error terms (National Research Council 1986), but often qualitative statements are the best that can be expected under the circumstances (Morgan and Henrion 1990, Cooke 1991). When the magnitude of negative impact to wildlife is high, risk assessment is warranted, along with uncertainty statements. Population Viability Analysis (PVA) is one form of risk assessment that is appropriate for application to wildlife.

Scientific generalizations depend largely on the scope of the investigation, with more confidence in generalizations stemming from studies encompassing larger areas and longer time periods. Larger-scale studies can include wider ranges of variation in measured variables, thereby expanding the portion of the environment that may be experienced by the study units and considered in the

conclusion. Scientific conclusions are considered more accurate and reliable when they are derived from methods and data that are specific to the study units at that particular place and most recently. The more grossly an indicator represents the study units, or the less the indicator has been functionally related to the study units, the less reliable are hypothesis tests or assessments stemming from the use of indicators (Simberloff 1998). Therefore, the scientific merits of a conclusion should be examined more closely when the assessment or hypothesis test involved a keystone species, umbrella species, sensitive species, or indicator species. They should also be examined more closely when species' numerical trends are determined from the trends in anecdotal, indicator data such as the frequency of road-kills, sightings, issuance of depredation permits, or hunter harvests.

Scientific conclusions are considered more reliable when the methods used to derive them are fully and clearly described so that the reader has the opportunity to repeat the study. When a project proponent or their consultants claim that the species in question has not been observed on the project site, the project proponent should explain the types of observations employed, when and how often the observations occurred, and how long of a time period was involved. Scientists also attach greater reliability to conclusions from experiments that suffer less from pseudoreplication (Hurlbert 1974). Many population studies are autonomous and involve no replication or interspersion of treatments. Relating the results of these studies to environmental conditions at the study site is a form of pseudoreplication, and should be interpreted conservatively. Also, some scientists expect more conservative conclusions from hypothesis-testing by considering Type II error or by conducting power analysis of trend data (Shrader-Frechette and McCoy 1992, Gerrodette 1987). A Type II error — not rejecting the null hypothesis when in fact it was false — can lead to no management actions being taken to halt the decline of a species or its habitat (Shrader-Frechette and McCoy 1992).

The accepted scientific methods for wildlife biologists are described in numerous publications, including Dasmann (1981), Verner et al. (1986), and Morrison et al. (1998), as examples. Some methods for reducing uncertainty are described by the National Research Council (1986), for example.

The scientific foundation of a conclusion has seven aspects that we identified. The highest standards would be, for example, to report the uncertainty of the conclusion quantitatively (aspect 1), assess the presence of the species across a larger area than the project area (aspect 2), and to use a research design that incorporates replication, control, and interspersion of treatments (aspect 7). The lowest standards correspond with no uncertainty specified for the conclusion (aspect 1), no study or data apparently used to assess presence or absence of the species (aspect 2), and no experimental or research design principles used to make the conclusion (aspect 7).

Soundness of biological information leading to conclusion

Not all conclusions or actions are scientific. The TWS Bylaws expect wildlife biologists to use sound biological information and the highest standards in all aspects of our profession. These standards pertain to many aspects of conclusions that are both scientific and nonscientific. The credibility of a conclusion can be judged based on the quality of the document reporting it, including the writing, the relevance and accuracy of premises, and the rigor in referencing source information. The following standards are intended to foster document preparation based on sound biological information.

Source material in environmental documents and decisions needs to be identified and referenced. So long as the reference is relevant to the conclusion, scientists usually prefer source material to consist of independently reviewed scientific documents (Smallwood et al. 1999), followed by scientific documents that were not reviewed, and personal communications or anecdotes. We recommend that personal communications be backed up by contact information of the individual(s) cited. Opinions should be accompanied by a statement of uncertainty (see above). All references of source information should be accurately represented. Referencing should also be comprehensive and balanced according to the arguments or anticipated counter arguments.

Evidence of sound biological information may be the qualifications of the analyst or assessor who prepared the conclusion, although qualifications are no guarantee that the conclusion was sound. Using correct spelling and accurate names of species also improves the soundness of the conclusion, as does clear and accurate use of key terms in the wildlife profession.

A conclusion involving wildlife can be considered more sound if greater thoroughness was applied to the issue. Thoroughness is increased by including data of more population or demographic parameters routinely studied by wildlife biologists, as well as more aspects of habitat or resources needed by the species. Thoroughness is also increased when inter-generation dynamics in demographic parameters are considered, when the entire region is included in the assessment or analysis, and when the species' use of habitat elements or food resources is compared to the available habitat elements or food resources.

Thoroughness bears on the soundness of biological information leading to conclusions of management impacts. Such conclusions can be considered more sound when the analysts have considered a full range of project

and mitigation alternatives, including a 'no project' alternative and all the benefits and disadvantages of each alternative (O'Brien 2000). Conclusions can be considered more sound when analysts rely upon risk analysis (PVA) of the proposed actions and alternatives, as well as the spatial requirements of specific demographic units. Conclusions of management impact are more sound when the analysts consider the indirect effects on ecosystem processes that affect the species (Ricklefs et al. 1984) and when they consider cumulative impacts (McCold and Holman 1995).

The soundness of biological information leading to a conclusion has 10 aspects that we identified. The highest standards include, for example, referencing of peer-reviewed scientific reports as sources of a conclusion (aspect 1), referencing of source information that is both comprehensive and balanced to the arguments (aspect 3), and estimated management impacts that consider the full range of project alternatives, spatial requirements of the species, PVA, an appropriately designed monitoring program, impacts on ecosystem processes that affect the species (indirect effects), and cumulative impacts (aspect 10). The lowest standards correspond with no referencing of source information (aspect 1) or biased, selective referencing (aspect 3), and the management impacts make no consideration of project alternatives or spatial or numerical requirements of the species, monitoring, ecosystem processes, nor cumulative impacts.

DO WE REALLY NEED THESE STANDARDS?

We have witnessed poorly prepared environmental documents, containing loosely founded, questionable conclusions and extraordinary claims regarding wildlife and their habitats. Examples illustrating this point are unfortunately all too commonplace, often relying on "gray literature", "white papers", "draft" documents, and personal communications when peer-reviewed research reports are available. Specific examples have the potential to perhaps embarrass rather than instruct, and will therefore be avoided here. Suffice it to say, the reliance on non-scientific opinion, anecdotal information, speculation, and the misuse of published literature, unpublished literature, and personal communications have an embarrassing effect on the profession.

Wildlife biologists often lack the funding and time needed to make *sound* or *scientific* biological conclusions. Project proponents will not wait, and neither will the news media or concerned citizens. The interests of wildlife biologists are also often at odds with the agendas of others who have substantial influence over the conclusions, such as politicians, attorneys, and non-biologist administrators or bosses. Wildlife biologists are often asked to provide hastily prepared conclusions or opinions, and they usually do the best they can under less than ideal circumstances. Nevertheless, the conclusions of wildlife biologists, made under these kinds of circumstances, have consequences for wildlife and for the wildlife profession.

Hastily prepared documents do not reflect well on the wildlife profession when species names are out-dated or misspelled, when citations do not appear in the list of references, when references listed in the back of the document were not cited in the main body of the document, or when scientific sources are misrepresented. Conclusions of species' absence reflect poorly on the profession when they are based on lack of records in California's Natural Diversity Data Base (NDDB), or when they are based on only GIS habitat maps (no ground searches) or cursory walkover searches of the project sites. Conclusions of species' absence reflect poorly on the profession when species are pigeon-holed into "preferred" or "optimum" habitat associations and then deemed absent for lack of these habitats on a project site (Lidicker 1995). Such mistakes evoke a sense of carelessness and inappropriate haste in coming to conclusions, and they suggest bias.

Unsupported conclusions of project impacts and mitigation effectiveness reflect poorly on the wildlife profession. Substantial support is warranted for conclusions that the project and its mitigation will provide protection or net benefits to the species, or that they will be conserved under the rubric of adaptive management or ecosystem management, or that they will produce no significant impact, no cumulative impact, and no indirect or synergistic effects. The quality of the supporting documents not only bears on the wildlife profession, but also bears on the credibility of the conclusions and ultimately the consequences to the species.

The wildlife profession does not benefit from careless or inconsistent use of its central terms, such as *habitat* (Hall et al. 1997), *corridor* (Beier and Loe 1992), *ecosystem* (Fauth 1997), and *population* (Smallwood 2000*b*). These terms endured rigorous scientific debate, which attributed specific definitions to them. Inconsistent use of definitions for such important terms creates confusion among wildlife biologists and others, and this confusion can have dire consequences for wildlife. If wildlife biologists present confusing arguments, then their case is weakened and the TWS objectives are vulnerable.

Conclusions can be embarrassing to the wildlife profession when they are said to be scientific or scientifically founded, but do not involve hypothesis testing, nor data or well accepted methods for reducing scientific uncertainty. The application of critical thinking is not necessarily the same as scientific thinking, although science relies largely on critical thinking. Scientific conclusions, in the form of estimates or assessments, should be accompanied by some statement of uncertainty, which can be quantitative, qualitative, or consist of a list of

alternative outcomes based on a likely range of conditions or different assumptions. Data that were considered, but then excluded from the analysis, need to be identified and an explanation provided for their exclusion. *Scientific conclusions must be accompanied by a description of the data, the data collection methods, the analytical methods, and the assumptions leading to the conclusion. A conclusion can qualify as scientific when the reader has sufficient information in the document to repeat the methods and possibly come to the same conclusion.*

We do not suggest that standards can be broadly agreed upon and implemented for every nuance of our profession. We suggest that there are core aspects of our profession that possibly could be ascribed standards upon which most of us could agree are appropriate (Table 1). We expect that a set of standards will improve our profession by being available as reminders to wildlife biologists of the factors they need to consider, and by being available for anybody to judge the credibility of environmental documents, decisions, determinations, and claims made by wildlife biologists or others. With such a set of standards, a reviewer of documents or conclusions could readily describe what TWS would expect as foundation for a particular conclusion. Standards established by wildlife biologists could empower many people in forming opinions about conclusions regarding actions and impacts involving wildlife. It could also promote better adherence to relevant environmental laws, such as the Endangered Species Act, National Environmental Policy Act, California Environmental Quality Act, and California Endangered Species Act, and be used to assess the conclusions of EIRs, EISs, EAs, HCPs, court or other public declarations or testimonies (depositions), press releases, commissioned reports, progress reports, and even scientific reports.

By publicly establishing standards we, as professional wildlife biologists, can ensure our work products meet or exceed these standards. Knowing that a more clearly and generally agreed-upon set of standards exists, the analyst is more likely to be vigilant in applying these standards. We believe wildlife biologists will provide conclusions that are more sound and scientific by having the ability to systematically check whether they or their colleagues employed a widely agreed-upon set of standards when establishing the foundation or support documentation for their conclusions. Others within and outside our profession can readily identify if and when deviations from the standards occur. We believe our standards will foster sound stewardship, sound biological information, and scientific management. These standards are broadly applicable to conclusions that bear on the welfare of wildlife. However, those who use Table 1 to criticize the foundation of others' conclusions should themselves be qualified to do so, and their credentials should accompany the critique.

IMPLEMENTING THE STANDARDS

When conclusions are made that grossly fall short of the standards of the wildlife biology profession, then professional colleagues, and even the Western Section itself, should use Table 1 to bring the shortfall to the attention of the interested parties. TWS-WS members could challenge an EIR in court by relying largely on the standards in Table 1. A judge could be convinced that the EIR is, in fact, not an informative document, which is a requirement for EIRs under CEQA. (Under CEQA law, "the court does not pass upon the correctness of the EIR's environmental conclusions, but only upon its sufficiency as an informative document" (County of Inyo v. City of Los Angeles (3rd Dist. 1977) 71 Cal. App. 3d 185, 189 [139 Cal. Reptr. 396, 399]), meaning that any conclusion in the EIR can be considered valid by the courts so long as foundation for the conclusion is summarized in the EIR.) Conversely, those who prepared an EIR could attach Table 1, along with all the items checked-off, thereby demonstrating the extra step they took to prepare the EIR. In either case, an explanation of the items checked should be provided so that careless use of Table 1 can be avoided.

These standards, or some later version of them, also could be codified into standard practice by case law, or by revisions to environmental laws or to the operations manuals of government agencies. However these standards might be used, they are a statement of what we currently believe is appropriate. Indeed, we expect the standards to change as our knowledge, methods, and technologies improve.

Biologists could also use Table 1 to support their arguments for additional time and funding to arrive at scientifically sound conclusions. The public could better assess what we are able and unable to do, given our funding and time constraints. These standards can also benefit our profession by inspiring debate over particular standards or their descriptions, ultimately leading to an improved set of standards.

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We thank Dale McCullough and an anonymous reviewer for helpful comments on an earlier draft of this paper.

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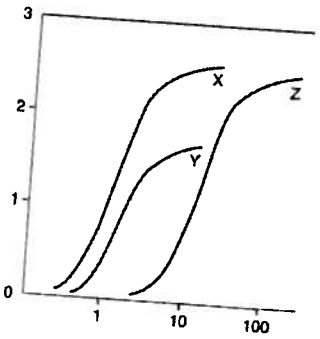
EXHIBIT C



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January 30, 2013

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Attn: Ms. Christina Caro

Subject: Comment Letter on Draft Environmental Impact Report for Casa Diablo IV Geothermal Development Project

Dear Ms. Caro,

At the request of Lozeau | Drury LLP (Lozeau Drury), Clark and Associates (Clark) has reviewed materials related to the above referenced project, including the Public Draft Joint Environmental Impact Statement (DEIS) and Environmental Impact Report (DEIR)[1] prepared for the Bureau of Land Management (BLM), the United States Forest Service (USFS), Inyo National Forest, and the Great Basin Unified Air Pollution Control District (GBUAPCD). The proponent, ORNI 50 LLC, a wholly-owned subsidiary of Ormat Nevada, Inc, is proposing to construct, operate, maintain and decommission a 33 megawatt (MW) geothermal power generating facility and related infrastructure near Mammoth Lakes in Mono County, California. According to the DEIS/DEIS, the Applicant's initial application was filed on February 17, 2010 by Mammoth Pacific, L.P. (MPLP). Since then, MPLP was acquired by Ormat Nevada Inc., which formed a wholly owned subsidiary (ORNI 50, LLC) for the CD-IV Project. ORNI 50, LLC submitted a revised application to BLM in June 2012.

[1] BLM. 2012. Casa Diablo IV Geothermal Development Project Public Draft Joint Environmental Impact Statement and Environmental Impact Report. State Clearinghouse No. 2011041008.

Clark's review of the materials in no way constitutes a validation of the conclusions or materials contained within the plan. If we do not comment on a specific item this does not constitute acceptance of the item.

Project Description

The majority of the CD-IV Project would be developed on National Forest System Lands where the surface resources are managed by the United States Forest Service (USFS), Inyo National Forest and the mineral resources are managed by the Bureau of Land Management (BLM), Bishop Field Office.

According to the DEIS/DEIR, the CD-IV Project would be located in the vicinity of the existing Mammoth Pacific L.P. (MPLP) geothermal complex located within the Mono-Long Valley Known Geothermal Resource Area (KGRA) near the town of Mammoth Lakes in Mono County, California. The DEIS/DEIR also describes the proposed location of the CD-IV Project as residing within the MPLP Geothermal Complex (Figure 1-1, Existing Facilities). The CD-IV Project would be the fourth geothermal power plant in the complex.[2]

The CD-IV Project would construct a new 33 net MW binary power plant, develop an expanded geothermal well field of up to 16 geothermal resource wells, construct pipelines to bring the geothermal brine to the power plant and pipelines to take the cooled brine to injection wells, and install an electric transmission line to interconnect to the Southern California Edison (SCE) Substation at Substation Road.

The CD-IV Project facility is described as:

1. A geothermal power plant consisting of two (2) Ormat Energy Converter (OEC) binary generating units (21.2 MW gross each) with vaporizers, turbines, generators, air-cooled condensers, preheaters, pumps and piping, and related ancillary

[2] BLM. 2012. Casa Diablo IV Geothermal Development Project Public Draft Joint Environmental Impact Statement and Environmental Impact Report. State Clearinghouse No. 2011041008. Page 1-4

equipment. The gross power generation of the CD-IV plant would be 42.4 MW. The estimated auxiliary and parasitic loads (power used within the project for circulation pumps, fans, well pumps, loss in transformers and cables) is about 9.4 MW, thus providing a net power output of about 33 MW. Additional components of the power plant would include:

a) A motive fluid system consisting of motive fluid (n-pentane) storage vessels (either one or two vessels in the range of 9,000 to 12,000 gallons) and motive fluid vapor recovery systems (VRUs). Each VRU would consist of a diaphragm pump and a vacuum pump.

b) A new substation would be constructed on the power plant site and would be connected to the SCE Casa Diablo Substation at Substation Road.

c) An overhead 33 kV transmission line connecting the power plant substation with the SCE Casa Diablo Substation approximately 650 feet (198 meters) long.

2. Up to 16 geothermal wells are proposed. Fourteen of the wells would be located in the Basalt Canyon Area and two wells would be located southeast of the proposed power plant east of U.S. Highway 395. The specific locations for these wells would be selected out of the 18 possible locations shown in Figure 2-2 of the DEIS/DEIR. The actual number may be less depending on the productivity of the wells. The final number and location of wells would be determined by modeling and actual drilling results. Approximately half of the wells would be production wells and the other half would be injection wells. Each production well would range in depth from 1,600 to 2,000 feet below ground surface (bgs), and each new injection well would be drilled to approximately 2,500 feet bgs. Production wells would be equipped with a down-hole pump powered by a

surface electric motor. Most of the well sites in Basalt Canyon have been analyzed previously for the development of exploratory wells, two of which were drilled in 2011. Additional detail is provided in Section 2.2.4.

3. Piping would extend from production wells to the power plant and from the power plant to the individual injection wells. Two main pipelines would parallel the existing Basalt Canyon pipeline and would cross beneath U.S. Highway 395 between the wellfield and the CD-IV power plant site. Where pipelines must cross another pipeline or a road, the crossings would be underground.
4. Power and control cables for the wells would be installed in above-ground cable trays placed on the pipeline supports. Appurtenant facilities include pumps, tanks, valves, controls, and flow monitoring equipment.

This DEIS/DEIR was issued prematurely without considering the serious flaws in the Proponent's analysis of the project, and these flaws are replicated in the DEIS/DEIR. The flaws include:

1. failure to provide a clear description of the project;
2. fails to adequately screen the project impacts when they fail to adequate describe the project and the project components;
3. failure to perform an adequate air quality analysis;
4. failure to adequately estimate the air quality burden the project will place on the air basin; and
5. failure to perform an odor analysis.

The DEIS/DEIR also fails to identify and adequately mitigate significant adverse impacts on air quality from Project construction. Finally, the proponent has a long track record of unauthorized releases above permit threshold levels. There is no evidence that conditions at the new facility will be maintained in a better manner.

I14-102

I. Failure To Provide Clear Description Of Project

The proponent fails to adequately describe the size and scope of the project, which must be viewed as a component of a larger existing facility. The MPLP Geothermal Complex currently includes 3 existing generating stations: the 14 MW Mammoth Pacific I unit (MP-1), the 15 MW Mammoth Pacific II unit (MP-II), and the 15 MW PLES-I unit (PLES-I) totaling 44 MW in net generating capacity at the site.

I14-103

The proponent of the project has also proposed to replace the MP-1 facility with a new structure. Since the MP-1 project has been approved by the County, the Applicant will increase the total gross generating capacity of the Casa Diablo Geothermal Complex from 44 MW to up to 96 MW with the addition of the CD-IV Project. Therefore, the actual potential Project involves the addition of 52 MW of generation to the existing complex. The parsing of the project into different DEIS/DEIR fails to meet CEQA's requirements for a complete description of the project. The proponent must analyze the impact the CD-IV Project will have on the whole MPLP Geothermal Complex, rather than parsing the project piecemeal in separate DEIRs.

II. The DEIS/DEIR Fails To Adequately Screen The Project Impacts When They Fail To Adequate Describe The Project And The Project Components.

I14-104

The CEQA Guidelines, Appendix G, establish that impacts on air quality would be "significant" if a project would violate any ambient air

quality standard or substantially contribute to an existing or projected violation of an ambient air quality standard. To determine whether such violations occur, it is common practice for lead agencies to compare ***project*** emissions to quantitative significance thresholds developed by local air districts as a screening tool for CEQA review.

Thresholds of significance for construction emissions are typically expressed on a short-term basis, *i.e.* daily or hourly basis to adequately capture impacts due to the high variability of emissions during different construction stages. The Project site is under the jurisdiction of the GVAPCD, which has not developed significance thresholds for construction like most other air districts. Given the lack of quantitative significance thresholds in the GVAPCD's guidance, the Proponent could have conducted ambient air quality dispersion modeling to evaluate whether ambient air quality standards would be violated during any of the construction phases. **I14-104 cont.**

The CD-IV Project is located in the Great Basin Valleys Air Basin (GBVAB), which includes Mono, Inyo, and Alpine Counties. Mono County is designated non-attainment for the federal and state standards for ozone and PM_{10}. Mono County is also has the highest population density of all the counties in the GBVAB, with the Town of Mammoth Lakes having the greatest population in the county. In the absence of quantitative significance thresholds from GVAPCD, the Proponent has used short-term significance thresholds developed by another air district, the Imperial County Air Pollution Control District (ICAPCD) to screen for significance of criteria pollutant emissions.

The Proponent notes that the Imperial County is a rural county similar to Mono County with existing and proposed geothermal development projects. The Imperial County Air Basin is also a federal and state non-attainment area for both ozone and particulate matter less

than 10 microns (PM_{10}).[3] The majority of air basins in California are a federal and state non-attainment area for both ozone and PM_{10}, including the basins immediately adjacent to GBVAB (the Mountain Counties, San Joaquin Valley, and Mojave Desert). What the proponent does not note is that ICAPCD has some of the highest published significance thresholds for particulate matter less than 10 microns (PM10) in the State of California.

Table 1:
CEQA significance thresholds for construction emissions from various air districts

Air district construction thresholds*	NOx (lbs/day)	ROG (lbs/day)	PM_{10} (lbs/day)	DPM (lbs/day)	$PM_{2.5}$ (lbs/day)	CO (lbs/day)
ICAPCD	55	55	150			550
BAAQMD	54	54	82		54	
SCAQMD	100	75	150		55	550
EDCAPCD	82	82				
SLOCAPCD				7		
MBUAPCD			82			550
FRAQMD	25	25	80			
SMAQMD	85					
YSAQMD	82	82	150			

ICAPCD = Imperial County Air Pollution Control District, CEQA Handbook, 2007;
SCAQMD = South Coast Air Quality Management District, CEQA Handbook, 1993;
BAAQMD = Bay Area Air Quality Management District, CEQA Guidelines 2009;
EDCAPCD = El Dorado County Air Pollution Control District, CEQA Guide, February 2002;
SLOCAPCD = San Louis Obispo County Air Pollution Control District, CEQA Air Quality Handbook, December 2009.
MBUAPCD = Monterey Bay Unified Air Pollution Control District, CEQA Air Quality Guidelines, June 2004,
FRAQMD = Feather River Air Quality Management District, http://www.fraqmd.org/CEQA_Thresholds.htm;
SMAQMD Sacramento Metropolitan Air Quality Management District, Guide to Air Quality Assessment, July 2004;
YSAQMD, Yolo-Solano Air Quality Management District, Air Quality Handbook, Guidelines for Determining Air Quality Thresholds of Significance and Mitigation Measures for Proposed Development Projects that Generate Emissions from Motor Vehicles, revised 2002

I14-104 cont.

Given the proximity of the major population center for Mono County (the Town of Mammoth Lakes) to the proposed project and the existing air quality burden that exists in the County, it would be prudent to use a lower significance threshold than the one proposed by the Proponent.

[3] BLM. 2012. Casa Diablo IV Geothermal Development Project Public Draft Joint Environmental Impact Statement and Environmental Impact Report. State Clearinghouse No. 2011041008. Pg 4.2.-6

Proponents should re-evaluate the potential impacts using a more conservative/health protective significance threshold in a Supplemental EIR (SEIR). I14-104 cont.

III. Failure To Perform An Adequate Air Quality Analysis

The DEIS/DEIR's air quality analysis is deficient and must be updated in a SEIR. The analysis fails to: (1) adequately characterize the potential impacts from construction activities; and, (2) analyze potential health risks from HAPs during the operational phase of the project. Therefore, a revised EIR should be prepared to include a thorough evaluation of all air quality issues associated with the project. I14-105

(1) The DEIS/DEIR fails to accurately estimate the potential emissions from construction activities for the Project. Proponents rely on emissions factors that are assumed to include typical control measures presumptively, producing lower than emissions than previously assumed.

A. The Emission Factors Used To Calculate PM_{10} Emissions Are 71% Lower Than Factors Published By USEPA

Using the U.S. EPA's AP-42[4] emission factor for construction related emissions of total suspended particulate of 1.2 tons per acre per month of activity. The California Air Resource Board (CARB) estimates that 64% of construction-related total suspended particulate emissions is PM_{10}. This yields the following **emission factors for uncontrolled construction-related PM_{10} emissions:** I14-106

- 0.77 tons per acre per month of PM_{10}, or
- 51 lbs. per acre per day of PM_{10}.

The emission factors utilized in the construction analysis performed by the Proponent were compiled by the Midwest Research Institute (MRI)

[4] U.S. EPA. 1995. Compilation of Air Pollutant Emission Factors, Volume I: Stationary, Point and Area Sources, AP-42, 5th Edition, January 1995 for further information

under contract to the PM_{10} Best Available Control Measure (BACM) Working Group. According to CARB, the bulk of the operations observed by MRI were site preparation-related activities.[5] The site estimates were combined with operation-specific emission factors from USEPA's AP-42 to produce an overall "average" emission factor of 0.11 tons PM_{10}/acre-month. CARB notes this was 71% lower than AP-42's 4th edition value.[6] As a daily emission factor, the MRI's average emission factor (0.11 tons PM_{10}/acre-month) is equivalent to 10 lbs PM_{10}/acre-day. **I14-106 cont.**

What proponents do not indicate in their analysis is that the MRI's value assumes the effects of typical control measures such as routine watering. A dust control of 50% is assumed for these measures. The MRI value therefore underestimates the potential emissions from construction activities.

B. The Emission Factors Used To Calculate PM_{10} Emissions Should Have Included A Worst Case Scenario Emission Factor Value Which Is Approximately 4 Times Higher

According to the CARB,[7] the MRI report also included an emission factor for worst-case emissions of 0.42 tons PM_{10}/acre month emission factor, the MRI's worst-case emission factor (0.42 tons PM_{10}/acre-month) is equivalent to 38.18 lbs PM_{10}/acre-day. **I14-107**

CARB notes that the worst-case emission factor is appropriate for large-scale construction operations, which involve substantial earthmoving operations.[8] The worst case scenario value has been utilized by SCAQMD to sites that involve substantial earthmoving operations.[9]

[5] CARB. 2002. Emission Inventory Source, Building Construction Dust. pg 7.7-2 http://www.arb.ca.gov/ei/areasrc/fullpdf/full7-7.pdf
[6] CARB. 2002. Emission Inventory Source, Building Construction Dust. pg 7.7-2 http://www.arb.ca.gov/ei/areasrc/fullpdf/full7-7.pdf
[7] CARB. 2002. Emission Inventory Source, Building Construction Dust. pg 7.7-2 http://www.arb.ca.gov/ei/areasrc/fullpdf/full7-7.pdf
[8] CARB. 2002. Emission Inventory Source, Building Construction Dust. pg 7.7-2 http://www.arb.ca.gov/ei/areasrc/fullpdf/full7-7.pdf
[9] CARB. 2002. Emission Inventory Source, Building Construction Dust. pg 7.7-2 http://www.arb.ca.gov/ei/areasrc/fullpdf/full7-7.pdf

Table 4.2-3 of the DEIS/DEIR, shows the maximum day emissions (in pounds per day) for the project as 98 lbs per day. This assumes all three phases of construction (power plant construction, well construction, and pipeline construction) occur simultaneously. Appendix C -1 of the DEIS/DEIR, indicates in Section 5 (page C-9) that 49.8 lbs of the emissions come from fugitive dust from trucks on unsaved roads. The remaining 35 lbs of PM_{10} comes from construction activities.

I14-107 cont.

Using the more conservative worst-case emission factor for PM_{10} emissions from construction, the 35 lbs of fugitive dust from construction activities increases to 133.63 lbs per day. The cumulative fugitive (fugitive dust from construction and traffic) is therefore as high as 183.43 lbs per day. This value exceeds all of the regulatory thresholds of significance shown in Table 1. The proponent must re-evaluate using the worst-case emission factor or use USEPA's factor.

(2) The proponents have failed to analyze potential health risks from hazardous air pollutants (HAPs) during the operational phase of the project. Proponents state that health risks are assessed qualitatively and full health risk assessment was not warranted.[10] Although they acknowledge the potential of releases of hydrogen sulfide or H_2S from drilling activities and diesel exhaust from construction equipment, Proponents fail to acknowledge that there are health consequences from short-term exposures to these chemicals and that they may be transported long distances.

I14-108

Hydrogen sulfide, H_2S, is a known respiratory irritant and hazardous air pollutant (HAP). Diesel exhaust contains nearly 40 toxic substances including toxic air contaminants (TACs) and may pose a serious public health risk for residents in the vicinity of the facility. TACs are airborne substances that are capable of causing short-term (acute) and/or long-term

[10] BLM. 2012. Casa Diablo IV Geothermal Development Project Public Draft Joint Environmental Impact Statement and Environmental Impact Report. State Clearinghouse No. 2011041008. Pg 4.2.-4

(chronic or carcinogenic, i.e., cancer causing) adverse human health effects (i.e., injury or illness). TACs include both organic and inorganic chemical substances. The current California list of TACs includes approximately 200 compounds, including particulate emissions from diesel-fueled engines.

Evidence exists that clouds of soot emitted by heavy-duty construction equipment can travel downwind for miles, then drift into heavily populated areas. For example, health impact studies from the South Coast Air Quality Management District[11] (SCAQMD) have documented that diesel emissions travel miles from the sources impacting residents.

I14-108 cont.

Diesel exhaust has been linked to a range of serious health problems including an increase in respiratory disease, lung damage, cancer, and premature death[12,13,14]. Fine diesel particles are deposited deep in the lungs in the smallest airways and can result in increased respiratory symptoms and disease; decreased lung function, particularly in children and individuals with asthma; alterations in lung tissue and respiratory tract defense mechanisms; and premature death.[15] Exposure to diesel exhaust increases the risk of lung cancer. It also causes non-cancer effects including chronic bronchitis, inflammation of lung tissue, thickening of the alveolar walls, immunological allergic reactions, and airway constriction.[16]

[11] SCAQMD MATES I, II, and III have documented the impacts for DPM in the SCAB.
[12] California Air Resources Board, Initial Statement of Reasons for Rulemaking, Proposed Identification of Diesel Exhaust as a Toxic Air Contaminant, Staff Report, June 1998.
[13] U.S. EPA, Health Assessment Document for Diesel Engine Exhaust, Report EPA/600/8-90/057F, May 2002.
[14] Environmental Defense Fund, Cleaner Diesel Handbook, Bring Cleaner Fuel and Diesel Retrofits into Your Neighborhood, April 2005; http://www.edf.org/documents/4941_cleanerdieselhandbook.pdf, accessed March 27, 2008.
[15] California Air Resources Board , Initial Statement of Reasons for Rulemaking, Proposed Identification of Diesel Exhaust as a Toxic Air Contaminant, Staff Report, June 1998.
[16] Findings of the Scientific Review Panel on The Report on Diesel Exhaust as adopted at the Panel's April 22, 1998 Meeting.

A recent analysis found that air pollution from diesel construction equipment is already taking a heavy toll on the health and economic well-being of Californians.[17,18]

In addition to potential releases of H_2S, the project could produce large quantities of ammonia.[19] Ammonia released to the environment has the potential during normal operation to create significant secondary particulate impacts. Ammonia emitted by the Project can react with sulfite (SO_3) and nitrogen dioxide (NO_2) downwind in the atmosphere to form ammonium sulfate, ammonium bisulfate, and ammonium nitrate according to the following reactions. (Seinfeld and Pandis 1998, pp. 529-534;[20] Matsuda *et al.* 1982;[21] Burke and Johnson 1982.[22]) I14-108 cont.

$$SO_3 + 2\ NH_3 \rightarrow (NH_4)_2SO_4 \quad (1)$$
$$SO_3 + NH_3 \rightarrow NH_4HSO_4 \quad (2)$$
$$NO_2 + OH + NH_3 \rightarrow NH_4NO_3 \quad (3)$$

The increase in PM in the region will only exacerbate the already serious air quality issues in the region.

IV. Failure To Adequately Estimate The Air Quality Burden The Project Will Place On The Air Basin

I14-109

The DEIS/DEIR fails to adequately characterize the operational

[17] These estimates are conservative because they do not include emissions from a large number of small construction projects (residential and commercial and projects smaller than 1 acre in size). Further, John Hakel, vice president of the Associated General Contractors, which represents construction equipment fleet owners and general contractors, indicated that the report appeared to underestimate the sheer volume of construction equipment.

[18] Union of Concerned Scientists, Digging up Trouble: Construction Pollution in the Bay Area; http://www.ucsusa.org/assets/documents/clean_vehicles/Bay-Area-Fact-Sheet.pdf, accessed March 27, 2008.

[19] J.M. Burke and K.L. Johnson, Ammonium Sulfate and Bisulfate Formation in Air Preheaters, Report EPA-600/7-82-025a, April 1982.

[20] John H. Seinfeld and Spyros N. Pandis, Atmospheric Chemistry and Physics, John Wiley & Sons, Inc., New York, 1998.

[21] S. Matsuda, T. Kamo, A. Kato, and F. Nakajima, Deposition of Ammonium Bisulfate in the Selective Catalytic Reduction of Nitrogen Oxides with Ammonia, Ind. Eng. Chem. Prod. Res. Dev., v. 21, 1982, pp. 48-52.

[22] J.M. Burke and K.L. Johnson, Ammonium Sulfate and Bisulfate Formation in Air Preheaters, Report EPA-600/7-82-025a, April 1982.

emissions of VOCs from the Facility. Fugitive emissions from the Casa Diablo Complex are likely to be substantial given the acceptable fugitive loss rate project for the CD-IV project.

The Draft EIS/EIR states that fugitive n-pentane emissions from the CD-IV Project will substantially exceed the emission rates designated by ICAPCD. The DEIS/DEIR states "[t]he fugitive n-pentane, which is considered an ROG (reactive organic gas), would be released to the atmosphere or would leak into the geothermal lines, as a result of fugitive leaks of vaporized n-pentane from the valves, connections, seals, and tubes of the closed power plant motive fluid system.[23] The Applicant has estimated a maximum fugitive n-pentane leak rate for the CD-IV Project of 410 lbs/day (74.825 tons/year), and has requested this amount as permit limit from the GBUAPCD. (*Id.*) I14-109 cont.

The Project's own 410 lbs/day estimate significantly exceeds the ICAPCD operational emissions of ozone precursor ROGs of just 55 lbs/day (almost 8 times higher), is almost double the GBUAPCD's best available control technology ("BACT") threshold of 250 lbs/day for VOC emissions from stationary sources, and does not include emissions from the rest of the Casa Diablo Complex.[24] Operational emissions from CD-IV are substantial and qualify as a significant air impact. The Draft EIR/EIS must be revised to fully analyze and mitigate this per se significant impact.

V. Failure to Perform An Odor Analysis

I14-110

According to the DEIS/DEIR odor impacts were identified as less than significant requiring no further analysis. Existing sources of odors that could affect the proposed project were not properly identified. The

[23] BLM. 2012. Casa Diablo IV Geothermal Development Project Public Draft Joint Environmental Impact Statement and Environmental Impact Report. State Clearinghouse No. 2011041008. Pg 4.2-4

[24] BLM. 2012. Casa Diablo IV Geothermal Development Project Public Draft Joint Environmental Impact Statement and Environmental Impact Report. State Clearinghouse No. 2011041008. Pg 4.2-4

project has the potential to release large quantities of hydrogen sulfide, H_2S, a known irritant.

CARB investigated the ability of H_2S to cause annoyance to the general population. This study (CARB 1985,[25] p. 2), concluded that "an unpleasant odor is at or above the threshold of annoyance for half the people, when its concentration reaches 5 times the average threshold of detection." Recent work using reliable test methods indicates that the detectable threshold for H_2S ranges from 0.4 $\mu g/m^3$ (in studies in the Netherlands using a dynamic flow method) to 0.7 $\mu g/m^3$ (in studies in Japan using a static test method in an odor-free test room[26]). Thus, the concentration of H_2S that would annoy half the people would range from 2 $\mu g/m^3$ to 3.5 $\mu g/m^3$.

I14-110 cont.

This is consistent with conclusions reached by the World Health Organization (WHO), which considered that a level of 0.008 mg/m^3 (0.005 ppm) averaged over 30 min should not produce odour nuisance in most situations.[27] Extrapolating this to a 1-hour averaging time, this is equivalent to 3.5 ug/m^3 for a 1-hour exposure. These values are consistent with the annoyance range of 2 to 3.5 ug/m^3 estimated using CARB guidance.

The Proponent must adequately document the sources of potential odors, perform dispersion modeling of the sources to determine the ground level concentrations in the affected community, and determine the frequency of exceedences in the community from the releases at the project. This information must be included in a SEIR.

[25] John E. Amoore, The Perception of Hydrogen Sulfide Odor in Relation to Setting an Ambient Standard, Prepared for California Air Resources Board, ARB Contract A4-046-33, April 10, 1985.

[26] Y. Hoshika and others, International Comparison of Odor Threshold Values of Several Odorants in Japan and in The Netherlands, Environmental Research, v. 61, 1993, pp. 78–83.

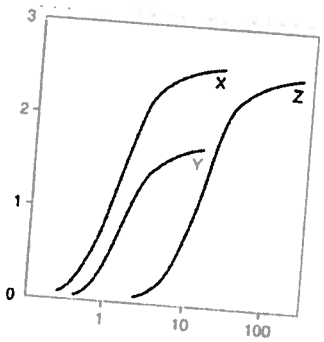
[27] World Health Organization, Hydrogen Sulfide, Environmental Health Criteria No. 19, 1981, p. 13; National Research Council, Hydrogen Sulfide, University Park Press, Baltimore, 1979; T. Lindvall, On Sensory Evaluation of Odors Air Pollutant Intensities, Nord. Hyg. Tidskr., Supplement v. 2, 1970, pp. 1-181.

Conclusion

The facts identified and referenced in this comment letter lead me to reasonably conclude that the Project will result in significant adverse impacts that were not identified in the DEIS/DEIR and that are not adequately mitigated. Many of the DEIS/DEIR's conclusions that environmental impacts are not significant or less than significant with mitigation are unsupported or contradicted by the evidence. As a result, several analyses presented in the DEIS/DEIR, including impacts on air quality fail to identify or disclose the magnitude of significant adverse impacts. To protect air quality and public health the Proponent must prepare a SEIR for the Project. I14-111

Sincerely,

James Clark, Ph.D.



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James J. J. Clark, Ph.D.

Principal Toxicologist

Toxicology/Exposure Assessment Modeling

Risk Assessment/Analysis/Dispersion Modeling

Education:

Ph.D., Environmental Health Science, University of California, 1995

M.S., Environmental Health Science, University of California, 1993

B.S., Biophysical and Biochemical Sciences, University of Houston, 1987

Professional Experience:

Dr. Clark is a well recognized toxicologist, air modeler, and health scientist. He has 20 years of experience in researching the effects of environmental contaminants on human health including environmental fate and transport modeling (SCREEN3, AEROMOD, ISCST3, Johnson-Ettinger Vapor Intrusion Modeling); exposure assessment modeling (partitioning of contaminants in the environment as well as PBPK modeling); conducting and managing human health risk assessments for regulatory compliance and risk-based clean-up levels; and toxicological and medical literature research.

Significant projects performed by Dr. Clark include the following:

LITIGATION SUPPORT

Case: James Harold Caygle, et al, v. Drummond Company, Inc. Circuit Court for the Tenth Judicial Circuit, Jefferson County, Alabama. Civil Action. CV-2009

Client: Environmental Litgation Group, Birmingham, Alabama

Dr. Clark performed an air quality assessment of emissions from a coke factory located in Tarrant, Alabama. The assessment reviewed include a comprehensive review of air quality standards, measured concentrations of pollutants from factory, an inspection of the facility and detailed assessment of the impacts on the community. The results of the assessment and literature have been provided in a declaration to the court.

Case Result: Settlement in favor of plaintiff.

Case: Rose Roper V. Nissan North America, et al. Superior Court of the State Of California for the County Of Los Angeles – Central Civil West. Civil Action. NC041739

Client: Rose, Klein, Marias, LLP, Long Beach, California

Dr. Clark performed a toxicological assessment of an individual occupationally exposed to multiple chemicals, including benzene, who later developed a respiratory distress. A review of the individual's medical and occupational history was performed to prepare an exposure assessment. The exposure assessment was evaluated against the known outcomes in published literature to exposure to respiratory irritants. The results of the assessment and literature have been provided in a declaration to the court.

Case Result: Settlement in favor of plaintiff.

Case: O'Neil V. Sherwin Williams, et al. United States District Court Central District of California

Client: Rose, Klein, Marias, LLP, Long Beach, California

Dr. Clark performed a toxicological assessment of an individual occupationally exposed to petroleum distillates who later developed a bladder cancer. A review of the individual's medical and occupational history was performed to prepare a quantitative exposure assessment. The results of the assessment and literature have been provided in a declaration to the court.

Case Result: Summary judgment for defendants.

Case: Moore V., Shell Oil Company, et al. Superior Court of the State Of California for the County Of Los Angeles

Client: Rose, Klein, Marias, LLP, Long Beach, California

Dr. Clark performed a toxicological assessment of an individual occupationally exposed to chemicals while benzene who later developed a leukogenic disease. A review of the individual's medical and occupational history was performed to prepare a quantitative exposure assessment. The exposure assessment was evaluated against the known outcomes in published literature to exposure to refined petroleum hydrocarbons. The results of the assessment and literature have been provided in a declaration to the court.

Case Result: Settlement in favor of plaintiff.

Case: Raymond Saltonstall V. Fuller O'Brien, KILZ, and Zinsser, et al. United States District Court Central District of California

Client: Rose, Klein, Marias, LLP, Long Beach, California

Dr. Clark performed a toxicological assessment of an individual occupationally exposed to benzene who later developed a leukogenic disease. A review of the individual's medical and occupational history was performed to prepare a quantitative exposure assessment. The exposure assessment was evaluated against the known outcomes in published literature to exposure to refined petroleum hydrocarbons. The results of the assessment and literature have been provided in a declaration to the court.

Case Result: Settlement in favor of plaintiff.

Case: Richard Boyer and Elizabeth Boyer, husband and wife, V. DESCO Corporation, et al. Circuit Court of Brooke County, West Virginia. Civil Action Number 04-C-7G.

Client: Frankovitch, Anetakis, Colantonio & Simon, Morgantown, West Virginia.

Dr. Clark performed a toxicological assessment of a family exposed to chlorinated solvents released from the defendant's facility into local drinking water supplies. A review of the individual's medical and occupational history was performed to prepare a qualitative exposure assessment. The exposure assessment was evaluated against the known outcomes in published literature to exposure to chlorinated solvents. The results of the assessment and literature have been provided in a declaration to the court.

Case Result: Settlement in favor of plaintiff.

Case: JoAnne R. Cook, V. DESCO Corporation, et al. Circuit Court of Brooke County, West Virginia. Civil Action Number 04-C-9R

Client: Frankovitch, Anetakis, Colantonio & Simon, Morgantown, West Virginia.

Dr. Clark performed a toxicological assessment of an individual exposed to chlorinated solvents released from the defendant's facility into local drinking water supplies. A review of the individual's medical and occupational history was performed to prepare a qualitative exposure assessment. The exposure assessment was evaluated against the known outcomes in published literature to exposure to chlorinated solvents. The results of the assessment and literature have been provided in a declaration to the court.

Case Result: Settlement in favor of plaintiff.

Case: Patrick Allen And Susan Allen, husband and wife, and Andrew Allen, a minor, V. DESCO Corporation, et al. Circuit Court of Brooke County, West Virginia. Civil Action Number 04-C-W

Client: Frankovitch, Anetakis, Colantonio & Simon, Morgantown, West Virginia.

Dr. Clark performed a toxicological assessment of a family exposed to chlorinated solvents released from the defendant's facility into local drinking water supplies. A review of the individual's medical and occupational history was performed to prepare a qualitative exposure assessment. The exposure assessment was evaluated against the known outcomes in published literature to exposure to chlorinated solvents. The results of the assessment and literature have been provided in a declaration to the court.

Case Result: Settlement in favor of plaintiff.

Case: Michael Fahey, Susan Fahey V. Atlantic Richfield Company, et al. United States District Court Central District of California Civil Action Number CV-06 7109 JCL.

Client: Rose, Klein, Marias, LLP, Long Beach, California

Dr. Clark performed a toxicological assessment of an individual occupationally exposed to refined petroleum hydrocarbons who later developed a leukogenic disease. A review of the individual's medical and occupational history was performed to prepare a qualitative exposure assessment. The exposure assessment was evaluated against the known outcomes in published literature to exposure to refined petroleum hydrocarbons. The results of the assessment and literature have been provided in a declaration to the court.

Case Result: Settlement in favor of plaintiff.

Case: Constance Acevedo, et al., V. California Spray-Chemical Company, et al., Superior Court of the State Of California, County Of Santa Cruz. Case No. CV 146344

Dr. Clark performed a comprehensive exposure assessment of community members exposed to toxic metals from a former lead arsenate manufacturing facility. The former manufacturing site had undergone a DTSC mandated removal action/remediation for the presence of the toxic metals at the site. Opinions were presented regarding the elevated levels of arsenic and lead (in attic dust and soils) found throughout the community and the potential for harm to the plaintiffs in question.

Case Result: Settlement in favor of defendant.

Case: Michael Nawrocki V. The Coastal Corporation, Kurk Fuel Company, Pautler Oil Service, State of New York Supreme Court, County of Erie, Index Number I2001-11247

Client: Richard G. Berger Attorney At Law, Buffalo, New York

Dr. Clark performed a toxicological assessment of an individual occupationally exposed to refined petroleum hydrocarbons who later developed a leukogenic disease. A review of the individual's medical and occupational history was performed to prepare a qualitative exposure assessment. The exposure assessment was evaluated against the

known outcomes in published literature to exposure to refined petroleum hydrocarbons. The results of the assessment and literature have been provided in a declaration to the court.

Case Result: Judgement in favor of defendant.

SELECTED AIR MODELING RESEARCH/PROJECTS

Client – Confidential

Dr. Clark performed a comprehensive evaluation of criteria pollutants, air toxins, and particulate matter emissions from a carbon black production facility to determine the impacts on the surrounding communities. The results of the dispersion model will be used to estimate acute and chronic exposure concentrations to multiple contaminants and will be incorporated into a comprehensive risk evaluation.

Client – Confidential

Dr. Clark performed a comprehensive evaluation of air toxins and particulate matter emissions from a railroad tie manufacturing facility to determine the impacts on the surrounding communities. The results of the dispersion model have been used to estimate acute and chronic exposure concentrations to multiple contaminants and have been incorporated into a comprehensive risk evaluation.

Client – Los Angeles Alliance for a New Economy (LAANE), Los Angeles, California

Dr. Clark is advising the LAANE on air quality issues related to current flight operations at the Los Angeles International Airport (LAX) operated by the Los Angeles World Airport (LAWA) Authority. He is working with the LAANE and LAX staff to develop a comprehensive strategy for meeting local community concerns over emissions from flight operations and to engage federal agencies on the issue of local impacts of community airports.

Client – City of Santa Monica, Santa Monica, California

Dr. Clark is advising the City of Santa Monica on air quality issues related to current flight operations at the facility. He is working with the City staff to develop a comprehensive strategy for meeting local community concerns over emissions from flight operations and to engage federal agencies on the issue of local impacts of community airports.

Client: Omnitrans, San Bernardino, California

Dr. Clark managed a public health survey of three communities near transit fueling facilities in San Bernardino and Montclair California in compliance with California Senate Bill 1927. The survey included an epidemiological survey of the effected communities, emission surveys of local businesses, dispersion modeling to determine potential emission concentrations within the communities, and a comprehensive risk assessment of each community. The results of the study were presented to the Governor as mandated by Senate Bill 1927.

Client: Confidential, San Francisco, California

Summarized cancer types associated with exposure to metals and smoking. Researched the specific types of cancers associated with exposure to metals and smoking. Provided causation analysis of the association between cancer types and exposure for use by non-public health professionals.

Client: Confidential, Minneapolis, Minnesota

Prepared human health risk assessment of workers exposed to VOCs from neighboring petroleum storage/transport facility. Reviewed the systems in place for distribution of petroleum hydrocarbons to identify chemicals of concern (COCs), prepared comprehensive toxicological summaries of COCs, and quantified potential risks from carcinogens and non-carcinogens to receptors at or adjacent to site. This evaluation was used in the support of litigation.

Client – United Kingdom Environmental Agency

Dr. Clark is part of team that performed comprehensive evaluation of soil vapor intrusion of VOCs from former landfill adjacent residences for the United Kingdom's Environment

Agency. The evaluation included collection of liquid and soil vapor samples at site, modeling of vapor migration using the Johnson Ettinger Vapor Intrusion model, and calculation of site-specific health based vapor thresholds for chlorinated solvents, aromatic hydrocarbons, and semi-volatile organic compounds. The evaluation also included a detailed evaluation of the use, chemical characteristics, fate and transport, and toxicology of chemicals of concern (COC). The results of the evaluation have been used as a briefing tool for public health professionals.

EMERGING/PERSISTENT CONTAMINANT RESEARCH/PROJECTS

Client: Ameren Services, St. Louis, Missouri

Managed the preparation of a comprehensive human health risk assessment of workers and residents at or near an NPL site in Missouri. The former operations at the Property included the servicing and repair of electrical transformers, which resulted in soils and groundwater beneath the Property and adjacent land becoming impacted with PCB and chlorinated solvent compounds. The results were submitted to U.S. EPA for evaluation and will be used in the final ROD.

Client: City of Santa Clarita, Santa Clarita, California

Dr. Clark is managing the oversight of the characterization, remediation and development activities of a former 1,000 acre munitions manufacturing facility for the City of Santa Clarita. The site is impacted with a number of contaminants including perchlorate, unexploded ordinance, and volatile organic compounds (VOCs). The site is currently under a number of regulatory consent orders, including an Immanent and Substantial Endangerment Order. Dr. Clark is assisting the impacted municipality with the development of remediation strategies, interaction with the responsible parties and stakeholders, as well as interfacing with the regulatory agency responsible for oversight of the site cleanup.

Client: Confidential, Los Angeles, California

Prepared comprehensive evaluation of perchlorate in environment. Dr. Clark evaluated the production, use, chemical characteristics, fate and transport, toxicology, and remediation of perchlorate. Perchlorates form the basis of solid rocket fuels and have recently been detected in water supplies in the United States. The results of this research

were presented to the USEPA, National GroundWater, and ultimately published in a recent book entitled *Perchlorate in the Environment*.

Client – Confidential, Los Angeles, California

Dr. Clark is performing a comprehensive review of the potential for pharmaceuticals and their by-products to impact groundwater and surface water supplies. This evaluation will include a review if available data on the history of pharmaceutical production in the United States; the chemical characteristics of various pharmaceuticals; environmental fate and transport; uptake by xenobiotics; the potential effects of pharmaceuticals on water treatment systems; and the potential threat to public health. The results of the evaluation may be used as a briefing tool for non-public health professionals.

PUBLIC HEALTH/TOXICOLOGY

Client: Brayton Purcell, Novato, California

Dr. Clark performed a toxicological assessment of residents exposed to methyl-tertiary butyl ether (MTBE) from leaking underground storage tanks (LUSTs) adjacent to the subject property. The symptomology of residents and guests of the subject property were evaluated against the known outcomes in published literature to exposure to MTBE. The study found that residents had been exposed to MTBE in their drinking water; that concentrations of MTBE detected at the site were above regulatory guidelines; and, that the symptoms and outcomes expressed by residents and guests were consistent with symptoms and outcomes documented in published literature.

Client: Confidential, San Francisco, California

Identified and analyzed fifty years of epidemiological literature on workplace exposures to heavy metals. This research resulted in a summary of the types of cancer and non-cancer diseases associated with occupational exposure to chromium as well as the mortality and morbidity rates.

Client: Confidential, San Francisco, California

Summarized major public health research in United States. Identified major public health research efforts within United States over last twenty years. Results were used as a briefing tool for non-public health professionals.

Client: Confidential, San Francisco, California

Quantified the potential multi-pathway dose received by humans from a pesticide applied indoors. Part of team that developed exposure model and evaluated exposure concentrations in a comprehensive report on the plausible range of doses received by a specific person. This evaluation was used in the support of litigation.

Client: Covanta Energy, Westwood, California

Evaluated health risk from metals in biosolids applied as soil amendment on agricultural lands. The biosolids were created at a forest waste cogeneration facility using 96% whole tree wood chips and 4 percent green waste. Mass loading calculations were used to estimate Cr(VI) concentrations in agricultural soils based on a maximum loading rate of 40 tons of biomass per acre of agricultural soil. The results of the study were used by the Regulatory agency to determine that the application of biosolids did not constitute a health risk to workers applying the biosolids or to residences near the agricultural lands.

Client – United Kingdom Environmental Agency

Oversaw a comprehensive toxicological evaluation of methyl-*tertiary* butyl ether (M*t*BE) for the United Kingdom's Environment Agency. The evaluation included available data on the production, use, chemical characteristics, fate and transport, toxicology, and remediation of M*t*BE. The results of the evaluation have been used as a briefing tool for public health professionals.

Client – Confidential, Los Angeles, California

Prepared comprehensive evaluation of *tertiary* butyl alcohol (TBA) in municipal drinking water system. TBA is the primary breakdown product of M*t*BE, and is suspected to be the primary cause of M*t*BE toxicity. This evaluation will include available information on the production, use, chemical characteristics, fate and transport in the environment, absorption, distribution, routes of detoxification, metabolites, carcinogenic potential, and remediation of TBA. The results of the evaluation were used as a briefing tool for non-public health professionals.

Client – Confidential, Los Angeles, California

Prepared comprehensive evaluation of methyl *tertiary* butyl ether (MTBE) in municipal drinking water system. MTBE is a chemical added to gasoline to increase the octane

rating and to meet Federally mandated emission criteria. The evaluation included available data on the production, use, chemical characteristics, fate and transport, toxicology, and remediation of MTBE. The results of the evaluation have been were used as a briefing tool for non-public health professionals.

Client – Ministry of Environment, Lands & Parks, British Columbia

Dr. Clark assisted in the development of water quality guidelines for methyl tertiary-butyl ether (MTBE) to protect water uses in British Columbia (BC). The water uses to be considered includes freshwater and marine life, wildlife, industrial, and agricultural (e.g., irrigation and livestock watering) water uses. Guidelines from other jurisdictions for the protection of drinking water, recreation and aesthetics were to be identified.

Client: Confidential, Los Angeles, California

Prepared physiologically based pharmacokinetic (PBPK) assessment of lead risk of receptors at middle school built over former industrial facility. This evaluation is being used to determine cleanup goals and will be basis for regulatory closure of site.

Client: Kaiser Venture Incorporated, Fontana, California

Prepared PBPK assessment of lead risk of receptors at a 1,100-acre former steel mill. This evaluation was used as the basis for granting closure of the site by lead regulatory agency.

RISK ASSESSMENTS/REMEDIAL INVESTIGATIONS

Client: Confidential, Atlanta, Georgia

Researched potential exposure and health risks to community members potentially exposed to creosote, polycyclic aromatic hydrocarbons, pentachlorophenol, and dioxin compounds used at a former wood treatment facility. Prepared a comprehensive toxicological summary of the chemicals of concern, including the chemical characteristics, absorption, distribution, and carcinogenic potential. Prepared risk characterization of the carcinogenic and non-carcinogenic chemicals based on the exposure assessment to quantify the potential risk to members of the surrounding community. This evaluation was used to help settle class-action tort.

Client: Confidential, Escondido, California

Prepared comprehensive Preliminary Endangerment Assessment (PEA) of dense non-aqueous liquid phase hydrocarbon (chlorinated solvents) contamination at a former printed circuit board manufacturing facility. This evaluation was used for litigation support and may be used as the basis for reaching closure of the site with the lead regulatory agency.

Client: Confidential, San Francisco, California

Summarized epidemiological evidence for connective tissue and autoimmune diseases for product liability litigation. Identified epidemiological research efforts on the health effects of medical prostheses. This research was used in a meta-analysis of the health effects and as a briefing tool for non-public health professionals.

Client: Confidential, Bogotá, Columbia

Prepared comprehensive evaluation of the potential health risks associated with the redevelopment of a 13.7 hectares plastic manufacturing facility in Bogotá, Colombia The risk assessment was used as the basis for the remedial goals and closure of the site.

Client: Confidential, Los Angeles, California

Prepared comprehensive human health risk assessment of students, staff, and residents potentially exposed to heavy metals (principally cadmium) and VOCs from soil and soil vapor at 12-acre former crude oilfield and municipal landfill. The site is currently used as a middle school housing approximately 3,000 children. The evaluation determined that the site was safe for the current and future uses and was used as the basis for regulatory closure of site.

Client: Confidential, Los Angeles, California

Managed remedial investigation (RI) of heavy metals and volatile organic chemicals (VOCs) for a 15-acre former manufacturing facility. The RI investigation of the site included over 800 different sampling locations and the collection of soil, soil gas, and groundwater samples. The site is currently used as a year round school housing approximately 3,000 children. The Remedial Investigation was performed in a manner

that did not interrupt school activities and met the time restrictions placed on the project by the overseeing regulatory agency. The RI Report identified the off-site source of metals that impacted groundwater beneath the site and the sources of VOCs in soil gas and groundwater. The RI included a numerical model of vapor intrusion into the buildings at the site from the vadose zone to determine exposure concentrations and an air dispersion model of VOCs from the proposed soil vapor treatment system. The Feasibility Study for the Site is currently being drafted and may be used as the basis for granting closure of the site by DTSC.

Client: Confidential, Los Angeles, California

Prepared comprehensive human health risk assessment of students, staff, and residents potentially exposed to heavy metals (principally lead), VOCs, SVOCs, and PCBs from soil, soil vapor, and groundwater at 15-acre former manufacturing facility. The site is currently used as a year round school housing approximately 3,000 children. The evaluation determined that the site was safe for the current and future uses and will be basis for regulatory closure of site.

Client: Confidential, Los Angeles, California

Prepared comprehensive evaluation of VOC vapor intrusion into classrooms of middle school that was former 15-acre industrial facility. Using the Johnson-Ettinger Vapor Intrusion model, the evaluation determined acceptable soil gas concentrations at the site that did not pose health threat to students, staff, and residents. This evaluation is being used to determine cleanup goals and will be basis for regulatory closure of site.

Client –Dominguez Energy, Carson, California

Prepared comprehensive evaluation of the potential health risks associated with the redevelopment of 6-acre portion of a 500-acre oil and natural gas production facility in Carson, California. The risk assessment was used as the basis for closure of the site.

Kaiser Ventures Incorporated, Fontana, California

Prepared health risk assessment of semi-volatile organic chemicals and metals for a fifty-year old wastewater treatment facility used at a 1,100-acre former steel mill. This evaluation was used as the basis for granting closure of the site by lead regulatory agency.

ANR Freight - Los Angeles, California

Prepared a comprehensive Preliminary Endangerment Assessment (PEA) of petroleum hydrocarbon and metal contamination of a former freight depot. This evaluation was as the basis for reaching closure of the site with lead regulatory agency.

Kaiser Ventures Incorporated, Fontana, California

Prepared comprehensive health risk assessment of semi-volatile organic chemicals and metals for 23-acre parcel of a 1,100-acre former steel mill. The health risk assessment was used to determine clean up goals and as the basis for granting closure of the site by lead regulatory agency. Air dispersion modeling using ISCST3 was performed to determine downwind exposure point concentrations at sensitive receptors within a 1 kilometer radius of the site. The results of the health risk assessment were presented at a public meeting sponsored by the Department of Toxic Substances Control (DTSC) in the community potentially affected by the site.

Unocal Corporation - Los Angeles, California

Prepared comprehensive assessment of petroleum hydrocarbons and metals for a former petroleum service station located next to sensitive population center (elementary school). The assessment used a probabilistic approach to estimate risks to the community and was used as the basis for granting closure of the site by lead regulatory agency.

Client: Confidential, Los Angeles, California

Managed oversight of remedial investigation most contaminated heavy metal site in California. Lead concentrations in soil excess of 68,000,000 parts per billion (ppb) have been measured at the site. This State Superfund Site was a former hard chrome plating operation that operated for approximately 40-years.

Client: Confidential, San Francisco, California

Coordinator of regional monitoring program to determine background concentrations of metals in air. Acted as liaison with SCAQMD and CARB to perform co-location sampling and comparison of accepted regulatory method with ASTM methodology.

Client: Confidential, San Francisco, California

Analyzed historical air monitoring data for South Coast Air Basin in Southern California and potential health risks related to ambient concentrations of carcinogenic metals and volatile organic compounds. Identified and reviewed the available literature and calculated risks from toxins in South Coast Air Basin.

IT Corporation, North Carolina

Prepared comprehensive evaluation of potential exposure of workers to air-borne VOCs at hazardous waste storage facility under SUPERFUND cleanup decree. Assessment used in developing health based clean-up levels.

Professional Associations

American Public Health Association (APHA)
Association for Environmental Health and Sciences (AEHS)
American Chemical Society (ACS)
California Redevelopment Association (CRA)
International Society of Environmental Forensics (ISEF)
Society of Environmental Toxicology and Chemistry (SETAC)

Publications and Presentations:

Books and Book Chapters

Sullivan, P., **J.J. J. Clark,** F.J. Agardy, and P.E. Rosenfeld. (2007). *Synthetic Toxins In The Food, Water and Air of American Cities.* Elsevier, Inc. Burlington, MA.

Sullivan, P. and **J.J. J. Clark**. 2006. *Choosing Safer Foods, A Guide To Minimizing Synthetic Chemicals In Your Diet.* Elsevier, Inc. Burlington, MA.

Sullivan, P., Agardy, F.J., and **J.J.J. Clark**. 2005. *The Environmental Science of Drinking Water.* Elsevier, Inc. Burlington, MA.

Sullivan, P.J., Agardy, F.J., **Clark, J.J.J.** 2002. *America's Threatened Drinking Water: Hazards and Solutions.* Trafford Publishing, Victoria B.C.

Clark, J.J.J. 2001. "TBA: Chemical Properties, Production & Use, Fate and Transport, Toxicology, Detection in Groundwater, and Regulatory Standards" in *Oxygenates in the Environment.* Art Diaz, Ed.. Oxford University Press: New York.

Clark, J.J.J. 2000. "Toxicology of Perchlorate" in *Perchlorate in the Environment.* Edward Urbansky, Ed. Kluwer/Plenum: New York.

Clark, J.J.J. 1995. Probabilistic Forecasting of Volatile Organic Compound Concentrations At The Soil Surface From Contaminated Groundwater. UMI.

Baker, J.; **Clark, J.J.J.**; Stanford, J.T. 1994. Ex Situ Remediation of Diesel Contaminated Railroad Sand by Soil Washing. Principles and Practices for Diesel Contaminated Soils, Volume III. P.T. Kostecki, E.J. Calabrese, and C.P.L. Barkan, eds. Amherst Scientific Publishers, Amherst, MA. pp 89-96.

Journal and Proceeding Articles

Tam L. K.., Wu C. D., Clark J. J. and **Rosenfeld, P.E.** (2008) A Statistical Analysis Of Attic Dust And Blood Lipid Concentrations Of Tetrachloro-p-Dibenzodioxin (TCDD) Toxicity Equialency Quotients (TEQ) In Two Populations Near Wood Treatment Facilities. Organohalogen Compounds, Volume 70 (2008) page 002254.

Tam L. K.., Wu C. D., Clark J. J. and **Rosenfeld, P.E.** (2008) Methods For Collect Samples For Assessing Dioxins And Other Environmental Contaminants In Attic Dust: A Review. Organohalogen Compounds, Volume 70 (2008) page 000527

Hensley A.R., Scott, A., Rosenfeld P.E., **Clark, J.J.J.** (2007). "Attic Dust And Human Blood Samples Collected Near A Former Wood Treatment Facility." *Environmental Research.* 105:194-199.

Rosenfeld, P.E., **Clark, J. J.,** Hensley, A.R., and Suffet, I.H. 2007. "The Use Of An Odor Wheel Classification For The Evaluation of Human Health Risk Criteria For Compost Facilities" Water Science & Technology. 55(5): 345-357.

Hensley A.R., Scott, A., Rosenfeld P.E., **Clark, J.J.J.** 2006. "Dioxin Containing Attic Dust And Human Blood Samples Collected Near A Former Wood Treatment Facility." The 26th International Symposium on Halogenated Persistent Organic Pollutants – DIOXIN2006, August 21 – 25, 2006. Radisson SAS Scandinavia Hotel in Oslo Norway.

Rosenfeld, P.E., **Clark, J. J.** and Suffet, I.H. 2005. "The Value Of An Odor Quality Classification Scheme For Compost Facility Evaluations" The U.S. Composting Council's 13th Annual Conference January 23 - 26, 2005, Crowne Plaza Riverwalk, San Antonio, TX.

Rosenfeld, P.E., **Clark, J. J.** and Suffet, I.H. 2004. "The Value Of An Odor Quality Classification Scheme For Urban Odor" WEFTEC 2004. 77th Annual Technical Exhibition & Conference October 2 - 6, 2004, Ernest N. Morial Convention Center, New Orleans, Louisiana.

Clark, J.J.J. 2003. "Manufacturing, Use, Regulation, and Occurrence of a Known Endocrine Disrupting Chemical (EDC), 2,4-Dichlorophnoxyacetic Acid (2,4-D) in California Drinking Water Supplies." National Groundwater Association Southwest Focus Conference: Water Supply and Emerging Contaminants. Minneapolis, MN. March 20, 2003.

Rosenfeld, P. and **J.J.J. Clark**. 2003. "Understanding Historical Use, Chemical Properties, Toxicity, and Regulatory Guidance" National Groundwater Association Southwest Focus Conference: Water Supply and Emerging Contaminants. Phoenix, AZ. February 21, 2003.

Clark, J.J.J., Brown A. 1999. Perchlorate Contamination: Fate in the Environment and Treatment Options. In Situ and On-Site Bioremediation, Fifth International Symposium. San Diego, CA, April, 1999.

Clark, J.J.J. 1998. Health Effects of Perchlorate and the New Reference Dose (RfD). Proceedings From the Groundwater Resource Association Seventh Annual Meeting, Walnut Creek, CA, October 23, 1998.

Browne, T., **Clark, J.J.J.** 1998. Treatment Options For Perchlorate In Drinking Water. Proceedings From the Groundwater Resource Association Seventh Annual Meeting, Walnut Creek, CA, October 23, 1998.

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ATTACHMENTS

SECTION 7.7

BUILDING CONSTRUCTION DUST

(Revised September 2002)

EMISSION INVENTORY SOURCE CATEGORY
Miscellaneous Processes / Construction and Demolition

EMISSION INVENTORY CODES (CES CODES) AND DESCRIPTION
630-622-5400-0000 (47357) Building Construction Dust – Residential

630-624-5400-0000 (47365) Building Construction Dust – Commercial

630-626-5400-0000 (47373) Building Construction Dust – Industrial

630-628-5400-0000 (54551) Building Construction Dust – Institutional

630-630-5400-0000 (60400) Building Construction Dust – Governmental

METHODS AND SOURCES

The building construction dust source category provides estimates of the fugitive dust particulate matter caused by construction activities while building residential, commercial, industrial, institutional, or governmental structures. The emissions result predominantly from site preparation work, which may include scraping, grading, loading, digging, compacting, light-duty vehicle travel, and other operations. Table 1 shows particulate matter emissions less than 10 microns (PM_{10}) estimates by county for construction activities. The process rates (PR) in acre-months/year used to calculate the emissions are also listed.

Dust emissions from construction operations are computed by using a PM_{10} emission factor developed by Midwest Research Institute (MRI) during 1996.[1] The emission factor is based on observations of construction operations in California and Las Vegas. Activity data for construction is expressed in terms of acre-months of construction. Acre-months are based on estimates of the acres disturbed for residential construction, and project valuation for other, non-residential construction. Activity data for 1999 are used to estimate construction operations emissions.

Emission Factor. The emission factor used for our estimates of geologic dust emissions from construction activities is based on work performed by Midwest Research Institute[1] under contract to the PM_{10} Best Available Control Measure (BACM) working group. For most parts of the state, the emission factor used is 0.11 tons PM_{10} /acre-month of activity (or 0.225 tons PM/acre-month). This emission factor is based on MRI's observation of the types, quantity, and duration of operations at eight construction

sites (three in Las Vegas and five in California). The bulk of the operations observed were site preparation-related activities. The observed activity data were then combined with operation-specific emission factors provided in U.S. EPA's AP-42 (5th Edition)[2] document to produce site emissions estimates. These site estimates were then combined to produce the overall average emission factor of 0.11 tons PM_{10}/acre-month. This emission factor is approximately 71% lower than the previous emission factor that was used from the 4th Edition of AP-42.

The construction emission factor is assumed to include the effects of typical control measures such as routine watering. A dust control effectiveness of 50% is assumed from these measures, which is based on the estimated control effectiveness of watering.[3] Therefore, if this emission factor is used for construction activities where watering is not used, it should be doubled to more accurately reflect the actual emissions. The MRI document lists their average emission factor values as uncontrolled. However, our judgement is that the activities observed and the emission estimates do include the residual effects of control. All of the test sites observed were actual operations that used watering controls as part of their standard industry practice in California and Las Vegas. So, even if in some cases watering was not performed during the actual site visits, the residual decreases in emissions from the watering controls and raising the soil moisture are thought to be included in the MRI estimates.

The MRI report also includes an emission factor for worst-case emissions of 0.42 tons PM_{10}/acre-month. This emission factor is appropriate for large-scale construction operations, which involve substantial earthmoving operations. The South Coast Air Quality Management District (SCAQMD) estimated that 25 percent of their construction projects involve these types of operations, and applied the larger emission factor to the activities. For the remainder of the state, such detailed information is not readily available, so the average emission factor of 0.11 tons PM_{10}/acre-month was used.

This methodology directly computes PM_{10} emissions. The PM emissions are PM_{10} x 2.04.[4]

Activity Data. For the purpose of estimating emissions, it is assumed that the fugitive dust emissions are related to the acreage affected by construction. Because region-wide estimates of the acreage under construction are not directly available, other construction activity data are used to derive acreage estimates. Activity data are estimated separately for residential construction, and the other types of construction (commercial, industrial, institutional, and governmental). The activity data for construction are based on 1999 estimates.

For residential construction, the number of new housing units, estimated by the Department of Finance[5] for 1999, are used to estimate acreage disturbed. The DOF data are shown in Table 2. Based on reference sources,[6,7,8] it is estimated that single-family living units (houses) are built on 1/7 of an acre in heavily populated counties, and 1/5 of an acre in less populated counties. Table 3 shows the acreage assumptions by county. It is also estimated that multiple living units, such as apartments, occupy 1/20 of an acre per living unit. For all of these residential construction activities, a project

duration of six months is assumed[6]. Applying these factors to the reported number of new units in each county results in an estimate of acre-months of construction. This, combined with the construction emission factor, is used to estimate residential construction particulate emissions.

For commercial, industrial, and institutional building construction, construction acreage is based on project valuations obtained from the Department of Finance[5] as shown in Table 4. Project valuations for Additions and Alterations were not included. According to the Construction Industry Research Board[9], most additions and alterations would be modifications within the existing structure and normally would not include the use of large earthmoving equipment. Most horizontal additions would usually be issued a new building permit. The valuations are 3.7, 4.0 and 4.4 acres per million dollars of valuation for the respective construction types listed.[8] Valuations are corrected from 1999 to 1977 values using the Annual Average Consumer Price Index (CPI-U-RS) provided by the U.S. Census Bureau[10]. The Census Bureau uses the Bureau of Labor Statistics' experimental Consumer Price Index (CPI-U-RS) for 1977 through 2000[11]. Valuations are corrected from 1999 to 1977 values because the acres per dollar valuation values are based on 1977 valuations. The CPI-U-RS for 1999 is 244.1 and the CPI-U-RS for 1977 is 100.0. The ratio of 1977 to 1999 dollars is 100.0/244.1 or 0.41. Each acre is assumed to be under construction for 11 months for each project type.[6] Sample calculations are provided below.

ASSUMPTIONS

1. The current methodology assumes that all construction operations in all parts of the state emit the same levels of PM_{10} on a per acre basis.
2. It is assumed that watering techniques are used statewide, reducing emissions by 50% and making it valid to apply the MRI emission factor without correction.
3. The methodology assumes that valuation is proportional to acreage disturbed, even for high-rise type building construction.
4. The methodology assumes that construction dust emissions are directly proportional to the number of acres disturbed during construction.
5. The estimates of acreage disturbed are limited in their accuracy. New housing units and project valuations do not provide direct estimates of actual acreage disturbed by construction operations in each county.
6. The methodology assumes that the Consumer Price Index (CPI-U-RS) provides an accurate estimate of 1977 and 1999 values.

TEMPORAL ACTIVITY

The temporal activity is assumed to occur five days a week between the hours of 8:00 a.m. and 4:00 p.m. The table below shows the percentage of construction activity that is estimated to occur during each month. The monthly activity increases during the spring and summer months. Some districts use a slightly different profile that has a larger peak during the summer months. Construction emissions for future years are based on construction activity projections.

Hours	Days	Weeks
8	5	52

JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
6.4	6.4	8.3	9.2	9.2	9.2	9.2	9.2	9.2	8.3	8.3	7.3

COMMENTS AND RECOMMENDATIONS

To improve the construction dust estimates, both the emission factor and activity data require attention. The emission factor could be improved by gathering more detailed site data to allow use of the more site-specific emission factors listed in the MRI document[1]. The emission factors could be better applied if the percentage of construction projects that involve substantial earthmoving operations could be determined for each county. Possible improvements to the activity data are better estimates of the actual acreage disturbed by projects and the duration of the projects. Dust emissions from governmental structures were not estimated due to lack of activity data.

CHANGES IN METHOD AND EMISSION ESTIMATES

The major change in this methodology from the previous methodology is the use of current activity data.

GROWTH PARAMETERS

For residential and commercial construction, the growth parameters were developed by Pechan (Categories 14 and 15 in their report, "Development of Emission Growth Surrogates and Activity Projections Used in Forecasting Point and Area Source Emissions, Final Report," February 26, 2001). The growth parameters are based on employment and output data in the construction sector (SIC codes 15 – 17). For the

remaining categories, the growth parameters were developed by Pechan and are based on employment in the construction sector (SIC codes 15 – 17).

SAMPLE CALCULATIONS

The table below provides an example of estimating residential, commercial, industrial and institutional building construction dust emissions for Fresno County.

Follow the steps shown below the table to estimate the construction dust emissions.

Estimating PM_{10} Construction Dust in Fresno County

		Residential Single Family	Residential Multiple Unit	Commercial	Industrial	Institutional
Step 1	Construction Basis	Units Built	Units Built	Valuation (1977 Dollars)	Valuation (1977 Dollars)	Valuation (1977 Dollars)
Step 2	Construction Basis Value	2646	386	$42.05 million	$35.14 million	$32.60 million
Step 3	Acres/Basis	1/5 acres/unit	1/20 acres/unit	3.7 acres/ million	4.0 acres/ million	4.4 acres/ million
Step 4	Project Duration	6 months	6 months	11 months	11 months	11 months
Step 5	Acre-months/year	3175.2	115.8	1711.4	1546.3	1578.0
Step 6	Emission Factor (tons PM10/acre-month)	0.11	0.11	0.11	0.11	0.11
Step 7	PM_{10} Emissions (tons/year)	349.3	12.7	188.3	170.1	173.6

Step 1: Construction Basis. Enter the units. For residential, the activity units are "Units Built". For non-residential, the activity units are "Valuation (1977 dollars)".

Step 2: Construction Basis Value. For residential construction, enter the number of units (either single or multiple) from Table 2. For commercial, industrial and institutional construction, enter the valuation from Table 4 converted to 1977 dollars. To convert the 1999 dollars to 1977 dollars, use the Consumer Price Index (CPI-U-RS)[10]. The CPI-U-RS for 1999 is 244.1 and the CPI-U-RS for 1977 is 100.0. The ratio of 1977 to 1999 dollars is 100.0/244.1 or 0.41. To obtain the valuations in 1977 dollars, multiply the 1999 valuations by 0.41 and divide by 1,000 to convert from thousands to millions of

dollars. In Table 4, valuations listed under "Other" are assumed to be institutional construction.

Step 3: Acres/Basis Unit. Enter the acres per construction units. For residential construction in Fresno County, this is 1/5 acres per home and 1/20 acres per multiple dwelling unit (see Table 3 for acreage assignments for single family living units). For commercial, industrial and institutional construction, the acres per unit are 3.7, 4.0 and 4.4 acres per million dollars valuation, respectively.

Step 4: Project Duration. Residential construction is estimated to take six months, while commercial, industrial and institutional construction are estimated to take 11 months.

Step 5: Compute Acre-Months. Multiply the values from steps 2, 3 and 4 together to get the acre-months.

Process Rate = Construction Basis Value x Acres/Unit x Months = Acre-Months.

Step 6: Emission Factor. Input the emission factor. ARB's default factor is 0.11 tons PM_{10}/acre-month when watering practices are employed.

Step 7: Compute Emissions. Multiply the values from step 5 and step 6 to compute the annual PM_{10} emissions.

Emissions = Acre-Months x Emission Factor.

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5. California Department of Finance, California Statistical Abstract – 2000, Section I, Construction, Economic Research Unit, (916) 322-2263,www.dof.ca.gov.

6. Midwest Research Institute, Inventory of Agricultural Tilling, Unpaved Roads and Airstrips and Construction Sites, prepared for the U.S. Environmental Protection Agency, PB 238-929, Contract 68-02-1437 (November 1974).

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9. Personal Communication with Ben Bartolotto, Research Director of the Construction Industry Research Board, (818) 841-8210 (August 2002).

10. U.S. Census Bureau, Income 2000, Supplemental Information: Annual Average Consumer Price Index (CPI-U-RS): 1947 to 2000, www.census.gov/hhes/income/income00.cpiurs.html.

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UPDATED BY

Cheryl Taylor
September 2002

Table 1. 1999 Building Construction Dust

				Residential		Commercial		Industrial		Institutional	
				EIC:630-622-5400-0000		EIC:630-624-5400-0000		EIC:630-626-5400-0000		EIC:630-628-5400-0000	
AB	CO	DIS	COUNTY NAME	PR (acre-mo/yr)	PM_{10} (tons/yr)	PR (acre-mo/yr)	PM_{10} (tons/yr)	PR (acre-mo/yr)	PM_{10} (tons/yr)	PR (acre-mo/yr)	PM_{10} (tons/yr)
GBV	2	GBU	ALPINE	33.0	3.6	9.5	1.0	0.0	0.0	13.4	1.5
	14	GBU	INYO	21.6	2.4	105.0	11.6	0.0	0.0	12.6	1.4
	26	GBU	MONO	160.2	17.6	0.0	0.0	64.2	7.1	5.1	0.6
LC	17	LAK	LAKE	194.4	21.4	22.0	2.4	0.0	0.0	63.2	7.0
LT	9	ED	EL DORADO	322.5	35.5	71.2	7.8	4.9	0.5	83.2	9.2
	31	PLA	PLACER	223.0	24.5	87.1	9.6	57.0	6.3	34.9	3.8
MC	3	AMA	AMADOR	292.8	32.2	6.9	0.8	158.8	17.5	95.8	10.5
	5	CAL	CALAVERAS	362.4	39.9	95.2	10.5	0.0	0.0	90.4	9.9
	9	ED	EL DORADO	1198.8	131.9	264.7	29.1	18.3	2.0	309.2	34.0
	22	MPA	MARIPOSA	88.8	9.8	4.2	0.5	0.0	0.0	57.9	6.4
	29	NSI	NEVADA	951.9	104.7	63.2	7.0	17.3	1.9	459.8	50.6
	31	PLA	PLACER	495.6	54.5	193.5	21.3	126.6	13.9	77.5	8.5
	32	NSI	PLUMAS	121.2	13.3	0.0	0.0	5.2	0.6	6.8	0.7
	46	NSI	SIERRA	16.8	1.8	0.0	0.0	0.0	0.0	3.7	0.4
	55	TUO	TUOLUMNE	232.8	25.6	58.0	6.4	0.0	0.0	122.6	13.5
MD	15	KER	KERN	632.8	69.6	125.7	13.8	42.7	4.7	243.4	26.8
	19	AV	LOS ANGELES	278.2	30.6	705.9	77.6	208.5	22.9	275.9	30.4
	33	MOJ	RIVERSIDE	182.8	20.1	68.3	7.5	32.4	3.6	37.2	4.1
	33	SC	RIVERSIDE	22.9	2.5	8.5	0.9	4.0	0.4	4.7	0.5
	36	MOJ	SAN BERNARDINO	1344.4	147.9	790.3	86.9	1385.5	152.4	385.1	42.4
NC	8	NCU	DEL NORTE	40.2	4.4	67.3	7.4	0.0	0.0	38.5	4.2
	12	NCU	HUMBOLDT	440.7	48.5	251.6	27.7	6.0	0.7	97.4	10.7
	23	MEN	MENDOCINO	322.2	35.4	22.1	2.4	54.4	6.0	139.6	15.4
	49	NS	SONOMA	370.9	40.8	138.7	15.3	107.3	11.8	87.4	9.6
	53	NCU	TRINITY	49.8	5.5	13.5	1.5	0.0	0.0	32.2	3.5
NCC	27	MBU	MONTEREY	1979.7	217.8	721.4	79.4	175.3	19.3	579.0	63.7
	35	MBU	SAN BENITO	695.4	76.5	123.7	13.6	75.7	8.3	95.1	10.5
	44	MBU	SANTA CRUZ	486.6	53.5	493.5	54.3	75.5	8.3	173.6	19.1
NEP	18	LAS	LASSEN	137.4	15.1	39.7	4.4	0.0	0.0	39.6	4.4
	25	MOD	MODOC	16.8	1.8	7.2	0.8	0.0	0.0	15.7	1.7
	47	SIS	SISKIYOU	165.9	18.2	90.7	10.0	0.0	0.0	79.5	8.7
SC	19	SC	LOS ANGELES	8414.8	1577.8	21352.2	4003.5	6306.0	1182.4	8347.0	1565.1
	30	SC	ORANGE	7986.6	1497.5	13285.4	2491.0	2217.7	415.8	2409.7	451.8
	33	SC	RIVERSIDE	9004.1	1688.3	3361.6	630.3	1595.5	299.2	1832.6	343.6
	36	SC	SAN BERNARDINO	4450.4	834.5	2616.2	490.5	4586.5	860.0	1274.7	239.0
SCC	40	SLO	SAN LUIS OBISPO	1919.4	211.1	497.3	54.7	222.6	24.5	455.8	50.1
	42	SB	SANTA BARBARA	609.3	67.0	771.8	84.9	339.7	37.4	626.9	69.0
	56	VEN	VENTURA	3372.9	371.0	2072.0	227.9	1052.8	115.8	1621.3	178.3
SD	37	SD	SAN DIEGO	10495.6	1154.5	7943.1	873.7	3491.7	384.1	3203.1	352.3
SF	1	BA	ALAMEDA	3033.6	333.7	5369.1	590.6	2480.5	272.9	971.5	106.9
	7	BA	CONTRA COSTA	3650.4	401.5	2134.9	234.8	328.2	36.1	1129.9	124.3
	21	BA	MARIN	610.2	67.1	226.2	24.9	0.0	0.0	644.0	70.8
	28	BA	NAPA	753.3	82.9	678.5	74.6	312.1	34.3	418.7	46.1
	38	BA	SAN FRANCISCO	1206.8	132.7	2461.4	270.8	0.0	0.0	203.3	22.4
	41	BA	SAN MATEO	698.2	76.8	5123.1	563.5	602.3	66.3	1123.7	123.6
	43	BA	SANTA CLARA	3960.0	435.6	7193.7	791.3	5087.5	559.6	2251.3	247.6
	48	BA	SOLANO	1292.3	142.2	414.6	45.6	206.7	22.7	256.4	28.2
	49	BA	SONOMA	2669.6	293.7	998.0	109.8	772.0	84.9	628.7	69.2
SJV	10	SJU	FRESNO	3291.0	362.0	1711.4	188.3	1546.3	170.1	1578.0	173.6
	15	SJU	KERN	2863.1	314.9	568.6	62.6	193.4	21.3	1101.4	121.2
	16	SJU	KINGS	591.6	65.1	137.5	15.1	291.7	32.1	104.0	11.4
	20	SJU	MADERA	618.6	68.0	146.2	16.1	128.0	14.1	63.9	7.0
	24	SJU	MERCED	1203.6	132.4	109.7	12.1	327.8	36.1	651.0	71.6
	39	SJU	SAN JOAQUIN	4844.4	532.9	1713.9	188.5	1514.8	166.6	1105.4	121.6
	50	SJU	STANISLAUS	2714.4	298.6	872.3	96.0	492.3	54.2	710.8	78.2
	54	SJU	TULARE	1859.4	204.5	570.5	62.8	62.0	6.8	1041.0	114.5
SS	13	IMP	IMPERIAL	394.2	43.4	81.1	8.9	322.7	35.5	4255.5	468.1
	33	SC	RIVERSIDE	2216.8	410.1	827.6	153.1	392.8	72.7	451.2	83.5
SV	4	BUT	BUTTE	1140.3	125.4	368.4	40.5	85.3	9.4	179.1	19.7
	6	COL	COLUSA	57.6	6.3	21.8	2.4	0.0	0.0	40.9	4.5
	11	GLE	GLENN	64.8	7.1	26.8	2.9	0.0	0.0	46.9	5.2
	31	PLA	PLACER	4237.6	466.1	1654.2	182.0	1082.6	119.1	662.5	72.9
	34	SAC	SACRAMENTO	7436.7	818.0	4183.7	460.2	1123.2	123.5	1331.2	146.4
	45	SHA	SHASTA	913.2	100.5	226.8	25.0	159.8	17.6	388.0	42.7
	48	YS	SOLANO	580.6	63.9	186.3	20.5	92.9	10.2	115.2	12.7
	51	FR	SUTTER	219.6	24.2	17.1	1.9	30.6	3.4	1151.5	126.7
	52	TEH	TEHAMA	184.2	20.3	51.7	5.7	8.9	1.0	105.8	11.6
	57	YS	YOLO	1065.9	117.2	588.5	64.7	625.0	68.8	182.9	20.1
	58	FR	YUBA	137.4	15.1	16.4	1.8	0.0	0.0	212.4	23.4
Total Statewide				112,645.1	14,871.1	95,228.1	13,684.9	40,701.3	5,646.3	46,637.4	6,238.4

Table 2
NUMBER AND VALUATION OF NEW HOUSING UNITS AUTHORIZED BY BUILDING PERMITS, CALIFORNIA, 1999

	Number of units			Valuation ($1,000)			
County	Single	Multiple	Total	Single	Multiple	Additions & Alterations	Total
Total	**101,711**	**38,426**	**140,137**	**$19,262,653**	**$3,187,535**	**$3,333,078**	**$25,783,265**
Alameda	3,016	1,495	4,511	828,966	146,334	$183,031	$1,158,331
Alpine	20	30	50	7,503	8,969	151	$16,623
Amador	240	16	256	29,471	1,190	3,360	$34,021
Butte	947	13	960	114,103	806	11,496	$126,405
Calaveras	302	0	302	54,363	0	5,910	$60,273
Colusa	48	0	48	6,148	0	1,466	$7,615
Contra Costa	4,081	508	4,589	853,526	44,769	165,019	$1,063,314
Del Norte	33	2	35	3,644	128	917	$4,689
El Dorado	1,212	223	1,435	263,487	17,013	25,356	$305,856
Fresno	2,646	386	3,032	340,238	16,082	22,479	$378,800
Glenn	54	0	54	5,264	0	1,577	$6,842
Humboldt	355	49	404	32,813	1,641	10,047	$44,501
Imperial	327	6	333	37,644	338	3,742	$41,724
Inyo	18	0	18	3,729	0	994	$4,724
Kern	2,832	325	3,157	320,812	17,954	22,375	$361,140
Kings	493	0	493	55,558	0	3,326	$58,884
Lake	161	4	165	23,044	326	3,791	$27,161
Lassen	114	2	116	11,780	158	1,450	$13,389
Los Angeles	7,858	6,525	14,383	1,852,937	586,734	865,352	$3,305,023
Madera	481	138	619	41,096	7,274	4,322	$52,692
Marin	699	37	736	176,687	6,883	113,851	$297,420
Mariposa	74	0	74	10,716	0	853	$11,569
Mendocino	268	2	270	21,126	59	8,682	$29,868
Merced	1,003	0	1,003	121,496	0	8,497	$129,993
Modoc	14	0	14	1,487	0	805	$2,292
Mono	107	106	213	23,347	13,278	1,532	$38,157
Monterey	1,506	575	2,081	298,338	39,311	63,401	$401,050
Napa	597	123	720	145,345	8,169	21,201	$174,714
Nevada	786	29	815	117,370	2,581	12,106	$132,057
Orange	7,686	4,662	12,348	1,655,568	372,559	234,364	$2,262,491
Placer	3,875	1,021	4,896	714,476	70,047	30,402	$814,925
Plumas	101	0	101	10,243	0	113	$10,357
Riverside	12,659	1,920	14,579	2,275,766	130,796	65,796	$2,472,358
Sacramento	5,682	2,061	7,743	982,841	139,106	115,550	$1,237,497
San Benito	579	2	581	80,403	120	2,244	$82,767
San Bernardino	6,593	479	7,072	1,154,664	19,633	75,898	$1,250,195
San Diego	9,993	6,434	16,427	2,247,394	527,131	211,434	$2,985,960
San Francisco	114	3,697	3,811	29,117	456,151	212,346	$697,614
San Joaquin	4,034	12	4,046	582,934	1,125	16,255	$600,314
San Luis Obispo	1,578	86	1,664	242,940	5,011	22,130	$270,080
San Mateo	768	133	901	213,773	15,135	205,843	$434,751
Santa Barbara	601	314	915	141,335	21,338	62,667	$225,340
Santa Clara	3,333	3,677	7,010	739,017	291,309	275,701	$1,306,027
Santa Cruz	372	134	506	84,618	13,542	34,183	$132,342
Shasta	745	64	809	100,393	3,785	10,739	$114,917
Sierra	14	0	14	1,763	0	705	$2,468
Siskiyou	133	21	154	21,063	1,565	3,748	$26,375
Solano	1,430	523	1,953	261,516	30,728	18,368	$310,612
Sonoma	2,361	691	3,052	409,934	40,112	54,615	$504,661
Stanislaus	2,246	64	2,310	284,175	3,208	19,212	$306,594
Sutter	183	0	183	27,599	0	4,340	$31,939
Tehama	153	2	155	18,751	144	2,128	$21,023
Trinity	40	6	46	4,438	350	948	$5,736
Tulare	1,515	138	1,653	181,946	9,164	9,053	$200,163
Tuolumne	194	0	194	22,727	0	8,522	$31,249
Ventura	3,662	780	4,442	829,693	54,009	56,786	$940,488
Yolo	696	769	1,465	131,577	53,604	8,971	$194,152
Yuba	79	142	221	9,950	7,869	2,929	$20,748

Note: Detail may not add to total because of rounding
Source: Construction Industry Research Board, http://www.cirbdata.com
Department of Finance, Economic Research Unit, (916) 322-2263, http://www.dof.ca.gov

Table 3
Estimated Acres Disturbed for Single Living Unit Construction in California, 1999

Alameda	1/7
Alpine	1/5
Amador	1/5
Butte	1/5
Calaveras	1/5
Colusa	1/5
Contra Costa	1/7
Del Norte	1/5
El Dorado	1/5
Fresno	1/5
Glenn	1/5
Humboldt	1/5
Imperial	1/5
Inyo	1/5
Kern	1/5
Kings	1/5
Lake	1/5
Lassen	1/5
Los Angeles	1/7
Madera	1/5
Marin	1/7
Mariposa	1/5
Mendocino	1/5
Merced	1/5
Modoc	1/5
Mono	1/5
Monterey	1/5
Napa	1/5
Nevada	1/5

Orange	1/7
Placer	1/5
Plumas	1/5
Riverside	1/7
Sacramento	1/5
San Benito	1/5
San Bernardino	1/7
San Diego	1/7
San Francisco	1/7
San Joaquin	1/5
San Luis Obispo	1/5
San Mateo	1/7
Santa Barbara	1/7
Santa Clara	1/7
Santa Cruz	1/5
Shasta	1/5
Sierra	1/5
Siskiyou	1/5
Solano	1/5
Sonoma	1/5
Stanislaus	1/5
Sutter	1/5
Tehama	1/5
Trinity	1/5
Tulare	1/5
Tuolumne	1/5
Ventura	1/7
Yolo	1/5
Yuba	1/5

Table 4
NONRESIDENTIAL CONSTRUCTION VALUATION
AUTHORIZED BY PERMITS, CALIFORNIA, 1999
(Thousands of dollars)

County	Commercial	Industrial	Other	Additions and Alterations	Total
Total	**$5,706,720**	**$2,256,165**	**$2,350,196**	**$6,269,200**	**$16,582,282**
Alameda	321,753	137,499	48,956	408,531	$916,738
Alpine	572	0	677	0	$1,249
Amador	413	8,801	4,826	715	$14,755
Butte	22,076	4,727	9,027	15,160	$50,990
Calaveras	5,705	0	4,558	2,029	$12,292
Colusa	1,304	0	2,061	5,205	$8,570
Contra Costa	127,939	18,192	56,940	128,974	$332,044
Del Norte	4,035	0	1,938	1,641	$7,614
El Dorado	20,133	1,287	19,774	10,182	$51,377
Fresno	102,559	85,716	79,521	73,635	$341,431
Glenn	1,604	0	2,364	735	$4,703
Humboldt	15,079	333	4,909	10,075	$30,396
Imperial	4,860	17,889	214,449	6,090	$243,288
Inyo	6,293	0	633	929	$7,855
Kern	41,608	13,087	67,769	41,928	$164,391
Kings	8,240	16,172	5,239	7,705	$37,355
Lake	1,316	0	3,184	1,970	$6,470
Lassen	2,377	0	1,994	8,672	$13,043
Los Angeles	1,321,869	361,114	434,538	1,558,733	$3,676,254
Madera	8,759	7,094	3,219	5,380	$24,452
Marin	13,557	0	32,453	48,992	$95,002
Mariposa	251	0	2,919	213	$3,384
Mendocino	1,324	3,016	7,036	7,941	$19,317
Merced	6,572	18,168	32,804	14,929	$72,473
Modoc	429	0	791	424	$1,644
Mono	0	3,556	255	174	$3,985
Monterey	43,234	9,719	29,179	30,906	$113,037
Napa	40,660	17,302	21,101	54,408	$133,470
Nevada	3,788	957	23,173	1,556	$29,475
Orange	796,154	122,935	121,433	573,906	$1,614,428
Placer	115,943	70,186	39,050	53,656	$278,834
Plumas	0	291	341	103	$734
Riverside	255,646	112,239	117,198	126,079	$611,162
Sacramento	250,714	62,260	67,082	188,818	$568,874
San Benito	7,414	4,198	4,791	2,128	$18,531
San Bernardino	204,143	331,039	83,643	139,794	$758,619
San Diego	476,008	193,553	161,412	505,656	$1,336,629
San Francisco	147,503	0	10,247	496,970	$654,719
San Joaquin	102,711	83,970	55,706	63,128	$305,515
San Luis Obispo	29,799	12,337	22,971	27,940	$93,047
San Mateo	307,010	33,386	56,629	217,028	$614,054
Santa Barbara	46,249	18,830	31,590	45,661	$142,329
Santa Clara	431,098	282,014	113,449	1,029,389	$1,855,950
Santa Cruz	29,574	4,184	8,749	19,380	$61,886
Shasta	13,593	8,856	19,555	10,557	$52,560
Sierra	0	0	186	33	$219
Siskiyou	5,437	0	4,008	3,487	$12,931
Solano	36,011	16,605	18,729	36,208	$107,553
Sonoma	68,119	48,739	36,085	73,286	$226,230
Stanislaus	52,273	27,288	35,819	33,165	$148,545
Sutter	1,026	1,695	58,028	5,835	$66,583
Tehama	3,101	495	5,334	1,202	$10,132
Trinity	812	0	1,622	941	$3,375
Tulare	34,189	3,435	52,457	32,130	$122,212
Tuolumne	3,477	0	6,177	1,686	$11,340
Ventura	124,166	58,359	81,700	102,461	$366,685
Yolo	35,264	34,646	9,218	29,173	$108,301
Yuba	980	0	10,704	1,569	$13,253

Source: Construction Industry Research Board, http://www.cirbdata.com
Department of Finance, Economic Research Unit, (916) 322-2263, http://www.dof.ca.gov

The Report on Diesel Exhaust

This page last reviewed July 29, 2008

Findings of the Scientific Review Panel On

The Report on Diesel Exhaust

As Adopted at the Panel's April 22, 1998 Meeting

Pursuant to Health and Safety Code section 39661, the Scientific Review Panel (SRP / Panel) has reviewed the report *Proposed Identification of Diesel Exhaust as a Toxic Air Contaminant* by the staffs of the California Air Resources Board (ARB or Board) and the Office of Environmental Health Hazard Assessment (OEHHA) describing the public exposure to, and health effects of, diesel exhaust. The Panel members also reviewed the public comments received on this report.

Panel members participated in workshops devoted to discussion of the exposure and health issues associated with diesel exhaust in September 1994, January 1996, July 1997, and March 1998. The SRP reviewed the issues at its meetings in October 1997 and April 1998. A special meeting of the SRP was held on March 11, 1998, to hear testimony on health issues including the quantitative risk assessment from highly respected scientists invited by the Panel. Based on these reviews and information provided at scientific workshops and meetings, the SRP makes the following findings pursuant to Health and Safety Code section 39661:

Exposure Related Conclusions:

1. Diesel exhaust is a complex mixture of gases and fine particles emitted by a diesel-fueled internal combustion engine.
2. The gaseous fraction is composed of typical combustion gases such as nitrogen, oxygen, carbon dioxide, and water vapor. However, as a result of incomplete combustion, the gaseous fraction also contains air pollutants such as carbon monoxide, sulfur oxides, nitrogen oxides, volatile organics, alkenes, aromatic hydrocarbons, and aldehydes, such as formaldehyde and 1,3-butadiene and low-molecular weight polycyclic aromatic hydrocarbons (PAH) and PAH-derivatives.
3. One of the main characteristics of diesel exhaust is the release of particles at a markedly greater rate than from gasoline-fueled vehicles, on an equivalent fuel energy basis. The particles are mainly aggregates of spherical carbon particles coated with inorganic and organic substances. The inorganic fraction primarily consists of small solid carbon (or elemental carbon) particles ranging from 0.01 to 0.08 microns in diameter. The organic fraction consists of soluble organic compounds such as aldehydes, alkanes and alkenes, and high-molecular weight PAH and PAH-derivatives, such as nitro-PAHs. Many of these PAHs and PAH-derivatives, especially nitro-

PAHs, have been found to be potent mutagens and carcinogens. Nitro-PAH compounds can also be formed during transport through the atmosphere by reactions of adsorbed PAH with nitric acid and by gas-phase radical-initiated reactions in the presence of oxides of nitrogen.

4. Diesel exhaust includes over 40 substances that are listed by the United States Environmental Protection Agency (U.S. EPA) as hazardous air pollutants and by the ARB as toxic air contaminants. Fifteen of these substances are listed by the International Agency for Research on Cancer (IARC) as carcinogenic to humans, or as a probable or possible human carcinogen. Some of these substances are: acetaldehyde; antimony compounds; arsenic; benzene; beryllium compounds; bis(2-ethylhexyl)phthalate; dioxins and dibenzofurans; formaldehyde; inorganic lead; mercury compounds; nickel; POM (including PAHs); and styrene.

5. Almost all of the diesel particle mass is in the fine particle range of 10 microns or less in diameter (PM10). Approximately 94 percent of the mass of these particles are less than 2.5 microns in diameter. Because of their small size, these particles can be inhaled and a portion will eventually become trapped within the small airways and alveolar regions of the lung.

6. The estimated population-weighted average outdoor diesel exhaust PM10 concentration in California for 1995 is 2.2 microgram per cubic meter ($\mu g/m^3$). Several independent studies have reported similar outdoor air diesel exhaust PM10 concentrations. The 1995 estimated average indoor exposure concentration is approximately 1.5 $\mu g/m^3$.

7. The population time-weighted average total air exposure to diesel exhaust particle concentrations across all environments (including outdoors) is estimated to be 1.5 $\mu g/m^3$ in 1995. This total exposure estimate may underestimate many Californians' actual total exposure because it excludes elevated exposures near roadways, railroad tracks, and inside vehicles. Near-source exposures to diesel exhaust may be as much as five times higher than the 1995 population time-weighted average total air exposure. It also excludes other routes of exposure to diesel exhaust, such as ingestion and dermal absorption.

8. Diesel engine exhaust contains small carbonaceous particles and a large number of chemicals that are adsorbed onto these particles or present as vapors. These particles have been the subject of many studies because of their adverse effects on human health and the environment. A recent study conducted for the Health Effects Institute showed that, despite a substantial reduction in the weight of the total particulate matter, the total number of particles from a 1991-model engine was 15 to 35 times greater than the number of particles from a 1988 engine when both engines were operated without emission control devices. This suggests that more fine particles, a potential health concern, could be formed as a result of new technologies. Further study is needed since the extent of these findings only measured exhaust from two engines and engine technologies.

9. The major sources of diesel exhaust in ambient outdoor air are estimated to emit approximately 27,000 tons per year in 1995. On-road mobile sources (heavy-duty trucks, buses, light-duty cars and trucks) contribute the majority of total diesel exhaust PM10 emissions in California. Other mobile sources (mobile equipment, ships, trains, and boats) and stationary sources contribute the remaining emissions.

10. Significant progress has been made as a result of federal and state regulations that have addressed particulate matter levels from diesel engines. Emissions of on-road mobile source diesel exhaust PM10 in California are expected to decline by approximately 85 percent from 1990 to 2010 as a result of mobile source regulations already adopted by the ARB.

11. The results of a study funded by the ARB at the University of California, Riverside, indicate that the diesel exhaust from the new fuel tested contained the same toxic air contaminants as the old fuel, although their concentrations and other components may differ. Further research would be

helpful to quantify the amounts of specific compounds emitted from a variety of engine technologies, operating cycles, and fuel to characterize better any differences between old and new fuels and technologies.

Health Effects Associated with Diesel Exhaust:

12. A number of adverse short-term health effects have been associated with exposures to diesel exhaust. Occupational exposures to diesel exhaust particles have been associated with significant cross-shift decreases in lung function. Increased cough, labored breathing, chest tightness, and wheezing have been associated with exposure to diesel exhaust in bus garage workers. A significant increase in airway resistance and increases in eye and nasal irritation were observed in human volunteers following one-hour chamber exposure to diesel exhaust. In acute or subchronic animal studies, exposure to diesel exhaust particles induced inflammatory airway changes, lung function changes, and increased the animals' susceptibility to infection.

13. A number of adverse long-term noncancer effects have been associated with exposure to diesel exhaust. Occupational studies have shown that there may be a greater incidence of cough, phlegm and chronic bronchitis among those exposed to diesel exhaust than among those not exposed. Reductions in pulmonary function have also been reported following occupational exposures in chronic studies. Reduced pulmonary function was noted in monkeys during long-term exposure. Histopathological changes in the lung of diesel-exposed test animals reflect inflammation of the lung tissue. These changes include dose-dependent proliferations of Type II epithelial cells, marked infiltration of macrophages, plasma cells and fibroblasts into the alveolar septa, thickening of the alveolar walls, alveolar proteinosis, and focal fibrosis.

14. Studies have shown that diesel exhaust particles can induce immunological reactions and localized inflammatory responses in humans, as well as acting as an adjuvant for pollen allergy. Intranasal challenge with diesel exhaust particles in human volunteers resulted in increased nasal IgE antibody production and a significant increase in mRNA for pro-inflammatory cytokines. Co-exposure to diesel exhaust particles and ragweed pollen resulted in a nasal IgE response greater than that following pollen or diesel exhaust particles alone. Effects of intratracheal, intranasal, and inhalation exposures of laboratory animals are supportive of the findings in humans. These effects include eosinophilic infiltration into bronchi and bronchioles, elevated IgE response, increased mucus secretion and respiratory resistance, and airway constriction.

15. Based on the animal studies, the U.S. EPA determined a chronic inhalation Reference Concentration value of 5 $\mu g/m^3$ for noncancer effects of diesel exhaust. This estimate takes into consideration persons who may be more sensitive than others to the effects of diesel exhaust. The report supports the recommendation of 5 $\mu g/m^3$ as the California Reference Exposure Level (REL) (Table 1). It should be noted that this REL may need to be lowered further as more data emerge on potential adverse noncancer effects from diesel exhaust.

16. Diesel exhaust contains genotoxic compounds in both the vapor phase and the particle phase. Diesel exhaust particles or extracts of diesel exhaust particles are mutagenic in bacteria and in mammalian cell systems, and can induce chromosomal aberrations, aneuploidy, and sister chromatid exchange in rodents and in human cells *in vitro*. Diesel exhaust particles induced unscheduled DNA synthesis *in vitro* in mammalian cells. DNA adducts have been isolated from calf thymus DNA *in vitro* following treatment with diesel exhaust particle extracts. DNA adducts have been shown to increase following inhalation exposure of rodents and monkeys to whole diesel exhaust. Elevated levels of DNA adducts have been associated with occupational exposure to diesel exhaust. Results of inhalation bioassays in the rat, and with lesser certainty

in mice, have demonstrated the carcinogenicity of diesel exhaust in test animals, although the mechanisms by which diesel exhaust induces lung tumors in animals remains uncertain.

17. Over 30 human epidemiological studies have investigated the potential carcinogenicity of diesel exhaust. These studies, on average, found that long-term occupational exposures to diesel exhaust were associated with a 40 percent increase in the relative risk of lung cancer. The lung cancer findings are consistent and the association is unlikely to be due to chance. These epidemiological studies strongly suggest a causal relationship between occupational diesel exhaust exposure and lung cancer.

18. Other agencies or scientific bodies have evaluated the health effects of diesel exhaust. The National Institute of Occupational Safety and Health first recommended in 1988 that whole diesel exhaust be regarded as a potential occupational carcinogen based upon animal and human evidence. The International Agency for Research on Cancer (IARC) concluded that diesel engine exhaust is probably carcinogenic to humans and classified diesel exhaust in Group 2A. Based upon the IARC findings, in 1990, the State of California under the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65) identified diesel exhaust as a chemical "known to the State to cause cancer." The U.S. EPA has proposed a conclusion similar to IARC in their draft documents. The 1998 draft U.S. EPA document concluded similarly that there was sufficient animal evidence of carcinogenicity and that the human evidence was limited.

19. There are data from human epidemiological studies of occupationally exposed populations which are useful for quantitative risk assessment. The estimated range of lung cancer risk (upper 95% confidence interval) based on human epidemiological data is 1.3×10^{-4} to 2.4×10^{-3} $(\mu g/m^3)^{-1}$ (Table 2). After considering the results of the meta-analysis of human studies, as well as the detailed analysis of railroad workers, the SRP concludes that 3×10^{-4} $(\mu g/m^3)^{-1}$ is a reasonable estimate of unit risk expressed in terms of diesel particulate. Thus this unit risk value was derived from two separate approaches which yield similar results. A comparison of estimates of risk can be found in Table 3.

20. Based on available scientific information, a level of diesel exhaust exposure below which no carcinogenic effects are anticipated has not been identified.

21. Based on available scientific evidence, as well as the results of the risk assessment, we conclude that diesel exhaust be identified as a Toxic Air Contaminant.

22. As with other substances evaluated by this Panel and after reviewing the field of published peer reviewed research studies on diesel exhaust, additional research is appropriate to clarify further the health effects of diesel exhaust. This research may have significance for estimating the unit risk value.

23. The Panel, after careful review of the February 1998 draft SRP version of the ARB report, *Proposed Identification of Diesel Exhaust as a Toxic Air Contaminant*, as well as the scientific procedures and methods used to support the data, the data itself, and the conclusions and assessments on which the Report is based, finds this report with the changes specified during our October 16, 1997, meeting and as a result of comments made at the March 11, 1998, meeting, is based upon sound scientific knowledge, methods, and practices and represents a complete and balanced assessment of our current scientific understanding.

For these reasons, we agree with the science presented in Part A by ARB and Part B by OEHHA in the report on diesel exhaust and the ARB staff recommendation to its Board that diesel exhaust be listed by the ARB as a Toxic Air Contaminant.

Comment Letter I14

I certify that the above is a true and correct copy of the findings adopted by the Scientific Review Panel on April 22, 1998.

Sincerely,
/s/
John R. Froines, Ph.D.
Acting Chairman
Scientific Review Panel

TABLE 1

NONCANCER HEALTH VALUES APPROVED BY THE

SCIENTIFIC REVIEW PANEL

1998

Compound	Health Value	End Point
Acetaldehyde	9 $\mu g/m^3$	Respiratory System
Diesel Exhaust	**5 $\mu g/m^3$**	**Respiratory System**
Inorganic Lead	4.6×10^{-4} ($\mu g/m^3)^{-1}$	Cardiovascular Mortality
Perchloroethylene	35 $\mu g/m^3$	Alimentary System (Liver)
$\mu g/m^3$: Microgram Per Cubic Meter		

TABLE 2

CANCER POTENCIES APPROVED BY THE SCIENTIFIC REVIEW PANEL

FROM 1984 TO 1998

(In Order of Cancer Potency)

Compound	Unit Risk $(\mu g/m^3)^{-1}$	Range $(\mu g/m^3)^{-1}$
Dioxins	3.8×10^{1}	2.4×10^{1} to 3.8×10^{1}
Chromium VI	1.5×10^{-1}	1.2×10^{-2} to 1.5×10^{-1}
Cadmium	4.2×10^{-3}	2.0×10^{-3} to 1.2×10^{-2}
Inorganic Arsenic	3.3×10^{-3}	6.3×10^{-4} to 1.3×10^{-2}
Benzo[a]pyrene	1.1×10^{-3}	1.1×10^{-3} to 3.3×10^{-3}
Diesel Exhaust	**3×10^{-4}**	**1.3×10^{-4} to 2.4×10^{-3}**
Nickel	2.6×10^{-4}	2.1×10^{-4} to 3.7×10^{-3}
1,3-Butadiene	1.7×10^{-4}	4.4×10^{-6} to 3.6×10^{-4}
Ethylene Oxide	8.8×10^{-5}	6.1×10^{-5} to 8.8×10^{-5}
Vinyl Chloride	7.8×10^{-5}	9.8×10^{-6} to 7.8×10^{-5}
Ethylene Dibromide	7.1×10^{-5}	1.3×10^{-5} to 7.1×10^{-5}
Carbon Tetrachloride	4.2×10^{-5}	1.0×10^{-5} to 4.2×10^{-5}
Benzene	2.9×10^{-5}	7.5×10^{-6} to 5.3×10^{-5}
Ethylene Dichloride	2.2×10^{-5}	1.3×10^{-5} to 2.2×10^{-5}
Inorganic Lead	1.2×10^{-5}	1.2×10^{-5} to 6.5×10^{-5}
Perchloroethylene	5.9×10^{-6}	3.0×10^{-7} to 1.1×10^{-5}
Formaldehyde	6.0×10^{-6}	2.5×10^{-7} to 3.3×10^{-5}
	5.3×10^{-6}	6.0×10^{-7} to 2.0×10^{-5}

Chloroform		
Acetaldehyde	2.7×10^{-6}	9.7×10^{-7} to 2.7×10^{-5}
Trichloroethylene	2.0×10^{-6}	8.0×10^{-7} to 1.0×10^{-5}
Methylene Chloride	1.0×10^{-6}	3.0×10^{-7} to 3.0×10^{-6}
Asbestos	1.9×10^{-4} (per 100 fiber/m^3)	Lung: 11 - 110 x 10^{-6} (per 100 fiber/m^3) Mesothelioma: 38 - 190 x 10^{-6} (per 100 fiber/m^3)
$\mu g/m^3$: Microgram Per Cubic Meter		

TABLE 3

COMPARISON OF OTHER ORGANIZATIONS' ESTIMATED 95 PERCENT UPPER CONFIDENCE LIMITS

OF LIFETIME RISK PER $\mu g/m^3$ DIESEL PARTICULATE MATTER FROM RISK ASSESSMENTS BASED ON EPIDEMIOLOGIC DATA WITH OEHHA ESTIMATES

Method	Unit Risk / Range	Basis of Assessment	Reference
Epidemiologic Analysis	3×10^{-4}	Based on Smoking-Adjusted Pooled RR	Smith, 1998
Epidemiologic Analysis[b]	**3.6×10^{-4} to 2.4×10^{-3}**	**Case-Control Study of Garshick et al., 1987**	**OEHHA, Part B, Section 7.3.3**
Epidemiologic Analysis	**2.8×10^{-4} to 1.8×10^{-3}**	**Cohort Study of Garshick et al., 1988**	**OEHHA, Part B, Section 7.3.4**
Epidemiologic Analysis	**1.3 to 7.2×10^{-4}**	**Cohort Study, Time Varying Conc., Roof (3,50) Pattern**	**OEHHA, Part B, Appendix D**
Epidemiologic Analysis	**3.8×10^{-4} to 1.9×10^{-3}**	**Cohort Study, Time Varying Conc., Ramp (1,50) Pattern**	**OEHHA, Part B, Appendix D**
Epidemiologic Analysis	1.4×10^{-3}	London Transport Study[c]	Harris, 1983

Epidemiologic Analysis	2×10^{-3}	Epidemiologic Data of Garshick (Top End of U.S. EPA's Range)	U.S. EPA, 1998
Epidemiologic Analysis	1.3×10^{-4} to 1.3×10^{-2}	Using Smoking-Adjusted RR and Exposures of 5 or 500 $\mu g/m^3$	OEHHA, Part B, Section 7.3; Bracketed Risk Bounds

a) Bolded values are included in OEHHA's range of risk.

b) Obtained by applying Harris' slope of 5×10^{-4} ($\mu g/m^3 \times yr)^{-1}$ to California life table.

Air Toxics Program
Particulate Emissions from Diesel-Fueled Engines as a TAC
Toxic Emisisons from Diesel-Fueled Engines

Cleaner Diesel Handbook

BRING CLEANER FUEL AND DIESEL RETROFITS INTO YOUR NEIGHBORHOOD

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Comment Letter I14

Cleaner Diesel Handbook

BRING CLEANER FUEL AND DIESEL RETROFITS INTO YOUR NEIGHBORHOOD

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Executive summary

Cost-effective steps to reducing diesel pollution

Environmental Defense's *Cleaner Diesel Handbook* is designed to empower the private sector, public officials and ordinary citizens with the means to reduce harmful pollution from diesel engines. This handbook focuses on methods of reducing pollution created by diesel engines, especially those used in construction and other nonroad sectors. The nonroad sector includes vehicles not typically found on roads, such as agricultural equipment, locomotives, ferries, snowmobiles and airplanes. Construction equipment is part of the nonroad sector. Collectively, nonroad engines discharge more dangerous fine sooty particles than any other source in the transportation sector. The solutions described here can reduce these harmful emissions by up to 90% and are a cost-effective response to the challenge of improving local air quality.

The health imperative: half of Americans live with unhealthy air

Diesel engines emit nearly 40 toxic substances, smog-forming oxides of nitrogen and fine particulate matter, and they contribute to a laundry list of adverse health effects including: asthma, cardiovascular and respiratory problems, strokes, heart attacks, lung cancer and premature death. Diesel exhaust is estimated to contribute to more than 75% of the added cancer risk from air toxics in the United States. Of special concern are two main pollutants: fine particulate matter, which lodges deep in the lungs, and oxides of nitrogen (NO_x), which are precursors to smog. Both can be reduced substantially with the tools described in this handbook.

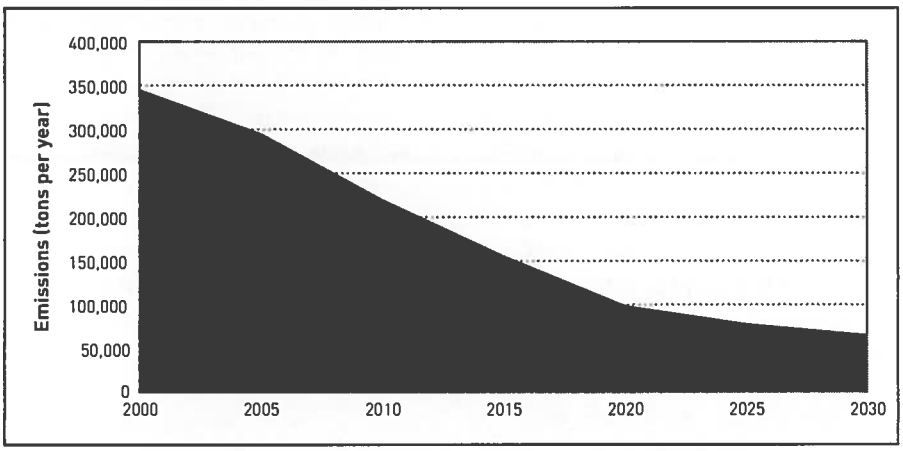
Recent data from the U.S. Environmental Protection Agency (EPA) shows that about half of all Americans live in places that fail to meet basic health standards for ozone (smog), fine particulates (soot) or both. On April 15, 2004, EPA found 474 counties—home to 159 million Americans—out of full compliance with the health-based eight-hour ozone standard. NO_x is a significant precursor in the formation of ground-level ozone and nonroad engines, as a vehicle class, emit almost one-fifth (more than 4 million tons) of the total national NO_x emissions from all sources.

As of April 2005, EPA classified 208 counties spanning 20 states as being out of full compliance with the health-based fine particulate ($PM_{2.5}$) standard. More than 57 million Americans live in counties that are not meeting the health-based particulate pollution standard. For the states and local communities that are struggling to trim every possible ton of pollution to meet federal health-based air quality standards and protect the health of their community, reducing pollution from existing diesel vehicles and equipment now is vitally important.

Cleaner air: bridging the 25-year gap

On May 10, 2004, EPA announced new air pollution regulations that will significantly lower pollution from new nonroad diesel engines used in construction, agriculture, manufacturing and services. As old diesel equipment is replaced over the coming years, this rule will deliver important public health benefits to communities across America. But the full pollution reductions and

FIGURE 1
Particulate pollution under phase-in of federal standards for diesel trucks, buses, and machinery



National $PM_{2.5}$ emissions under phase-in of federal standards for onroad diesel trucks and buses, and nonroad diesel equipment. (Estimated from EPA, 2000 and EPA, 2004a)

public health benefits of this rule will not be realized for more than 20 years due to the lag in time before the emissions standards come into effect and because of the long life spans of heavy-duty diesel engines. Many nonroad engines, like those used on construction or marine vehicles, may have life spans of several decades. A child born today may still be breathing soot from a backhoe in her neighborhood when she graduates from college—unless that backhoe is replaced with a clean one or retrofit with emissions controls.

Figure 1 shows national particulate pollution under the phase-in of the federal emissions standards for diesel trucks, buses and nonroad machinery.

While the health benefits from full implementation of EPA national diesel emissions standards are extremely important, the incremental phase-in of these benefits indicates that thousands of premature deaths each year could be prevented by speeding the cleanup of diesel engines. The shaded area under the curve represents the pollution a retrofit program could prevent.

Cost-effective diesel pollution reduction

This handbook demonstrates that cleaning up diesel engines is a cost-effective way to reduce the adverse health effects of diesel pollution and outlines some simple steps, like enforcing idling laws and using clean fuels—like ultra-low sulfur diesel (ULSD)—with best available retrofit technologies that can cut diesel emissions by up to 90%.

The three "Rs" of emissions reduction

Repower. Replace the engine, or entire vehicle, with newer, cleaner technologies that meet or exceed EPA's newest standards and/or uses alternative fuels.
Refuel. Alternative fuels, ultra-low sulfur diesel fuel and other clean fuels or additives are important first steps.
Retrofit. Reduce diesel exhaust with best available pollution control technology.

The handbook describes the "3Rs" of engine operations, as well as the use of best practices in equipment management. It gives particular attention to the subjects of cleaner fuels and retrofit technologies. The main goal is to reduce emissions of both fine particulate matter and NO_x. Appendices to the handbook will include some information on the manufacturers of retrofit technology and distributors of cleaner fuels. Together, this information is meant to serve as a starting point for anyone seeking to cut harmful diesel pollution.

Right now, there are a variety of cleaner fuels and demonstrated retrofit technologies available to reduce emissions of particulate matter (PM), oxides of nitrogen (NO_x), hydrocarbons (HC), carbon monoxide (CO), smoke and odor from existing diesel engines. It is important to remember that not all technologies and fuels target the same pollutants, and that appropriate technologies or fuels may vary in different contexts. Generally, a combination of multiple technologies and emissions control strategies is necessary for maximum emissions reduction.

In addition to describing the tools available for diesel pollution reduction, this handbook examines a variety of methods for implementing successful retrofit programs. The handbook provides examples of successful programs such as government and private sector efforts, contract specifications, voluntary retrofit programs, and economic or market incentive programs that provide financial support for cleaner technology or fuels.

Ultimately, the handbook demonstrates the need to reduce diesel engine emissions and presents the means to design and implement measures to clean up diesel technology. Together, these tools can be used to build a successful retrofit program in any community.

CHAPTER 1

Introduction: achieving cleaner, healthier air today

Science is very clear that air pollution from diesel engines endangers human health. Fortunately, cost-effective and practical technologies exist to substantially reduce diesel pollution. Across the country, we find successful diesel emissions-reduction programs, from school buses and trucks to construction equipment and ferries. Such programs can cut diesel pollution from targeted fleets by up to 90%. Yet far too many communities still have not taken advantage of these opportunities to win healthier air. This handbook is a guide to how to bring that success to your community, your company and your local government.

The purpose of this handbook is to provide practical information for decision-makers in the public and private sectors to use in creating and implementing effective emissions-reduction projects for construction and other nonroad diesel fleets.[1] Because the nonroad sector is so dirty, and because the emissions-reduction solutions are not yet widely disseminated for this sector, this handbook focuses attention on construction fleets and other nonroad applications. The handbook's basic concepts, however, are applicable across the diesel sector.

This handbook sets forth:

- the health imperative for reducing diesel pollution today;
- an overview of technologies and fuels that can reduce diesel pollution, with detailed follow-up information;
- information about successful retrofit programs;
- examples of contract specifications and other incentives for cleaning diesel engines.

Together, these tools can be used by any citizen concerned about diesel pollution to inform local policymakers and contractors about the benefits of, and the steps involved in, implementing a successful retrofit program.

This handbook focuses on how to reduce pollution from vehicles, engines and equipment used for construction. Construction vehicles are classified as "mobile sources" because they move. Mobile sources are divided into the "onroad" and "nonroad" sectors. The onroad sector includes vehicles used on roads for transportation of passengers or freight.

The nonroad sector includes vehicles that are not typically found on roads, such as agricultural equipment, locomotives, ferries, snowmobiles and airplanes. Construction equipment is part of the nonroad sector. However, the technologies, fuels, and techniques found herein are frequently applicable across the diesel sector (onroad engines and other nonroad engines) as well. For more information, visit the EPA Mobile Source web site at: http://www.epa.gov/otaq/invntory/overview/examples.htm.

Since 1996, EPA has required new nonroad diesel engines to meet specific emissions levels. Until 1996, those standards were not very strong, and as a result they allowed for high levels of pollution. On May 10, 2004, EPA announced air pollution regulations that will lower pollution from *new* nonroad diesel engines used in construction, agriculture, manufacturing and services by more than 90%.

To meet this rigorous emissions standard, EPA requires a combination of cleaner engines, pollution control technology and cleaner fuel. Based on

EPA estimates, when the full inventory of older nonroad engines has been replaced, the nonroad diesel program will annually prevent up to 12,000 premature deaths, one million lost work days, 15,000 heart attacks and 6,000 children's asthma-related emergency room visits.[2] According to EPA, the overall benefits of the nonroad diesel program outweigh the costs by a ratio of 40 to 1.[3]

But the full pollution reduction and public health benefits of the nonroad rule will not be realized for more than 20 years due to the lag in time before the emissions standards come into effect and because of the long life spans of heavy-duty diesel engines. EPA estimates that by 2030 the entire inventory of nonroad vehicles covered by this new rule should be upgraded.[4]

Given that nonroad engines remain in use for a very long time, even decades, strategies to retrofit existing machinery and the use of ultra-low sulfur diesel (ULSD) fuel are extremely important to win public health gains now. Figure 1 (page v) shows the national particulate pollution under the phase-in of the federal emissions standards for diesel trucks and buses, and nonroad machinery.

The public health benefits will likewise be phased in over time. EPA estimates, for example, that only about 30% of the ultimate level of annual benefits under its recently announced standards for nonroad diesel engines will be realized by 2015; just over 50% will be realized by 2020. While the health benefits from full implementation of EPA national diesel emissions standards are extremely important, the incremental phase-in of these benefits indicates that thousands of premature deaths each year, occurring now, could be prevented by accelerating the cleanup of diesel engines.

Right now, there are a variety of demonstrated retrofit technologies available to reduce particulate matter (PM), oxides of nitrogen (NO_x), hydrocarbon (HC), carbon monoxide (CO), smoke and odor created by existing diesel engines. Therefore, programs to reduce pollution from existing diesel engines are critical. This handbook explores a variety of methods for implementing successful retrofit programs.

ENVIRONMENTAL DEFENSE

Children are particularly vulnerable to the harmful health effects of diesel exhaust.

CHAPTER 2

The dangers of diesel emissions

According to recent EPA data, about half of all Americans now live in counties that fail to meet basic healthy air standards. On April 15, 2004, EPA found 474 counties, home to 159 million Americans, out of full compliance with the health-based eight-hour ozone standard.[5] In April 2005, EPA also found 208 counties representing more than 57 million Americans out of full compliance with the health-based particulate pollution standard.[6]

For the states and local communities that are struggling to trim every possible ton of pollution to meet federal health-based air quality standards, reducing pollution from existing diesel vehicles and equipment now is vitally important. Retrofits and the use of clean fuels are one of the most cost-effective ways to reduce diesel emissions and restore healthy air.

Diesel engines, including the construction engines that are the focus of this handbook, emit nearly 40 toxic substances (Table 1), smog-forming oxides of nitrogen and fine particulate matter ($PM_{2.5}$), which can penetrate the lungs and enter the bloodstream. Due to their small size, particulates are easily inhaled and reach deep into the lungs where they can trigger an inflammatory response. Exposure to particulate matter is associated with heart attacks, irregular heartbeat, asthma attacks, reduced lung function and bronchitis.

Several organizations, including EPA, have designated diesel exhaust as a probable or potential human carcinogen (Table 2). It is estimated that diesel exhaust contributes more than 70% of the cancer risk from air toxics in the United States.[7] Diesel emissions are also estimated to be the hazardous air pollutant with the highest contribution to cancer risk in many areas across the country;[8] according to Environmental Defense's Scorecard, this is true in New York, Los Angeles, Houston, Denver, Chicago and Atlanta.[9]

Smog-forming nitrogen oxides

Nitrogen oxides (NO_x) and volatile organic compounds (VOCs) that are created by diesel exhaust are precursors to ground-level ozone, or smog. Non-road engines, as a vehicle class, also emit more than 4 million tons of NO_x each year—this is approximately 19% of the total national NO_x emissions from all sources (22,349,000 tons).[10] As well as being significant contributors to ground-level ozone or smog, nitrogen oxides are also significant contributors to acid deposition, eutrophication of coastal bodies of water, fine particulate emissions and haze.

Fine particulate matter

There is a well-researched body of epidemiological studies from around the world that documents the serious threats associated with exposure to $PM_{2.5}$. These studies have linked $PM_{2.5}$ to adverse health effects, such as asthma, cardiovascular and respiratory problems, strokes, heart attacks[11] and lower birth weight[12] leading to increased use of asthma medications, doctor visits, emergency room visits, hospital admissions, school absenteeism and premature death.[13] Researchers estimate that as many as 60,000 Americans die prematurely each year because of exposure to fine particles.[14] Children, the elderly and the ill are particularly vulnerable. National $PM_{2.5}$ emissions from mobile sources totaled approximately 452,000 short

tons in 2001. Nonroad vehicles created the majority of those emissions, 64%, and almost 50% of total $PM_{2.5}$ emissions originated from nonroad diesel sources (221,000 short tons). Construction and surface mining equipment was the largest contributor (30%) to nonroad diesel source $PM_{2.5}$ emissions.

Asthma

People working at and living near construction sites are especially affected by nonroad vehicles' emissions. In urban areas, overall asthma prevalence has increased dramatically over the past two decades, rising 75% between 1980 and the average in 1993–4. While the highest prevalence of asthma is in children ages 5 to 14, the greatest increase in asthma prevalence has occurred in children ages 0 to 4 which increased 160% over the 15-year period.[15] For example, New York City residents suffer from alarmingly high asthma rates (1 out of every 8 adults has been diagnosed with asthma at some point in their lives[16]) and New York City air fails to meet many basic health standards. To learn about air quality conditions in your area, visit Environmental Defense's Scorecard web site at: http://www.scorecard.org/.

TABLE 1
Toxic air contaminants and hazardous air pollutants found in diesel exhaust

Acetaldehyde*	Chlorine	Methyl ethyl ketone
Acrolein	Chlorobenzene	Naphthalene*
Aluminum	Chromium compounds*	Nickel*
Ammonia	Cobalt compounds*	4-nitrobiphenyl*
Aniline*	Copper	Phenol
Antimony compounds*	Cresol	Phosphorus
Arsenic*	Cyanide compounds	POM (including PAHs)
Barium	Dibenzofuran	Propionaldehyde
Benzene*	Dibutylphthalate compounds*	Selenium
Beryllium compounds*	Ethyl benzene	Silver
Biphenyl	Formaldehyde*	Styrene*
Bis (2-ethylhexyl) phthalate*	Hexane	Sulfuric acid
Bromine	Lead compounds*	Toluene*
1,3-butadiene*	Manganese compounds	Xylene isomers and mixtures
Cadmium*	Mercury compounds*	Zinc
Chlorinated dioxins*	Methanol	

*This compound or class of compounds is known by the state of California to cause cancer or reproductive toxicity. See California EPA, Office of Environmental Health Hazard Assessment, "Chemicals Known to the State to Cause Cancer or Reproductive Toxicity," May 31, 2002.

Note: Toxic air contaminants on this list either have been identified in diesel exhaust or are presumed to be in the exhaust, based on observed chemical reactions or presence in the fuel or oil. See California Air Resources Board, "Toxic Air Contaminant Identification List Summaries, Diesel Exhaust," September 1997, available online at http://www.arb.ca.gov/toxics/tac/factshts/diesex.pdf.

TABLE 2
History of determinations of the carcinogenicity of diesel exhaust

Year	Agency	Determination
1988	National Institute for Occupational Safety and Health (NIOSH)	Potential occupational carcinogen
1989	International Agency for Research on Cancer (IARC)	Probable human carcinogen
1990	State of California (under provisions of Proposition 65)	Known by the state to cause cancer
1995	Health Effects Institute (HEI)	Potential to cause cancer
1996	World Health Organization International Programme on Chemical Safety (WHO-IPCS)	Probable human carcinogen
1998	California Air Resources Board (CARB)	Toxic air contaminant (determination based substantially on the cancer risk to humans)
2000	U.S. Department of Health and Human Services National Toxicology Program (U.S. DHHS/NTP)	Reasonably anticipated to be human carcinogen
2001	American Council of Government Industrial Hygienists (ACGIH) (proposed)	Suspected human carcinogen
2002	U.S. Environmental Protection Agency (EPA)	Probable human carcinogen

Sources:

National Institute for Occupational Safety and Health, "Carcinogenic Effects of Exposure to Diesel Exhaust," Current Intelligence Bulletin 50. August 1988. Available online at http://www.cdc.gov/niosh/88116_50.html . Last accessed August 13, 2004.

International Agency for Research on Cancer (IARC), Diesel and Gasoline Engine Exhausts and Some Nitroarenes. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, no. 46 (Lyons: World Health Organization, 1989), pp. 41-185.

California Environmental Protection Agency, Chemicals Known to the State to Cause Cancer or Reproductive Toxicity (Proposition 65, 1997), revised May 31, 2002.

Health Effects Institute, Diesel Exhaust: A Critical Analysis of Emissions, Exposure and Health Effects. Cambridge, MA: Health Effects Institute, 1995. Online resource, available at: http://www.healtheffects.org/Pubs/diesum.htm Last accessed on August 13, 2004.

American Conference of Governmental Industrial Hygienists, "Documentation of the Threshold Limit Values and Biological Exposure Limits, Notice of Intended Changes," 2001.

International Programme on Chemical Safety, World Health Organization, "Diesel Fuel and Exhaust Emissions," Environmental Health Criteria 171 (1996).

"The Toxic Air Contaminant Identification Process: Toxic Air Contaminant Emissions from Diesel-fueled Engines," fact sheet. Online resource, available at: http://www.arb.ca.gov/toxics/dieseltac/factsht1.pdf Last accessed on August 13, 2004.

U.S. Environmental Protection Agency, Draft Health Assessment Document for Diesel Exhaust, July 2000, EPA/600/8-90/057E.

California Air Resources Board, "Statewide Portable Equipment Registration Program." Online resource, available at: http://www.arb.ca.gov/perp/perp.htm Last accessed on August 13, 2004.

FIGURE 2
National NO_x emissions by source category, 2001 (22.3 million short tons)

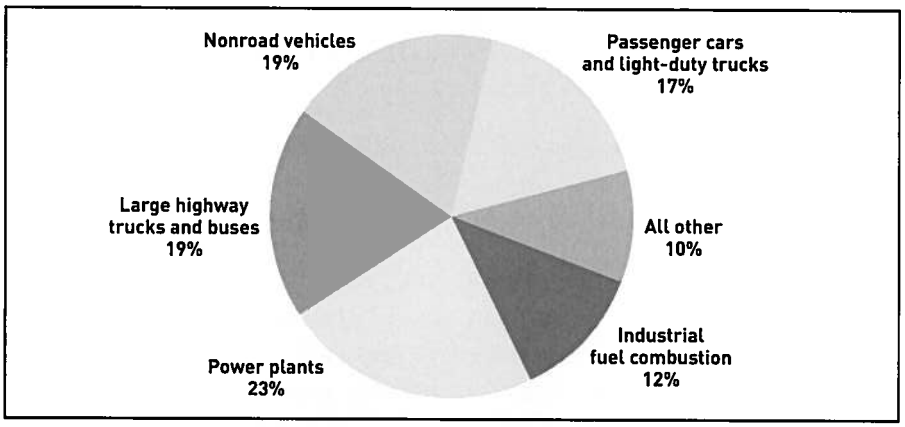
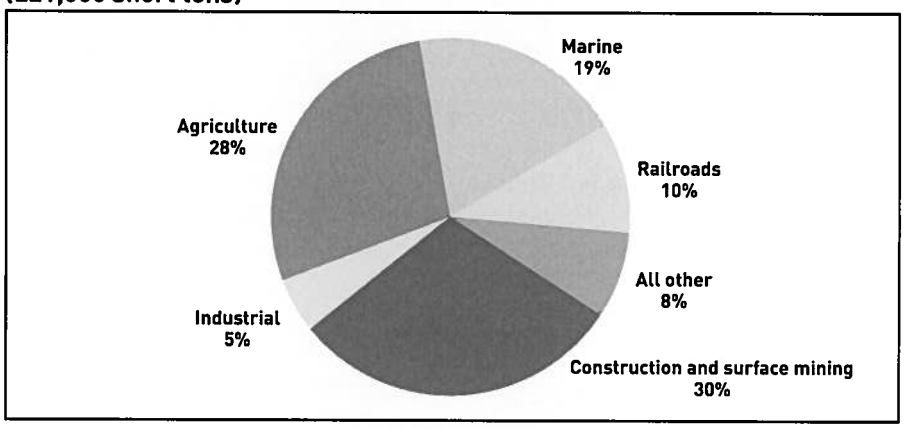
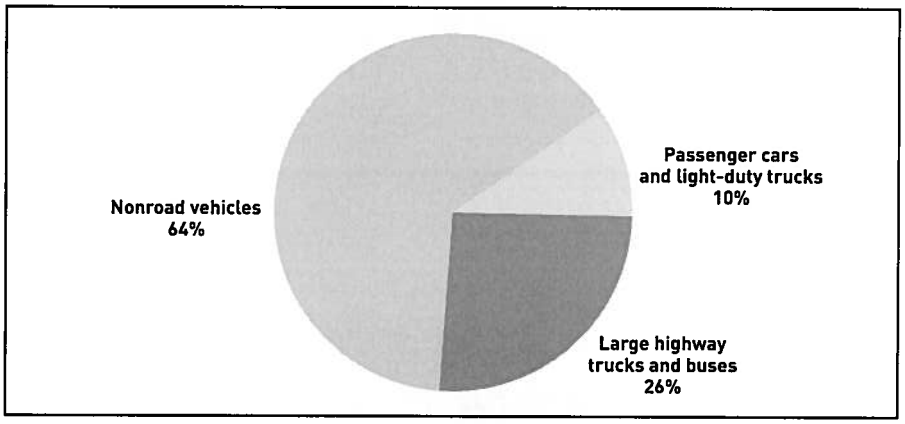


FIGURE 3
National $PM_{2.5}$ emissions from all nonroad diesel sources, 2001 (221,000 short tons)



Source (Figures 2, 3, 4): National Emission Inventory (NEI): Air Pollutant Emission Trends. 1999 Online resource, available at: http://www.epa.gov/ttn/chief/net/1999inventory.html Last accessed 03/01/05.

FIGURE 4
National $PM_{2.5}$ emissions from all mobile sources, 2001 (452,000 short tons)



CHAPTER 3

Cost-effective ways to reduce health threats

There are many options for reducing pollution from diesel engines in use today. This section describes, first, the "3 R's" for cleaning up diesel engines and, second, behavioral solutions that can help reduce pollution from diesel exhaust. For existing engines, our goal is to substantially reduce pollution today and, as soon as feasible, bring the pollution level down so that it is at least equivalent to the standards for new engines. Until old engines have been replaced with new and regulated technology, these measures are a cost-effective means of reducing diesel pollution.

A systems approach is the most effective way to curb diesel engine pollution. A systems approach takes into account all aspects of engine operations—from fuel type used, to retrofit technologies, to best practices such as anti-idling and proper maintenance practices—all of which are discussed in detail in the next few chapters of the handbook.

Fleet operators should note that, before undertaking any engine modifications, they should determine what effects retrofitting may have on equipment warranties and resolve any issues. Major engine manufacturers have now issued letters and other guidance with respect to warranty implications of cleaner fuels and retrofits, and "in most cases, engine manufacturers will continue to honor engine warranties if emissions control systems are sized, installed and maintained properly."[17]

The "3 R's" for cleaning up diesel engines

The "3 R's" listed below can be used to substantially reduce air pollutant emissions from construction equipment. Environmental Defense strongly encourages combinations of the 3 R's in order to maximize emissions reductions. Neither repowering nor refueling alone can achieve the PM reductions that a retrofit can and, similarly, retrofitting alone cannot achieve the NO_x reductions that many repowers can. Repowering or replacing in addition to retrofitting can maximize reductions in PM and NO_x pollution. In addition, refueling with ULSD fuel can result in even more reductions.

1. REPOWER (OR REPLACE)

One way of ensuring emissions reductions is to replace an entire piece of old construction equipment with a model that meets EPA 2008 standards. Another, less costly, strategy to reduce emissions from older, higher-polluting equipment is the replacement of the in-use engine (i.e., repower) with an emissions-certified engine instead of rebuilding the existing engine to its original specifications. Significant NO_x and PM benefits may be achievable due to the high emissions levels of the uncontrolled engine being replaced.

Depending on the engine and rating of older, higher polluting equipment, average emissions reductions may vary from 25% up to 75%.[18] In some instances, higher emissions reductions may be achievable. For example, replacing a 475 horsepower engine in a MY 1975–1986 Caterpillar 631-D Scraper with a Caterpillar engine meeting EPA Tier One standards[19] would produce a 40% reduction in NO_x and a 62% reduction in PM. Replacing the same engine with one meeting Tier Two standards would produce a 62% reduction in NO_x and an 81% reduction in PM.[20] It is important to note, that while

Environmental Defense strongly encourages repowering where possible, there are significant technical issues that may make it impossible for some older, higher polluting engines (Tier 0 and Tier 1) to be repowered with newer, cleaner engines (Tier 2 and Tier 3).

2. REFUEL

Using alternative fuels or cleaner petroleum-based fuels can also help reduce diesel engine pollution. Alternative fuels are defined in this handbook as any fuel other than petroleum-based fuels such as gasoline or diesel fuel. Emissions reductions can also be achieved by using diesel fuels with very low levels of sulfur, for example ULSD with a maximum sulfur content of 15 parts per million. Fuel emulsifiers, or fuel-borne catalysts are fuel additives that can be added to ULSD to cut emissions even further. In many cases, use of ULSD at 15 parts per million (ppm) of sulfur or less is a prerequisite to effective use of advanced retrofit technologies. Generally, it is not the fuel itself that is "clean", it is the engineered system (i.e. fuel, combustion engineering and exhaust after-treatment). Therefore, to achieve the greatest emissions reductions, a combination of repowered or replaced engines, retrofit technology and cleaner fuels must be used.

3. RETROFIT

"Retrofitting" is incorporating a device into a piece of diesel equipment to reduce pollution.[21] A wide range of pollution-control, or "retrofit" technologies exist today, and can be used in combination with each other and with cleaner fuels to achieve powerful emissions reductions. Different technologies fit different engine operating needs—the key is to select the combination that achieves maximum clean air benefits for a given machine and use.

For example, a retrofit could be a Diesel Particulate Filter (DPF), which traps particles from engine exhaust until the trap becomes loaded to the point that a regeneration cycle is implemented to burn off the trapped particulate matter.[22] DPFs are normally built with a porous ceramic, metal mesh or silicon

ENVIRONMENTAL DEFENSE

A delivery of ultra low sulfur diesel fuel to New York's World Trade Center site. In late 2006, ULSD will be widely available across the United States.

carbide filter housed in a metal container similar to a muffler. However, DPFs are just one of many technologies available to retrofit diesel engines, and many of these technologies serve different in-use functions. There are other examples of retrofit technologies, in addition to more detail about DPFs, in other sections of this handbook.

A combination of clean fuels and retrofits can reduce some hazardous diesel emissions by up to 90%, improving both environmental conditions and public health. Retrofits are remarkably cost-effective when compared to other means of reducing air pollution. For example, the average cost for most applications of a diesel oxidation catalyst (DOC) is approximately $2,500[23] (excluding installation) and for a DPF between $7,000–12,000[24] (excluding installation). The California Air Resources Board estimates that the average cost of retrofitting an engine of 275 horsepower with a catalyzed diesel particulate filter ranges between $6,900–$9,000.[25] By comparison, the average base price for a 200 to 300 horsepower wheel loader is $275,000.[26] Retrofitting an engine with a catalyzed DPF in this price range or with a $2,500 DOC costs only a small fraction (2.5 to 3.2% and less than 1%, respectively) of the cost of replacing the entire vehicle with one that pollutes less.

Moreover, the use of diesel fuel with 15 ppm of sulfur or less can benefit engine operation and maintenance by reducing wear and tear on heavy equipment. This translates into prolonged engine life and less frequent replacement of parts like pistons and cylinder liners.[27] Fleet operators using ULSD may therefore realize a dividend in avoided maintenance.[28] EPA expects these benefits to be equivalent to reducing the cost of the fuel by 3.3 cents per gallon.[29]

Environmental Defense recommends that construction fleet operators who have decided to take steps towards reducing harmful emissions from their construction vehicles contact their Original Equipment Manufacturer (OEM) or other appropriate technology experts to determine the most effective way to reduce diesel emissions from specific machine models in their fleet. Retrofit technology manufacturers and OEMs will probably need information about the fleet in order to advise construction fleet operators on which retrofit solutions will work best for their individual needs. It is always advisable for construction fleet operators to maintain a full inventory of construction machinery (including model and serial number of equipment, year of manufacture, engine displacement, horsepower and serial number of engine, and engine certification for post-1996 engines) working at a given site. This inventory should also include all machinery used to transport debris and construction material to and from a construction site.

Fleet operators who wish to install retrofit technology should also seek information from manufacturers about the proper monitoring, maintenance and operation of retrofit technology.[30] Finally, fleet operators should check with both OEMs and retrofit technology manufacturers about how installing retrofit equipment or using alternative fuels will affect equipment warranties. Most manufacturers have provided guidance to ensure that warranties are not threatened by any use of clean fuels or retrofits.

Equipment management and behavioral solutions to emissions reductions

In addition to the "3 R's" above, there are fleet management and behavioral solutions that can be implemented to reduce pollution. These common sense practices can be implemented immediately

and can be a good first step in any retrofitting/diesel emissions reduction plan.

Stop engine idling. Users of heavy-duty diesel equipment (both onroad and nonroad) often keep their engines idling when their equipment is not in use. Reducing or eliminating unnecessary idling can save fuel, and therefore money, as well as reduce emissions. According to EPA, a typical heavy-duty truck or bus can burn approximately one gallon of diesel fuel for each hour it idles, generating significant amounts of pollution, wasting fuel, and causing excessive engine wear.[31] Instead of idling, vehicle owners can purchase small generators or auxiliary power units specifically designed for trucks and buses that provide heat, air conditioning and/or power while a vehicle is not in motion.[32] These devices substantially reduce the fuel consumed and emissions generated during long-duration idling. Many communities across the county have anti-idling rules, but there is a need for enforcement and compliance with these rules and a need to develop and enforce worksite specific rules to govern idling.

Improve equipment maintenance and inspection. Proper maintenance, engine tuning and emissions testing is critical to success. This includes replacing worn out parts, cleaning, tuning and generally maintaining the engine. Whether a retrofit device is installed and/or cleaner fuel is being used, it is always important to ensure that the engine is properly tuned and maintained. This is essential not only for the engines to operate efficiently, but also to ensure that emissions reduction technologies can be used effectively. As with onroad vehicles, nonroad equipment should have regular inspections, including smoke testing. Proper maintenance will ensure complete fuel combustion and as a result PM exhaust is minimized. Proper maintenance can also improve fuel economy and extend engine life.

In addition to reducing idling time and instituting inspection and maintenance programs, the following measures can also help reduce exposure to diesel pollution:

- establishing a staging zone for trucks that are waiting to load or unload material at the work zone in a location where diesel emissions from the trucks will have minimum impact on abutters and the general public; and
- locating construction equipment away from sensitive receptors such as fresh air intakes to buildings, air conditioners and operable windows.

The remainder of this handbook focuses on using cleaner fuel and retrofits to reduce pollution from construction equipment. Reducing pollution from existing nonroad diesel equipment is vital to protecting the public from the health and environmental harms caused by hazardous diesel emissions. Even a relatively new engine can reduce pollution by installing a retrofit and using a cleaner fuel. The goal of these retrofit or emissions control technologies is to reduce emissions, up to and beyond what is required by EPA regulation[33] without negatively impairing the performance of the machine for its intended use.

CHAPTER 4

Successes and regional programs

A variety of regional programs have proven successful at reducing harmful diesel pollution. This section of the handbook provides examples of voluntary government or private sector leadership in retrofitting construction equipment, including: New York City's efforts at the World Trade Center and through Local Law 77, Boston's Big Dig Project, Connecticut's New Haven Harbor Crossing Corridor Improvement Program, the Port of Houston Retrofit Program and retrofits at Washington's Puget Sound. Additionally, this section examines examples of successful economic or market incentive programs that provide financial support for cleaner technologies or fuels, such as the Texas Emissions Reduction Plan, the Carl Moyer Program in California, or the EPA Voluntary Diesel Retrofit Program. The diversity of programs described reflects the varying needs of individual projects with respect to equipment, location, fuel availability and other related factors. When planning a retrofit project, it is always important to take individual situation characteristics into account.

"Best available retrofit technologies": New York City

New York City has demonstrated a strong commitment to reducing pollution from diesel engines. This case study discusses three NYC projects:

- the 7 World Trade Center Diesel Emission Reduction project,
- lower Manhattan redevelopment construction commitments, and
- NYC's Local Law 77.

7 WORLD TRADE CENTER SITE[34]

The Clean Air Communities Diesel Emissions Reduction Project at 7 World Trade Center is the first public-private endeavor of its kind in the city. As former Northeast States for Coordinated Air Use Management (NESCAUM) Executive Director, Ken Colburn stated, "through the application of advanced emission control technology and the use of ultra low sulfur diesel fuel, this Clean Air Communities initiative demonstrates that innovative, clean air progress is possible even at large-scale urban construction sites across the nation."[35]

In October of 2002, the site converted to ULSD for all equipment. Six pieces of construction equipment have already been retrofitted, and one electric crane is being used in lieu of the typical diesel engine crane technology. It is important to note that these strategies target PM, HC, and CO reductions, not NO_x.

LOWER MANHATTAN REDEVELOPMENT[36]

Lower Manhattan is a thriving mix of apartments, art galleries, shops and restaurants. More than 4,000 children live throughout lower Manhattan in neighborhoods as diverse as TriBeCa, Chinatown and Battery Park City. With the rebuilding of the World Trade Center site, lower Manhattan will become one of the nation's largest construction sites, teeming with diesel engines. These engines will be operating just steps from school, playgrounds, parks, homes and offices.

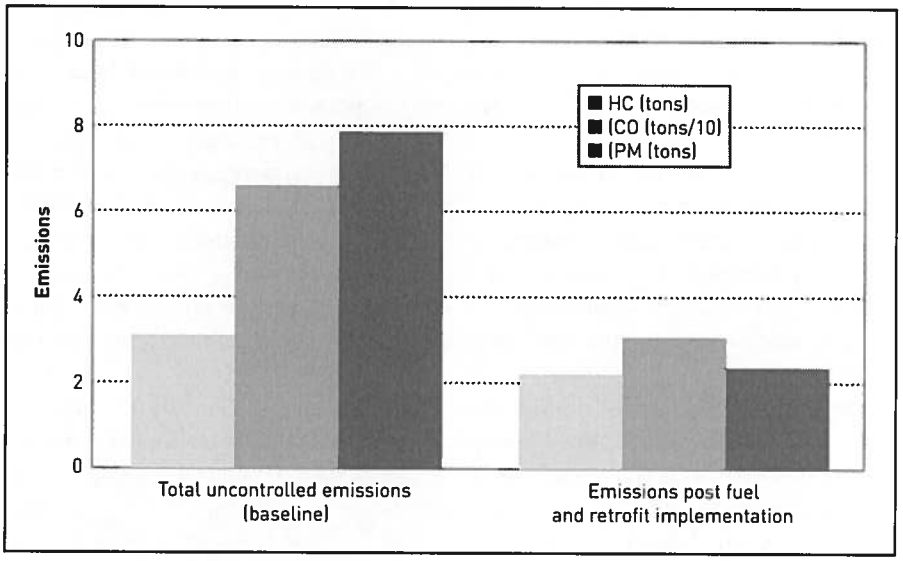
Governor Pataki and New York City have pledged to use the best available retrofits and cleaner diesel fuel in all of the reconstruction efforts. In 2002,

TABLE 3
7 World Trade Center retrofits

Date	Equipment	Retrofit technology
March 2003	Stationary Generator Excavator (CAT 245D, 14.7 l) Excavator (Komatsu PC200, 5.9 l)	DOC DOC DOC
January 2004	Stationary Generator (Rudox, 125 kw, 6.8 l)	Active DPF (Rypos RT500)
May and June 2004	A two-stroke and a four-stroke crane	Metallic High Performance DOC Clean Cat® known by the trade name of "diesel particulate reactors" (by Environmental Solutions Worldwide, Inc.)
Pending	The site has plans to retrofit one more piece of equipment, a concrete pump, with a DOC. Rather than purchasing a new DOC, the retrofit will reuse a high-efficiency DOC from one of the cranes after crane use is finished.	

Source Information provided by Glenn Goldstein at NESCAUM.

FIGURE 5
Total emissions reductions for 7 World Trade Center project



Courtesy of NESCAUM. Includes emissions from equipment that was not retrofit.

Governor Pataki committed to the use of ULSD and best-available retrofits in all state-controlled lower Manhattan construction projects, including at the World Trade Center site. The New York State Assembly and Senate followed Governor Pataki's lead and passed legislation on June 22, 2004 codifying Governor Pataki's commitment.[37] The law was unanimously approved in both the House and the Senate and was recently signed into effect by the governor.[38] It requires contractors and subcontractors using diesel-powered nonroad vehicles with an engine horsepower rating of 60 HP and above to use only ULSD and to retrofit, where practicable, their equipment with oxidation catalysts, particulate filters or technology with "comparable or better effectiveness."[39]

The pollution reduction efforts at 7 World Trade Center have been paralleled at other redevelopment sites in lower Manhattan. In the PATH reconstruction project, for example, three pieces of construction equipment were chosen for retrofits: a Caterpillar XQ2000 Genset and two Caterpillar 966G TG-22 Loaders. Caterpillar, the original manufacturer of all of the pieces of equipment, was chosen to perform the retrofits.

Caterpillar chose to utilize a passive DPF, the CRT™, manufactured by Johnson Matthey. The CRT™ particulate filter is a patented emissions control technology that contains both a platinum oxidation catalyst and a particulate filter. Caterpillar specifies the minimum exhaust temperature must be at least 260°C for at least 40% of the operating time. Though loaders met these minimum requirements, a detailed engineering analysis on the generator's exhaust temperature found that it was an unsuitable candidate for a DPF. The generator was only being used consistently at approximately 20% of its rate and thus lacked sufficient exhaust temperature.

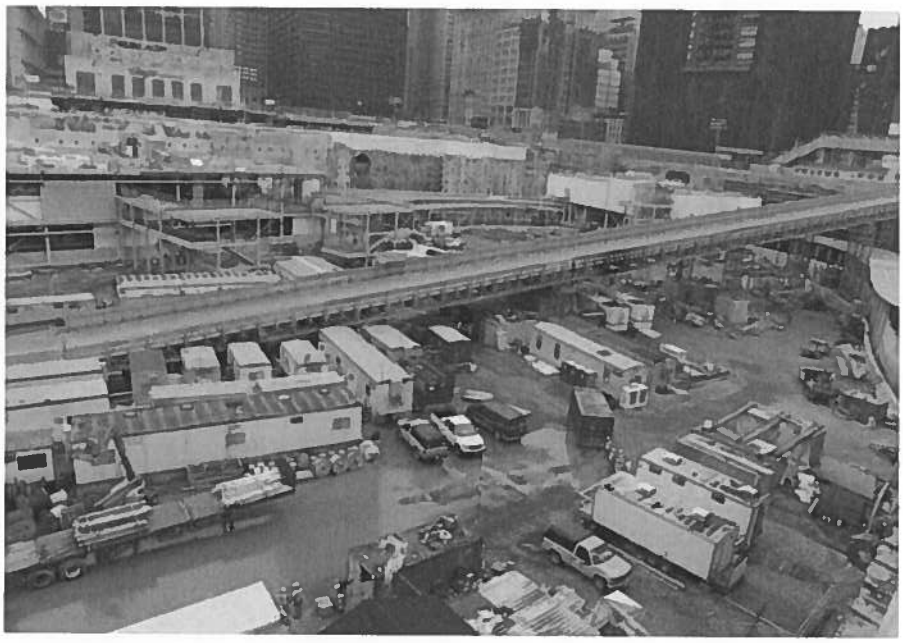
In August of 2003, H.O. Penn (Caterpillar's local dealership) and Caterpillar design engineers installed the DPFs on the two 966G Loaders. The installation process took eight to ten hours, which was approximately double the expected installation time. This delay can probably be attributed to these retrofits being the first installations of this kind performed by H.O. Penn as well as the need to modify several brackets/components during installation. During the emissions testing, the time required to remove the original muffler and replace it with the DPF was cut in half.

One concern about using DPF technology is failure of the DPF to regenerate, which could lead to excessive engine backpressure. Backpressure must be checked so that it does not increase to levels that may ultimately damage the engine. For this reason, Caterpillar decided to provide an integrated exhaust backpressure alarm with the retrofits to alert the driver if the backpressure is too much. The alarm, mounted in the cab of the loader, is both visual and audible. If a pre-specified backpressure is exceeded for more than a set time interval the alarm lights up.

The installed cost of the DPFs for the wheel loaders was approximately $15,000 each. This cost is probably higher than the future cost of retrofits of this type because this was the first installation on a Caterpillar 966G loader for both Caterpillar and H.O. Penn. After the first few installations, labor efficiencies are typically realized, as evidenced by the decreased installation time from the initial installation to the emissions testing installation. Further, as market demand increases, capital costs are expected to decrease. Additional project costs came from the April 2005 price premium of $0.01–$0.18 per gallon of ULSD in the New York City area. The use of ULSD is not expected to change maintenance schedules or cost, however, using DPFs is expected to slightly increase maintenance responsibilities and cost. Specifically, the filter technology must be cleaned to maintain emissions reduction benefits. A cleaning contract was not negotiated for this project, but other negotiated contract prices in the New York City area range from $300 to $500 per cleaning event. The DPFs have not yet been in service for a year, and have experienced no operational problems.

To establish the emissions reduction potential of the different strategies (ULSD vs. ULSD/DPF), emissions testing was performed using two different types of portable emissions monitoring systems: the Clean Air Technologies

Construction at the World Trade Center site.



ENVIRONMENTAL DEFENSE

International Montana system and the Environment Canada DOES2 system. Emissions testing was conducted for two weeks between September and October of 2003; significant PM emissions reductions were documented. Both monitoring systems identified PM emissions reductions of 15 to 20% for the use of ULSD alone, and of greater than 90% when ULSD was combined with the DPF. Additionally, the use of the DPF also produced significant CO emissions reductions. The switch to ULSD alone produced CO emissions reductions in the range of 1 to 10%, and more than 85% reductions were achieved when the DPF technology was used with ULSD.[40]

NEW YORK CITY LOCAL LAW 77

Recently, New York City committed to emissions reduction measures for all city-funded construction. New York City Local Law 77 calls on New York City to use clean fuels and advanced emissions-control technologies in all city construction fleets and contracts. The law requires two fundamental steps.[41] First, it requires the use of ULSD with a maximum sulfur content of 15 ppm in all city contracts, on a schedule set forth in the law. Second, it requires use of "best available" emissions control technology for any class of engine to which the law applies.

Local Law 77 provides a high standard for what shall constitute best available technology, calling on the City to use technologies that reduce both fine particulate matter (PM) and oxides of nitrogen (NO_x). Specifically, Local Law 77 requires that agencies use technologies that "shall be primarily based on the reduction in emissions of particulate matter and secondarily based upon the reduction in emissions of nitrogen oxides."[42] The DEP recently promulgated rules defining "best available technology."[43]

Retrofits and ULSD have been tested at the 7 World Trade Center site, incorporated into Lower Manhattan Development Corporation design guidelines, and now every Environmental Impact Statement for major reconstruction projects in lower Manhattan, from the Fulton Street transit center to Route

Even private NY contractors have joined the diesel retrofit effort. After Pavarini-McGovern Construction Company was found in violation of a local emissions regulation, they retrofit a 1971 380 HP crane with a DOC and committed to using the fuel-borne catalyst Platinum Plus.

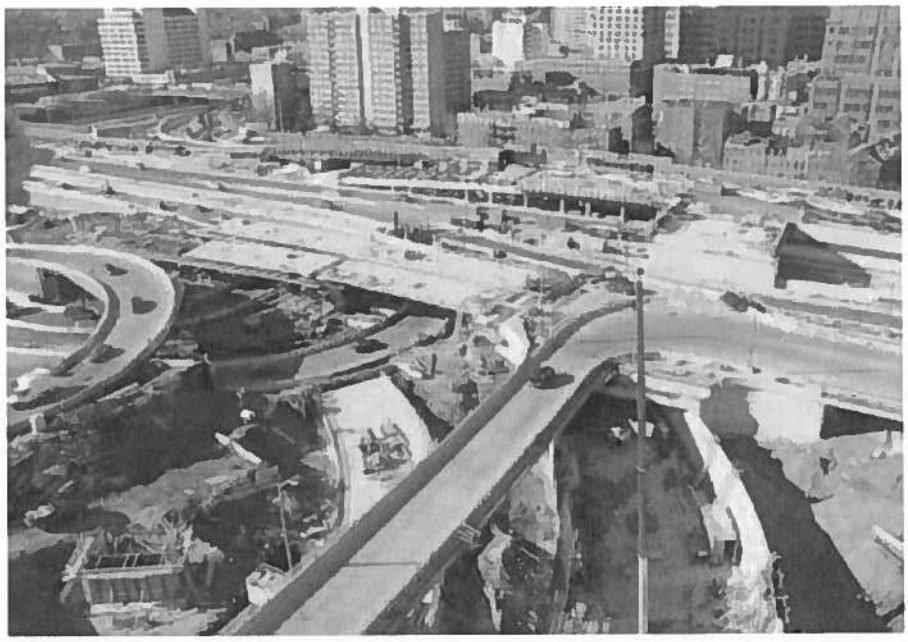
9A, has committed to using advanced retrofits in their environmental impact statements. For example, the Fulton Street Transit Center draft environmental impact statement requires the use of Tier 2 compliant equipment with PM emissions reductions at 85%.[44] Additionally, many projects in lower Manhattan are already moving ahead with emissions-reduction strategies based on a wide range of technologies.

The Big Dig[45]

The Central Artery Project in Boston, also known as the "Big Dig," has built 161 lane miles of highway in a 7.5-mile corridor directly through the middle of densely populated downtown. The project, which began in September 1991 and is currently scheduled to be substantially completed by the end of 2005,[46] presented an historic opportunity to test and demonstrate the feasibility of pollution control retrofits. Use of these retrofits helps to minimize the impact of such a large-scale project by reducing air pollution and lessening the health impact of a major construction project on workers, neighborhoods and regional air quality.

The Massachusetts Turnpike Authority (MTA) in collaboration with the Massachusetts Department of Environmental Protection (DEP) and NESCAUM, chose to retrofit construction equipment with diesel oxidation catalysts. Although other technologies achieve higher particulate reduction rates than DOCs, the MTA preferred DOCs for several reasons—primarily because the very clean diesel fuel (15 ppm of sulfur or less) needed to operate other technologies was not available at the time the Big Dig began.

Retrofit requirements were incorporated into Big Dig construction contracts.



MASSACHUSETTS TURNPIKE AUTHORITY

The Big Dig retrofit project has resulted in the installation of DOCs on approximately 200 pieces of construction equipment—this includes small in-tunnel cranes,[47] lifts, excavators, bulldozers, generators and compressors. This effort will achieve air emissions reductions that are the equivalent of removing 1,300 diesel buses off of Boston streets for a full year.[48]

The Big Dig retrofit project is a true success: **No adverse operational problems or additional maintenance costs have been experienced by Big Dig construction equipment retrofitted with DOCs.**[49] Additionally, preliminary estimates of area-wide emissions reductions from the retrofitted equipment amount to approximately 36 tons per year for carbon monoxide, 12 tons per year of hydrocarbons, and 3 tons per year of PM.[50]

The Massachusetts Highway Department provided funding to contractors to purchase the emissions control devices. According to Alex Kasprak, Environmental Engineer, Massachusetts Turnpike Authority, one of the lessons learned from the Big Dig project is that it is best to include the requirement for emissions control equipment as part of the contract's bid package. By doing so, the cost of the retrofit equipment can be included as part of the overall contract cost. This will also ensure that the maximum number of offroad pieces of equipment can be retrofitted.[51] Overall, the Big Dig retrofit program is now being used as a model by regulatory agencies to encourage other construction projects to utilize retrofitted diesel equipment.[52]

I-95 New Haven Harbor Crossing Corridor Improvement (NHCC Project)[53]

Eighty-three diesel oxidation catalysts have successfully been installed at the Connecticut NHCC project. In addition, construction contractors have volunteered to use low sulfur diesel (500 ppm sulfur content) on all their nonroad equipment. The NHCC project is part of Connecticut's Clean Air Construction Initiative and was launched to protect laborers as well as residents from harmful construction emissions along a densely populated corridor. Construction began in 2001.

The Connecticut Clean Air Initiative was a mutual effort of the Connecticut Department of Transportation (ConnDOT), the Connecticut Department of Environmental Protection, the Connecticut Department of Motor Vehicles, and the Connecticut Construction Industry Association to come up with real-world solutions to air quality problems. With compromise, a contract specification was evolved from the above mentioned agencies to improve the quality of life through this long duration construction project.

ConnDOT is requiring all contractors and subcontractors to take part in the Connecticut Clean Air Construction Initiative. The cost to purchase the DOCs and the cleaner fuels was included in the overall contract cost, as bid by each contractor. At present, all contractors have decided to install DOCs. Although other technologies achieve higher particulate reduction rates than DOCs, they were preferred primarily because low sulfur diesel fuel

"The Big Dig diesel construction retrofit program has proven that retrofitting construction equipment with DOCs is very feasible, and provides beneficial air quality improvements in terms of emission reduction and odor control."

—Alex Kasprak, Environmental Engineer, Massachusetts Turnpike Authority, CA/T Project

"I am very proud of Connecticut's success in this Clean Air Construction Initiative. The State of Connecticut's various Departments and the Connecticut Construction Industry Association (CCIA) worked and are still working to benefit the people of Connecticut by trying to improve the quality of life in locations where transportation projects are occurring. We are sensitive to those that live or work in an area were construction is going on, day after day, and how it affects those people's lives. This Initiative is a step in the right direction. As technologies improve, greater air quality can be achieved."

—Donna Weaver, Transportation Planner, Office of Environmental Planning, Connecticut Department of Transportation

(500 ppm sulfur content), rather than the ULSD (15 ppm of sulfur or less) needed to operate other technologies, was used for the project. Estimates for reduced emissions from the program are 20 tons per year for carbon monoxide, 2 tons per year for fine particulate matter (with clean fuels or oxidation catalysts) and 8 tons per year for hydrocarbons (with oxidation catalysts only).[54]

Because of the success of the Connecticut Clean Air Initiative on ConnDOT projects, other agencies such as the Connecticut Department of Public Works and the Connecticut Department of Economic and Community Development are also requiring their construction contractors to follow the ConnDOT specification. Three or four diesel oxidation catalysts have been installed on two projects as a result.

Port of Houston[55]

The Port of Houston is the sixth largest port in the world,[56] and a significant contributor to NO_x emissions in the eight counties of the Houston-Galveston area. All eight counties in this region fail to comply with EPA's health-based eight-hour ozone standards.[57] Although the Port of Houston Authority is not the largest contributor to emissions in the area, they have become the region's leader in emissions reduction activities and commitments.

Through demonstration testing of the alternative fuel PuriNOx™ on rubber-tire gantry crane with a 550 horse-power engine, the Port of Houston Authority (PHA) has reduced NO_x emissions by 25% and PM emissions by 50%.[58] In September of 2003, the Port Authority converted 39 yard tractors and yard cranes to PuriNOx and enacted the requirement that any new equipment purchased be able to use the technology.[59] Approximately 49 pieces of cargo-handling equipment are currently operating on PuriNOx for a NO_x emissions reduction of approximately 21 tons per year at a total cost of $216,000. According to Roger Guenther, container facilities manager at Barbours Cut Container Terminal, "It's just a different fuel, nothing special has to be done to the equipment. I could put diesel back in any of the offroad vehicles and they would run just fine. I can't tell any difference from one to the other."[60]

The PHA also applied for and received $337,000 in state funding (see the Texas Emissions Reduction Program section below) to replace two Fireboat FARNSWORTH propulsion engines with engines that produced 5.6 tons less NO_x per year.[61] Additionally, the PHA has purchased several new yard tractors and container handlers with clean engine technology, resulting in NO_x emissions reductions of 6.9 tons per year at a cost of $21,500.[62] Further, the PHA purchased 33 ultra-low emissions vehicles or propane vehicles for their onroad fleet.[63] The PHA plans to extend its retrofit program (which involves either retrofitting vehicles with oxidation catalysts,

PORT AUTHORITY OF HOUSTON

New equipment purchased by the Port of Houston Authority must run on PuriNox, an alternative fuel that reduces NO_x emissions.

switching their fuel use to PuriNOx, or both) to between 50 and 250 vehicles.[64] In total, the PHA has reduced NO_x emissions by 33.5 tons per year with the assistance of $574,000 in TERP funding.

Puget Sound in Washington[65]

Washington State's Puget Sound Clean Air Agency has formed a coalition, known as Diesel Solutions®, to dramatically reduce diesel engine pollution in the region. The first step in this program was to work with Conoco/Phillips and U.S. Oil to ensure that ULSD was locally available. Since ULSD was made available, 800 school buses have been retrofit, mostly with DOCs.

Approximately two dozen pilot projects used DPFs for the retrofits. The average retrofit cost has been between $1,200 and $8,000 per vehicle, and projects are financed through a statewide retrofit program developed as part of the EPA Voluntary Diesel Retrofit Program. The next step in the program is to retrofit diesel engine construction equipment with pollution control technology. As part of this effort, the Puget Sound Clean Air Agency has requested retrofits in their comments on local project environmental impact statements, and has been speaking with a number of construction companies.[66]

The Texas Emissions Reduction Program[67]

In 2001, the Texas State Legislature established the Texas Emissions Reduction Program, enacted through Senate Bill (SB) 5. The goals of the TERP, as stated in SB 5, are to: "assure that the air in the state is safe to breathe and meets minimum federal standards established under the Federal Clean Air Act (42. U.S.C. Section 4707); develop multi-pollutant approaches to solving the state's environmental problems; and adequately fund research and development that will make the state a leader in new technologies that can solve the state's environmental problems while creating new business and industry in the state."[68]

The TERP covers 41 counties in the state where air quality violates or is close to violating EPA standards.[69] Projects are eligible for financial assistance through a number of programs, including: the Emissions Reduction Initiative Grants Program, which offers incremental funding for NO_x emissions reduction activities; the Small Business Program, which offers grants to small businesses for pollution reduction measures; the Heavy-Duty Motor Vehicle Purchase or Lease Incentive Program, which allows the Texas Com-

mission on Environmental Quality to reimburse a purchaser or lessee of a new onroad heavy-duty vehicle for the difference in price between that vehicle or a higher-emitting diesel-powered vehicle; and the Light-Duty Motor Vehicle Purchase or Lease Incentive Program, which (though currently unfunded) is intended to provide financial incentives for the purchase of light-duty motor vehicles that are EPA-certified at a lower NO_x emissions standard than regular light-duty motor vehicles.

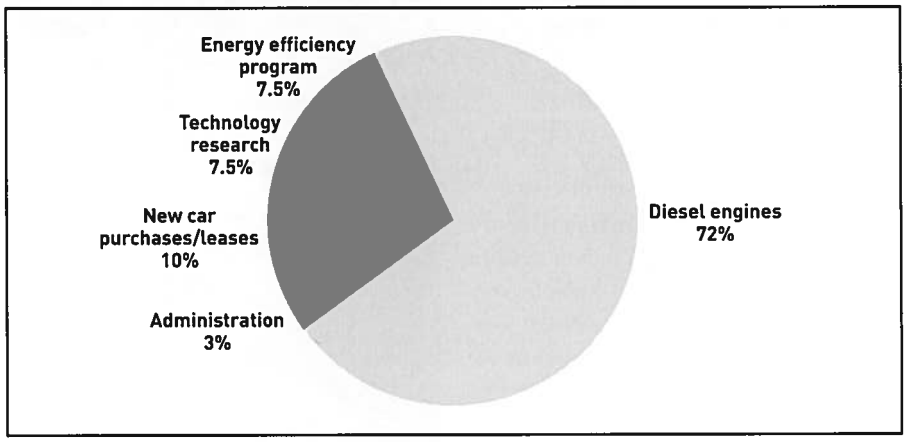
TERP will offer a total of approximately $130 million in funding for emissions reductions programs each year over the next three years.[70]

In the 2004 grant application period, the Texas Commission on Environmental Quality had approximately $127.5 million available for grant programs. Eligible projects include new purchases, replacements, retrofits, repowers, and refueling projects.[71] The projects from the first round of grants are expected to reduce NO_x emissions by over 3,500 tons over their lifetime, at an average cost of about $5,175 per ton reduction.[72] The projects funded by the second round of these grants are expected to reduce NO_x emissions by almost 13,600 tons over the life of the projects, at an average cost of $5,960 per ton reduction.[73] In 2004, the average cost per ton reduction of NO_x emissions was approximately $5,800. This represents a lower average cost per ton NO_x emissions reduction than achieved by 2002-2003 grants funds, which offered over $28 million in funding to reduce NO_x emissions by over 4,100 tons over the life of the projects at an average cost of approximately $8,362 per ton.[74] The Emissions Reduction Grant Incentive Program NO_x cost-effective criteria will be capped at $7,000 per ton reduction in 2005.[75] Grant award details are available at: http://www.tnrcc.state.tx.us/oprd/sips/terp.html and more information can be found at: http://www.tnrcc.state.tx.us/oprd/sips/terp.html.

California's Carl Moyer Program[76]

The Carl Moyer Memorial Air Quality Standards Attainment Program

FIGURE 6
TERP funding distribution, 2001 (approximately $130 million)



When the Texas Emissions Reduction Plan is fully implemented, the majority of funds will go toward replacing older diesel engines with cleaner-burning models.
Source: TNRCC. "Clean Air Incentives." Natural Outlook, Fall 2001. Online resource, available at: http://www.tceq.state.tx.us/assets/public/comm_exec/pubs/pd/020/01-04/clean_air.pdf Last accessed 04/12/05.

provides funds on an incentive basis for the incremental cost of cleaner than required engines and equipment. Funding is available for nonroad equipment 50 hp or greater. Eligible projects include cleaner onroad, offroad, marine, locomotive and stationary agricultural pump engines, as well as forklifts, airport ground support equipment, and auxiliary power units. The program achieves near-term reductions in NO_x emissions, which are necessary for California to meet its clean air commitments under the State Implementation Plan. In addition, local air districts use these NO_x emissions reductions to meet commitments in their conformity plans, thus preventing the loss of federal funding for local areas throughout California. The program also seeks to reduce particulate matter (PM) and hydrocarbons.

The California Air Resources Board (CARB) is responsible for the development and oversight of the majority of the Carl Moyer Program. CARB distributes Carl Moyer funding to California's 35 local air districts, which then screen applications and distribute the funding to diesel engine owners. The program has provided grants for projects such as repowering nonroad equipment, agricultural irrigation pumps, sweepers, tractors and marine vessels. It has also helped to fund the purchase of new natural gas refuse trucks and buses.

Governor Schwarzenegger recently signed AB923, which authorized increasing motor vehicle registration fees and tire fees to support programs, such as the Carl Moyer Program, that reduce air pollution. Through year six of the Carl Moyer Program, it had received approximately $154 million dollars in total funding.[77] With its recent reauthorization, up to $140 million a year of incentive funding is available for air pollution mitigation technologies.[78] More information is available on the Carl Moyer Program web site at: http://www.arb.ca.gov/msprog/moyer/moyer.htm.

The EPA Voluntary Diesel Retrofit Program

The Environmental Protection Agency, through the Office of Transportation and Air Quality, has developed a program to encourage voluntary diesel retrofits. This program uses economic incentives, which can be applied at the federal, regional, state, and local levels, to produce emissions reductions through the use of pollution control technology. One tool used by this program is grants, which have been awarded to various parties to help fund the cost of retrofit projects. Information on recent grants is available on the EPA Voluntary Diesel Retrofit Program web site.

EPA is also in the process of developing a policy to allow diesel engine retrofits to count as credits that can be traded or used to offset stationary source emissions. As a corollary to this program, EPA has developed a verification program to ensure that pollution control technology providers advertised emissions reductions. More information on the EPA verification process is available in the "Onroad and Nonroad EPA/CARB Verification" section of this handbook. Further information on the Voluntary Diesel Retrofit Program, verified technologies, and financial incentives for the use of pollution control technology can be found on the EPA Voluntary Diesel Retrofit web site, at: http://www.epa.gov/otaq/retrofit/index.htm.

CHAPTER 5

Fueling a cleaner tomorrow

Ultra-low sulfur diesel fuel (ULSD)

The sulfur in diesel fuel directly contributes to the amount of pollution emitted, such as engine-out PM emissions[79] and secondary emissions of SO_4.[80] Currently, the EPA standard for onroad diesel fuel is 500 ppm (also referred to as No. 2 Diesel). The current nonroad standard for diesel fuel is 5,000 ppm, but sulfur levels are generally around 3,400 ppm. As of September 2006, 15 ppm sulfur content (ULSD) will become mandatory for all onroad diesel engines[81] and in 2010, 15 ppm sulfur content fuel will become mandatory for many nonroad engines.[82]

Because ULSD is not required nationally until September 2006, its current availability and costs vary depending on location, whether ULSD has to be specially trucked in for a project, and the quantities needed. The map below shows areas within a 250-mile radius of where ULSD is refined,[83] or areas where ULSD should be available as of August 2004. Once ULSD becomes mandatory for the onroad sector in 2006, it will be readily available across the United States and cost differentials between low sulfur diesel (500 ppm) and ULSD should be minimal.

ULSD reduces harmful emissions, allows for aggressive retrofit devices, and reduces maintenance costs. EPA states: "While the estimated added cost for low-sulfur fuel is about seven cents per gallon, the net cost is projected to average about four cents per gallon because the use of ULSD could significantly reduce engine maintenance expenses."[84] The maintenance dividend for low sulfur fuel in large onroad vehicles (e.g. trucks and buses) is about $600 over the life of the engine or a fuel cost savings of about 1 cent per gallon.[85] The cost savings for nonroad equipment may be higher, because baseline sulfur levels in nonroad fuel are up to six times higher than onroad fuel.

The program has been a tremendous success. In the short period from October 1, 2004 to February 1, 2005, the Lane Clean Diesel Project received commitments from its partners to purchase over 2 million gallons of ULSD.

By switching from onroad diesel fuel (500 ppm) or from nonroad diesel fuel (about 2000 ppm-3000 ppm) to ULSD, particulate matter, smoke and sulfate emissions will be reduced.[86] ULSD used in combination with advanced retrofit technology allows for dramatic reductions of up to 90% of the PM, HC and CO found in diesel exhaust. Those who wish to design a retrofit program should talk with local fuel providers to determine whether ULSD is available in their market, and if it is not yet available, the timeline within which it will be

An Oregon success story

Sharon Banks of the Lane Regional Air Pollution Authority (LRAPA), Oregon successfully built a market for ULSD fuel in Lane County, Oregon. The objective was to bring ULSD fuel to Lane County at an affordable price ahead of the September 2006 mandate.

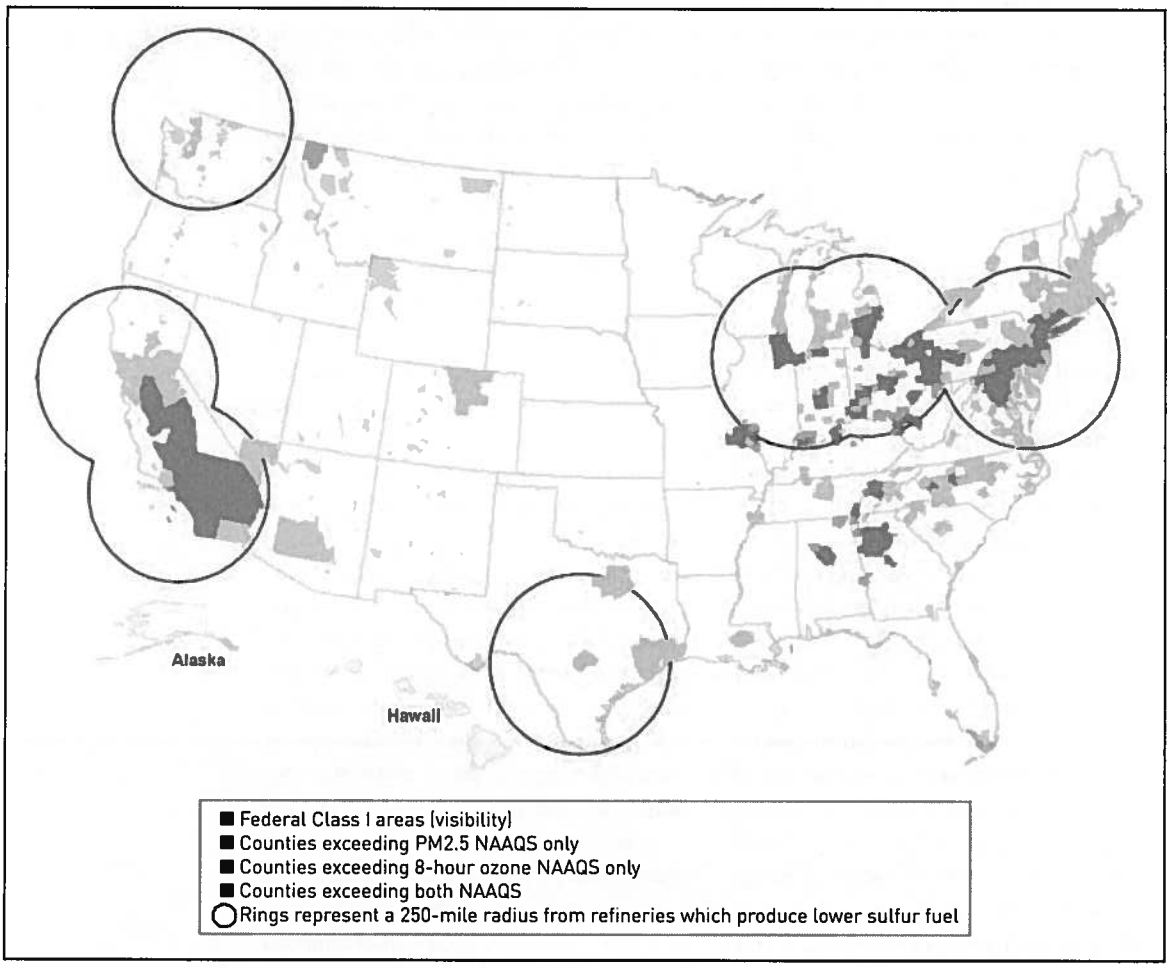
To bring the price of ULSD fuel down to a competitive level, Ms. Banks built enough demand in Lane County to make ULSD fuel attractive to users. City managers, County administrators, school districts, transit authorities, municipal waste haulers, large private fleets, fuel distributors and public utilities were all involved in the endeavor.

available. EPA rules mandate that all new onroad diesel vehicles use ULSD by 2006, at which point the fuel will be widely available nationwide.[87] New EPA rules do not require the use of ULSD in the nonroad sector before 2010, but the widespread availability of the fuel by September 2006 makes it easy for any nonroad fleet to begin using the fuel ahead of the EPA nonroad schedule.[88]

Emulsified diesel fuel

Emulsified diesel fuel is diesel fuel (LSD or ULSD) blended with up to 20% water and a proprietary additive. The water emulsion has to be stirred regularly when kept in a stationary tank to ensure that the water molecules are completely enclosed by fuel molecules. Stirring is important to avoid separation, which could cause engine corrosion and decreased lubricity. Storage tanks can be equipped with stirring devices such as circulation pumps. Though the timeframe for recirculation needs may vary based on individual product specifications, Lubrizol's PuriNOx can be stored at room temperature

FIGURE 7
Ultra low sulfur diesel fuels availability



Source: http://www.epa.gov/otaq/retrofit/fuelsmap.htm

for 3–4 weeks before recirculation becomes necessary.[89]

Emulsified diesel fuels generally do not require engine modifications. However, fleet operators should check with OEMs before using a fill-and-go system like emulsified diesel and fleet operators should confirm warranty compatibility with the equipment/engine manufacturer before using emulsified fuels. Emulsified fuels have been tested for many onroad and nonroad diesel engines, although only Lubrizol's PuriNOx summer blend has received EPA verification. Summer blend PuriNOx cannot be used when ambient temperatures fall below 20 degrees Fahrenheit.[90] EPA has verified PuriNOx for both on and nonroad use and has confirmed a 16.8–23.3% reduction in PM and a 17–20.2% reduction in NO_x for nonroad applications.[91]

CARB has verified PuriNOx for onroad engines model years 1988-2003 at 50% PM (Level 2) reduction and 15% NO_x reduction.[92] In addition, CARB has verified PuriNOx and AZ Purimuffler or AZ Purifier System for 1996 through 2002 diesel engines used in off-road applications specifically at the ports, railway yards and other intermodal/freight handling operation applications only. The PuriNOx and AZ Purimuffler or AZ Purifier System uses a diesel oxidation catalyst and an emulsified diesel fuel to achieve a 50% reduction in PM emissions, qualifying it for a Level 2 CARB verification. The system also achieves a 20% reduction in NO_x emissions.[93]

Using retrofit technology in conjunction with emulsified fuels significantly reduces both PM and NO_x. For example, use of an emulsified fuel with a DPF produces PM emissions reductions of 95%, HC reductions of 85%, CO reductions of 75% and NO_x reductions of 25%. Use of emulsified diesel fuel in conjunction with a DOC produces PM emissions reductions of 65%, HC reductions of 60%, CO reductions of 70% and NO_x reductions of 25%.[94] Thus, Environmental Defense recommends that if emulsified fuel is used, it be used in conjunction with a retrofit device whenever possible to maximize emissions reductions.

While many applications have been successful, some have raised concerns regarding fuel separation in equipment that is not being used regularly, loss of power, slower hydraulic movement, injector pump failure in newer engines and acceleration.[95] When considering the emissions reduction rates of emulsified fuel, possible loss of engine power and fuel efficiency should be taken into consideration. Fuel efficiency depends highly on the duty cycle, and Lubrizol reports that a typical loss is between 5 and 10%.[96] Since water does not contribute energy, emulsified diesel fuel can decrease engine power by approximately 10–13%[97] depending on how much water has been added.[98] Engine power is also highly dependent on the duty cycle and current engine sizing of the vehicle. PuriNOx has successfully been used in a variety of both low and high horsepower offroad engines, from small little John Deere Gators (all terrain vehicles) to tractors, loaders, scalars, dozers, haul trucks, cranes, marine vessels, etc.[99]

Availability and cost of emulsified fuel should be addressed with the local fuel distributor. If a centralized fuel storage tank is available on site, the emulsified fuel can be blended on site, which may be less expensive than when it has to be trucked in. According to Lubrizol, for example, PuriNOx prices vary by distributor, but a good approximation of cost nationwide is $0.25 per gallon over diesel fuel.[100] However, depending on where PuriNOx is sold and depending

on the price of regular diesel fuel, it can also be the same price or less expensive than regular diesel fuel.[101]

Fuel-borne catalyst

A fuel-borne catalyst (FBC) is a liquid fuel additive that conditions diesel fuel, improving combustion and reducing emissions. An FBC can either be added to bulk fuel or directly to the construction vehicle's fuel tank. An FBC typically contains small amounts of precious metals such as platinum, cerium, or iron compounds. Use of an FBC product can also improve fuel economy by up to 10% and increase horsepower by up to 5%.[102]

EPA has verified only one FBC, called Platinum Plus®, so far.[103] EPA verified reduction rates for the FBC used in conjunction with a DOC are 25-50% for PM, 16-50% for CO and 0–5% for NOx. According to Platinum Plus' manufacturer, only about 2% of the platinum gets into the environment because the platinum bonds with the hot surfaces of the engine.[104] Platinum in the environment has a limited potential to produce allergy-like symptoms for sensitive populations, such as: conjunctivitis, coughing, wheezing or asthma attacks.[105] However, a recent study by the United Kingdom's Committee on Toxicity of Chemicals in Food, Consumer Products, and the Environment reported: "platinum emissions from the platinum based fuel catalyst were unlikely to be in an allergenic form."[106]

To address the amount of platinum released into the environment and to achieve the maximum possible emissions reductions, Environmental Defense recommends that an FBC be used in conjunction with retrofit equipment, such as a DPF or the catalyzed wire mesh filter mentioned in the technology section.[107]

Alternative fuels

To reduce emissions of hazardous pollutants, construction fleet operators can use an alternative fuel. The use of alternative fuels provides not only environmental benefits, but also can reduce dependency on foreign petroleum and improve energy security through supply diversification. As with all vehicles and equipment, to achieve the maximum possible environmental benefits, alternatively fueled vehicles must be properly maintained.

This section of the handbook explores the specific advantages of biodiesel, compressed natural gas, liquefied natural gas and propane fuels. It is important to note that alternative fuels might be right for some fleets but not for others, especially because, at this time, alternative fuels do not have the same easily accessible infrastructure that diesel fuel does. Information on the availability of these, and other, alternative fuels is available from the Department of Energy's Alternative Fuels Data Center, which can be accessed online at: http://afdcmap.nrel.gov/locator/LocatePane.asp.

Additionally, federal and state tax incentives may be available to help defray increased purchasing costs for alternative fuel vehicles. More information on tax and other financial incentives for alternative fuel use is available from the Department of Energy's Alternative Fuels Data Center at: http://www.eere.energy.gov/cleancities/afdc/laws/incen_laws.html.

BIODIESEL

Biodiesel is a renewable, biodegradable, low-sulfur fuel that is produced from many types of feedstocks including vegetable oils (soybeans, rapeseeds, canola oil) or animal fat. Biodiesel is high in oxygen content (oxygenates) which leads to lower PM emissions.

Typically, biodiesel is blended with conventional diesel in a 20% biodiesel to 80% conventional diesel solution (B20). At B20, most of the potential PM benefits have been achieved while minimizing potential NO_x emissions increases. Biodiesel can also be blended with ULSD fuel, and in fact, makes up for ULSD's low lubricity. For example, using a 1% biodiesel and 99% ULSD blend increases lubricity 65% over pure ULSD, which is essentially equivalent to regular diesel fuel.[108]

EPA has statistically determined that PM, HC and CO emissions decrease and NO_x emissions increase slightly with B20 mixtures, when compared with conventional diesel. B20 increases NO_x by about 2%, decreases PM by approximately 10%, decreases HC by around 21% and decreases CO by approximately 11%.[109] Thus, biodiesel helps decrease emissions of some air pollutants, but it slightly increases NO_x emissions.[110] Due to the slight NO_x increase, biodiesel may only be appropriate for use in areas that are attaining the public health based standards for ozone—and even then, only in combination with other NO_x reduction strategies. B20 may also be appropriate for areas that have achieved their air quality standards but must work actively to maintain that status (maintenance areas).[111]

Biodiesel may also be used alone (B100) rather than blended with conventional or ULSD fuel. EPA has verified Biodiesel blends ranging from B1 to B100 for use in voluntary retrofit initiatives.[112] According to EPA, B100 is 5–11% less fuel efficient than conventional diesel.[113] Specifically, B100 reduces emissions of hydrocarbons by an average of 67%, carbon monoxide by an average of 48%, and particulate matter by an average of 47%.[114] On average, B100 emits about 10% more NO_x than conventional diesel fuels do.[115]

COMPRESSED NATURAL GAS AND LIQUEFIED NATURAL GAS

Compressed natural gas (CNG) is a colorless, tasteless, and non-toxic fuel that is mostly derived from methane. Although naturally odorless, an odorant is frequently added to CNG supplies to warn of its presence, a precaution made necessary by its flammability.[116] CNG is extracted from extensive underground reserves in gas wells or in conjunction with crude oil production and is commonly used to power water heaters, stoves, and laundry machines. However, CNG's utility is not limited to the household—it can also be an excellent and clean alternative fuel for mobile sources and has been used in the heavy-duty onroad sector.[117]

The U.S. Department of Energy describes CNG as "clean burning" producing significantly fewer harmful emissions than reformulated gasoline or diesel when used in natural gas vehicles. According to the U.S. Department of Energy, commercially available medium- and heavy-duty natural gas engines have demonstrated over 90% reductions of CO and PM and more than 50% reduction in NO_x relative to commercial diesel engines.[118] To use CNG, one must purchase a vehicle designed specifically for CNG use. At this time, CNG is not commercially available for nonroad use, although several hand-built demonstration units exist.

Liquefied natural gas (LNG) is natural gas that has been cooled to temperatures of 260 degrees below zero, but it is typically kept at high pressure so that it does not have to be so cold. The fuel's freezing temperatures increase the need for safety training by those operating LNG fueled vehicles. Skin contact with the fuel must be avoided, and machines that use LNG can vent a flammable gas mixture when not in use and parked in-

doors. Additionally, LNG must be used in a context where the LNG facility or terminal meets all applicable state or local government safety and siting rules. Similar to compressed natural gas, LNG has been used in the heavy-duty onroad sector,[119] but is not commercially available for the nonroad sector at this time.

PROPANE

Propane, known also as Liquefied Petroleum Gas, is a colorless and non-toxic fuel produced as a byproduct of natural gas processing or crude oil refining. Application of moderate pressure can convert the gas into a liquid, increasing the ease with which it is stored and transported. Although propane is less fuel efficient than gasoline, its higher octane rating means that engines run more smoothly and efficiently. Propane also produces less pollution than gasoline, and it can lower carbon dioxide, carbon monoxide and non-methane hydrocarbon emissions.[120] Additionally, propane is readily available—fueling stations are found in all 50 states. This fuel is widely used in the onroad sector, and has been successfully used by non-road vehicles such as fork-lifts or loaders.[121]

According to the U.S. Department of Energy, propane vehicles can produce fewer ozone-forming emissions than vehicles powered by reformulated gasoline. In addition, tests on light-duty, bi-fuel vehicles have demonstrated a 98% reduction in the emissions of toxics, including benzene, 1,3 butadiene, formaldehyde, and acetaldehyde, when the vehicles were running on propane rather than gasoline.[122]

CHAPTER 6

Filtering out pollutants

One of the most effective ways to reduce diesel pollution from existing equipment is to combine the cleaner fuels, discussed previously, with retrofit technology. In this handbook, the term *retrofit* is defined as incorporating any device into diesel equipment to reduce pollution. The term *retrofit technology* is used interchangeably with *emissions control technology*, *pollution control technology* and/or *after-treatment technology*.

There are a variety of demonstrated retrofit technologies available to significantly reduce PM, HC, CO, NO_x, toxics and odor emissions from existing heavy-duty diesel vehicles. Many technologies to reduce diesel PM are commercially available today and have been used for more than 25 years on nonroad diesel engines in construction equipment.[123] A number of NO_x control technologies that can significantly reduce pollution are still in development, although some are currently available.[124] Additionally, companies are making substantial investments to develop and commercialize diesel exhaust emissions control technologies. In fact, just 12 of the over 40 member companies that make up the Manufacturers of Emission Controls Association (MECA) have invested more than $1.8 *billion* in R&D and capital expenditures to help reduce pollution from the onroad and offroad diesel sectors.[125]

Thus, available retrofit technologies and applications are expanding rapidly and the industry is working aggressively to pursue solutions to address heavy-duty diesel emissions control.[126] Hundreds of scientists and engineers across the country are contributing to key developments to speed the evolution of diesel emissions control technology[127] and EPA has already formed partnerships with state, local and industry stakeholders in numerous states and the District of Columbia to reduce pollution from existing diesel engines.[128]

This part of the handbook introduces some of the many different options available for retrofitting.[129] It also provides information on the verification status of each technology:

- *Verified* means that the technology has been approved for use in either the onroad or the nonroad sector by the Environmental Protection Agency or the California Air Resources Board;
- *In development* means that the technology has not yet been verified, but may currently be in use in the onroad or nonroad sector, undergoing field testing, or in development.

Retrofit technologies can be geared towards PM or NO_x reduction, though many also reduce CO and HC emissions as well. Most advanced pollution control technologies require diesel fuels with very low levels of sulfur (15 parts per million of sulfur or less) to work properly and many can be combined for even deeper pollution cuts. Please talk to your fleet managers and Original Equipment Manufacturers (OEM) to determine the best options to meet your air quality goals.

Particulate matter reduction

DIESEL PARTICULATE FILTERS (VERIFIED)[130]

A diesel particulate filter (DPF) is an emissions control technology that traps diesel particulate matter from engine exhaust until the trap becomes loaded to the point that a regeneration cycle is implemented to

DPF in-use reduction numbers	
NO_x	0%
PM	Up to 90%
HC	Up to 90%
CO	Up to 90%

burn off the trapped particulate matter.[131] DPFs are normally built with a porous ceramic and metal mesh or silicon carbide filter housed in a metal container similar to a muffler. There are two main categories of DPFs: active and passive. The difference between the two is in the methods used to regenerate the filters. Passive systems rely on a catalyst to lower the temperature at which the collected soot will burn and, therefore, rely solely on the duty-cycle of the vehicle and resulting exhaust gas temperatures to ensure that regeneration occurs as frequently as required. Active systems use supplemental heat to supply the necessary energy to burn the collected particulate matter. The heat is provided by either onboard or offboard burners or electrical heaters. The type of DPF suitable for a specific application depends, in addition to other factors, upon the exhaust gas temperature, the daily duty cycle of the subject construction equipment and the availability of ULSD. Passive DPFs require the use of ULSD fuel to facilitate regeneration and prevent catalyst poisoning that would render them inoperable.[132] Active DPFs do not require ULSD fuel.

Active filter systems can be used on a broader range of vehicles because regeneration is accomplished by supplemental means that do not rely on the operation of the vehicle and the resulting duty-cycle. However, an active system can cost more than a passive system.

Although DPFs work by forcing the exhaust through porous walls, PM is collected without obstructing the flow of exhaust gases or damaging the engine or vehicle. Diesel particulate filters can reduce $PM_{2.5}$, PM_{10}, HC, and CO emissions by up to 90% and significantly reduce emissions of other toxics, including aldehydes.[133] However, DPFs do not remove NO_x.

Prior to installing DPFs, engines must be data-logged to ensure timely and consistent regeneration and tested to determine whether the required exhaust gas temperature is achievable for the necessary amount of time during the daily duty cycle. In addition, a back-pressure monitor must also be installed

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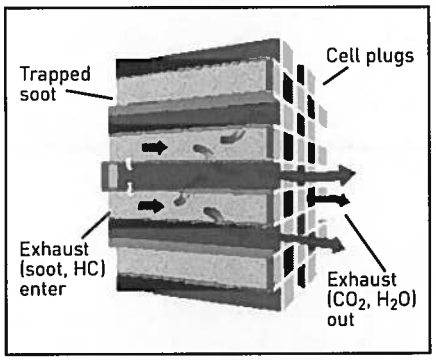
Construction equipment retrofit with a diesel particulate filter.

FIGURE 8
Schematic of a diesel particulate filter



MECA, "Minimizing NO2 Emissions from Catalyst-Based Diesel Particulate Filters." IDRAC Meeting, February 6, 2002. Online resource, available at: http://www.arb.ca.gov/diesel/presentations/020602/mecano2resolution.pdf Last accessed 03/03/05

to allow real-time monitoring of DPF performance and to ensure consistent in-use regeneration. If there is insufficient regeneration, the DPF will become plugged with soot, increasing exhaust gas backpressure levels beyond engine manufacturer specifications.

Particulate filters can be installed on new or existing equipment, sometimes as muffler replacements, to trap particulate matter in the exhaust.[134] Because DPFs tend to be larger and heavier than a diesel oxidation catalyst or a regular muffler, DPFs require some engineering to be properly installed on construction equipment. Installation of a DPF is more complex, time consuming and costly than the installation of a DOC. However, the installation of a DPF is worthwhile, because DPFs reduce PM, HC, and CO by up to 90%, whereas DOCs only reduce PM by approximately 20–30%, and HC and CO by approximately 50–70%. According to retrofit manufacturers, installation of a DPF takes about 5–7 hours and a DOC can be installed by the equipment operator in about 1–2 hours.

Depending on the application and size of the equipment, most DPF applications cost between $7,000 and $12,000 excluding installation.[135] Because DPFs are currently more effective at reducing particulate matter than other technologies, Environmental Defense strongly encourages the use of DPFs whenever possible.

Although DPFs are not as common as DOCs, an increasing number of DPFs are already being used at a number of construction sites. Worldwide, DPFs have been installed on over 70,000 heavy-duty vehicles, primarily trucks and buses.[136] Over 20,000 DPFs have been installed on nonroad engines worldwide.[137]

PASSIVE DIESEL PARTICULATE FILTER (VERIFIED)[138]

There are two different types of passive DPFs: catalyzed and regular. A catalyzed DPF will remove the soluble organic

TABLE 4
Examples of nonroad DPF installations

Type of equipment	Type of DPF	Location
Generator (600 kw)	Active DPF (by Rypos)	World Trade Center 7, NYC
Wheel Loader (CAT966)	Passive DPF (by Johnson Matthey)	World Trade Center 7, NYC
Wheel Loader (CAT 966GII)	Passive DPF (by Johnson Matthey)	American Asphalt, CA
Dump Trucks (Cummins, CAT and ITEC engines)	Passive DPF (by Johnson Matthey)	LA and surrounding areas, Seattle, Riverside County, San Diego

fraction (SOF) portion of the PM emissions in addition to regenerating the elemental carbon (soot) fraction of the PM.[139] In addition, the exhaust gas temperature required to ensure proper regeneration is slightly lower for the catalyzed passive DPF than for the regular passive DPF. The catalyzed DPF requires a temperature of approximately 210°C, depending on the catalyst used. The catalyst can also be added to the fuel as a fuel-borne catalyst. CARB staff has evaluated the catalyzed DPF as the most effective control technology because it can reduce PM emissions by over 85%.[140]

A regular DPF typically requires a greater than 260–320°C operating temperature for a significant portion of the duty cycle and has found limited application because of this.[141] If the necessary exhaust gas temperature cannot be achieved for the required portion of the daily duty cycle, an active DPF (see below) should be considered.

ACTIVE DIESEL PARTICULATE FILTER (VERIFIED)[142]

Active filters are used when the engine exhaust temperature is too low for a passive DPF and for older and dirtier engines. Because these systems do not rely on exhaust gas temperatures for regeneration, but rather on heat addition to the exhaust gas stream by use of burners or other means, an active DPF can successfully operate at low exhaust gas temperature. To increase the exhaust temperature for efficient regeneration, some commercial filter systems have incorporated burners, electrical heaters or fuel injection into the exhaust stream. These burners or electric heaters use about 1% of the total fuel consumption.[143]

Although emissions reductions are maximized with the use of ULSD, an active DPF typically does not require the use of ULSD fuel.[144] Like passive DPFs, an active DPF can be used alone or in conjunction with a DOC to reduce gaseous hydrocarbons and carbon monoxide. The California Air Resources Board has verified Lubrizol's actively regenerated DPF, the Combifilter™, for off-road applications in 1996–2004 diesel engines. The Combifilter system is verified for an 85% reduction in PM emissions.[145]

FLOW-THROUGH FILTERS (VERIFIED)[146]

There are three types of flow-through filters: 1) the catalyzed wire mesh filter; 2) the pertubated path metal foil filter; and 3) the catalytic particulate oxidizer. Flow-through filters can be comprised of wire mesh or pertubated path metal foils. Like other filter materials they can be used with active systems or be catalyzed and perform as a passive system.

CWMF EPA verified reduction numbers (when used with FBC)	
NO_x	0–9%
PM	55–76%
HC	75–89%
CO	50–66%

First, the catalyzed wire mesh filter (CWMF) is a new technology that has been EPA-verified for onroad use in conjunction with a fuel-borne catalyst.[147] A CWMF requires an exhaust gas temperature of 225°C for at least 25% of the daily duty cycle, which is lower than a DPF typically requires.[148] Thus, if a certain application does not allow for a DPF due to low exhaust gas temperatures, a CWMF might work. A CWMF weighs about the same as a DPF. EPA has verified the following emissions reduction rates for Clean Diesel Technologies, Inc.'s CWMF when used with a fuel borne catalyst: 0–9% for NO_x, 55-76% for PM, 75–89% for HC and 50–66% for CO.[149]

Generally, CWMFs should be visually inspected once per year, and in the event that the back pressure monitor signals an unreversed back pressure buildup,

the CWMF should be returned to an authorized dealer for thermal cleaning.[150] However, several CWMF units that have been in operation for over a year have been essentially maintenance free.[151] Currently, with limited quantities in production, the price range for a CWMF is $5,500 to $7,000.[152] As with all emerging technologies, prices could decline as demand for the technology grows.

Second, the pertubated path metal foil flow-through filter is an emerging technology of similar performance. It can also be catalyzed both for emissions control performance and regeneration characteristics.

Third, a Catalytic Particulate Oxidizer (CPO)[153] is a new technology developed for heavy and medium duty onroad and offroad diesel engines. The CPO has recently begun the CARB verification process but, as of February 16, 2005, has not been EPA or CARB verified.[154] The CPO has been certified[155] in Europe and is currently undergoing another verification process in Switzerland.[156] The technology does not trap or filter particulates but oxidizes them continuously. Oxidization is the process of adding oxygen to break down pollutants.[157] The chemical reaction between catalyst material and exhaust gases, according to the manufacturer's data, results in over 90% reduction of HCs, CO and PM. The CPO requires a minimum exhaust temperature of 190°C. According to the manufacturer's specifications, the CPO does not store ash, eliminating the need to open and clean the filter regularly. The CPO typically creates less backpressure than a DPF. CPOs costs range between $6,000–$8,000, depending on the size of the equipment.[158]

DIESEL OXIDATION CATALYSTS (VERIFIED)[159]

A diesel oxidation catalyst (DOC) is a type of catalyst (catalytic converter), which chemically converts HC, CO, soluble organic fraction (SOF) and polycyclic aromatic hydrocarbons (PAH) to water vapor and carbon dioxide. A DOC is a flow-through metal or ceramic substrate coated with a precious metal catalyst (e.g. platinum). The outside of the DOC is metal and looks similar to an exhaust muffler. DOCs are a "bolt on" application and they can be easily installed, typically as a direct muffler replacement. DOCs do not require engine modifications and generally are maintenance free. Although ULSD fuel is not required, PM emissions reductions are increased with the use of low sulfur or ultra-low sulfur diesel fuel. DOCs can be installed on old and new pieces of equipment; for example, some new Caterpillar equipment already comes with a DOC.

DOC in-use reduction numbers

NO$_x$	0%
PM	20-30%
HC	50-90%
CO	70-90%

A DOC is a proven and efficient technology that destroys large fractions of toxic emissions. Typically, DOCs reduce approximately 50–90% HC and 70-90% CO.[160] As to PM reduction, DOCs are effective for reducing the SOF component of the particulate matter.[161] The SOF portion of PM is composed of organic material from engine fuel and lube oil that forms on the surface of elemental carbon (black soot).[162] The SOF part of the particulate matter is often referred to as *wet PM*.[163] As a result, depending on the SOF concentrations in the particulate matter of diesel exhaust, DOCs reduce approximately 20–30% of PM.[164] SOF concentrations tend to decrease with newer engines.[165] If the reduction of black soot (solid fraction) is the goal, a DPF or a CWMF are more effective technologies than a DOC.

DOCs also cut down on aldehyde, smoke and odor.[166] However, DOCs do

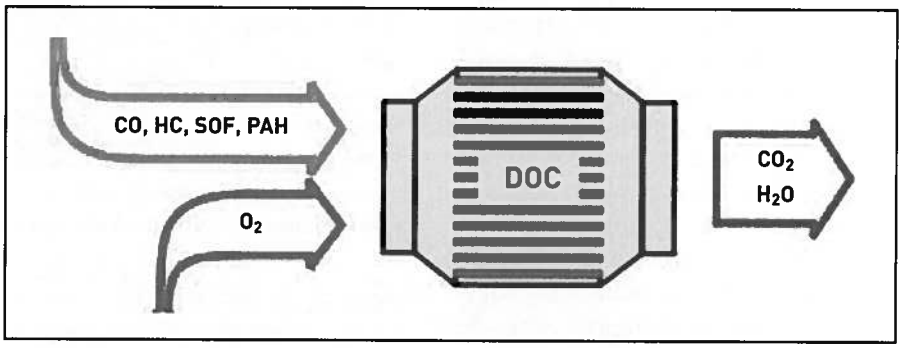
Construction equipment retrofit with a diesel oxidation catalyst.

COURTESY OF DONNA WEAVER, CONNECTICUT DEPARTMENT OF TRANSPORTATION

not remove NO_x. To increase emissions reductions, DOCs can be combined with other after-treatment technologies, including particulate filters. DOCs have already enjoyed widespread use in the onroad and nonroad sector. In fact, over 250,000 DOCs have been installed in new and retrofitted nonroad engines worldwide.[167] The cost of an oxidation catalyst is about 1–2% of the cost of new construction equipment. For example, the average cost for a DOC at the Boston Big Dig was about $2,500 per piece of construction equipment.[168] (See also the section on "Successes and Regional Programs.") Costs vary depending on the size of the equipment. Retrofit manufacturers will be able to give accurate cost estimates for each piece of equipment.

Overall, if a high number of construction vehicles should be retrofitted but funds are limited, DOCs might be an attractive option. DOCs might also be an attractive option if ULSD fuel is not available in the area. If ULSD fuel is not available, Environmental Defense encourages the use of low sulfur diesel (500 ppm) instead of typical nonroad diesel.

FIGURE 9
Schematic of a diesel oxidation catalyst



CRANKCASE EMISSIONS FILTRATION SYSTEMS WITH DOC (VERIFIED)

Crankcase emissions, on average, make up between 10–25% of total engine emissions over a prescribed test cycle but become very high (50–80%) on a relative basis when idling.[169]

Crankcase filter with DOC in-use reduction numbers	
NO_x	0%
PM	25-33%
HC	12-34%
CO	42-52%

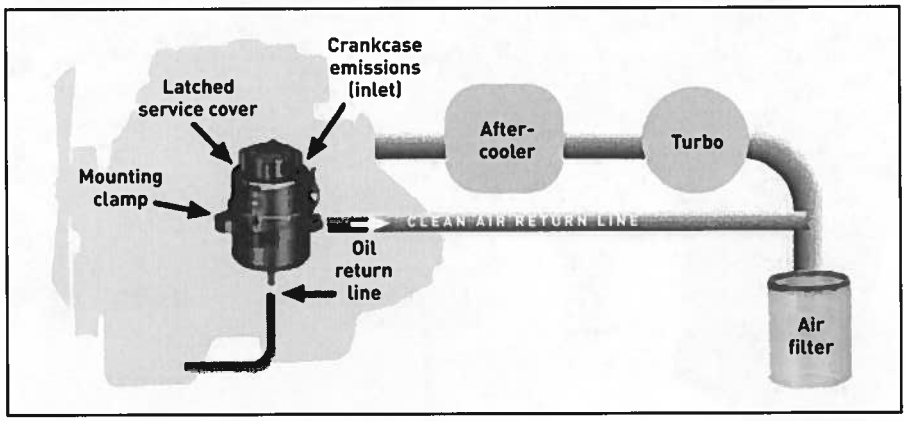
Targeting these emissions with pollution control technology can reduce overall engine exhaust pollution.

One example of a crankcase emissions filtration system is the Donaldson Spiracle™ crankcase filter. According to Donaldson, the filter eliminates 100% of all crankcase emissions and also eliminates under-hood fumes, reduces oil consumption by about 2–6 gallons/year and provides for a cleaner engine compartment. Donaldson reports that the Spiracle crankcase filter can be used alone, without other pollution control technologies, but EPA and CARB verification only apply the Spiracle when used with a DOC.

When combined with tailpipe pollution reduction technology, such as a DOC or a DPF, crankcase emissions filtration systems can achieve even greater emissions reductions. The Donaldson Spiracle crankcase filter is the only crankcase emissions reduction system that has been verified for use, when used with a DOC, by both EPA and CARB. The overall system reductions are based on the tailpipe reductions. Donaldson has approval for two different catalysts, depending upon the fuel sulfur level.[170] The use of a DOC with a Spiracle filter has been verified to reduce PM emissions by 25–33%, HC emissions by 12–34%, and CO emissions by 42–52%.[171] According to Donaldson, a DPF could be combined with the Spiracle filter in lieu of a DOC for a total engine emissions reduction of 89%. Neither EPA nor CARB have verified use of the Spiracle crankcase filter with a DPF.

The Spiracle system has a broad range of applications such as medium-duty and heavy-duty trucks, buses, off-road equipment and industrial generator sets.[172] For the retrofit market, the Spiracle system is available in two different sizes. For medium-duty applications, the end-user price for the system is approximately $325. For heavy-duty

FIGURE 10
Schematic of a crankcase emissions filtration system



Source: http://www.donaldson.com/en/engine/datalibrary/002509.pdf

applications, the end-user price is approximately $435.[173]

Nitrogen oxides reduction

In general, the retrofits discussed above do not reduce NOx, a key precursor to ozone/smog. Thus, to achieve NO_x emissions reductions, additional strategies must be used. There are a number of ways to reduce NO_x pollution, but not all are retrofit devices. NO_x pollution control technology includes: Selective Catalytic Reduction (SCR), NO_x adsorbers, lean NO_x catalysts, exhaust gas recirculation and fuel emulsifiers. The California Air Resources Board has determined that NO_x removal is cost effective at a cost of up to $13,600 per ton of NO_x reduced.[174] The Texas Emissions Reduction Program follows a similar standard of $13,000 per ton of NO_x reduced.[175]

SELECTIVE CATALYTIC REDUCTION (IN DEVELOPMENT)[176]

SCR systems add a reductant[177] (usually ammonia or urea) to diesel exhaust to convert NO_x to N_2. The exhaust and reductant are processed by a catalyst to reduce PM, HC and NO_x. Initial results from SCRs being used in combination with other technologies, such as a DOC, show the following possible reduction rates: 60%–80% NO_x, 25% PM, 50–70% HC and CO.[178] SCR systems must maintain a careful balance of proper urea injection and exhaust temperature. Typically, a mobile SCR needs to reach an exhaust gas temperature of 200–250°C to work. As soon as the required exhaust gas temperature is reached, NO_x is being reduced. Thus, unlike a DPF, no minimal daily duty cycle is necessary for the SCR to function properly. However, if too much urea is injected, ammonia slip (ammonia being emitted through exhaust pipe) may occur. Also, low exhaust temperatures can actually increase NO_x formation.[179] To avoid ammonia slip, proper control of the correct amount of urea injection is needed. For that reason, some mobile SCRs have a NO_x sensor before and a NO_x sensor after the urea injector to remotely record data.[180]

SCR combined with DOC in-use reduction numbers

NO_x	60–80%
PM	25%
HC	50–90%
CO	70–90%

While aided by the use of ULSD fuel, SCRs can be used with low sulfur fuel (500 ppm).[181] SCR's high NO_x reduction potential makes them an attractive option for NO_x emissions reduction. SCRs can be combined with a DOC or a DPF. SCRs can be used in stationary (i.e. generator set, compressors and pumps) as well as mobile applications. Marine vessels, ferries and trains have successfully installed SCRs.[182] Mobile SCRs are currently being used in a number of construction pilot programs.[183] As of February 11, 2005, the only SCR system that EPA/CARB have verified is Extengine's ADEC system. Another verification of a mobile SCR system for onroad engines is expected by the end of 2005.[184]

Urea, the reductant that is typically used in SCR systems, is a substance that is contained in agricultural fertilizer. Thus, urea is plentiful in the United States and while supply should not cause a problem, lack of infrastructure sometimes does. If a fleet of several vehicles is being retrofitted with SCRs, a urea dispenser can be set up at the construction site. Infrastructure problems sometimes occur if only one or two vehicles are being retrofitted because of the small quantities of urea needed. Urea distribution costs range between $0.70 and $35 per gallon.[185] The amount of urea needed per engine is a function of engine-out NO_x levels, which differ depending on the year the engine was built, and vehicle

size.[186] For every gallon of diesel fuel, about 5–10 ounces of urea are needed.[187]

The cost range for SCR systems varies greatly depending on the engine horsepower and the application. Mobile SCR systems in the 200–750 hp range cost between $12,500 and $15,000 for small quantities of SCR units.[188] These mobile SCR units are similar to an automotive type of system. Large stationary power generating SCR systems in the 750–2000 hp range can cost up to $80,000.[189]

NO_x ADSORBERS (IN DEVELOPMENT)

A NO_x adsorber, also sometimes referred to as a NO_x trap, works in two stages to remove NO_x from diesel exhaust. First, it uses a catalyst to adsorb NO_x emissions during lean operation.[190] Adsorb means to accumulate liquids or gases on a surface and "lean operation" occurs when the air-to-fuel ratio is high (perhaps 50 parts air to one part fuel), for example when a vehicle is going downhill or has a light load. Then, after the adsorber has been fully saturated with NOx, the system is regenerated (cleans itself) when the engine runs rich.[191] An engine runs "rich" when the air-to-fuel ratio is low (perhaps 29 parts air to one part fuel), for example when a vehicle is going uphill or has a heavy load. Also the exhaust gas temperature is very hot when an engine runs rich, which helps burn off the NO_x.

Unlike the other pollution controls discussed in this section, NO_x adsorbers are *not retrofittable*, i.e. they are not muffler replacements like diesel oxidation catalysts or diesel particulate filters and they can not be "added-on" like SCR. Instead they must be incorporated into the engine/vehicle design by the original equipment manufacturer. Although adsorbers have a high potential for NO_x emissions reductions, when sulfur-rich fuel is used the NO_x adsorption process is rapidly deactivated and rendered ineffective.[192] According to MECA, "To make this technology a commercial reality, low sulfur fuel is a requirement."[193] Near zero sulfur levels (less than 15 ppm sulfur) enable the application of catalyst and adsorption technology to run without interference.[194]

According to MECA, NO_x adsorber systems (in a low sulfur fuel environment) have the potential to provide "a high level of NO_x reduction across a wide range of operation conditions (temperature and NO_x concentration)—conditions which are consistent with the diversity in engine-out exhaust associated with both light- and heavy-duty diesel applications."[195] In fact, one manufacturer, Catalytica Energy Systems, states: "while still in early-stage development, our after-treatment approach is designed to offer a continuous production of a reactive reductant across a broad operating range to enable up to a 50% reduction in NO_x."[196] The operating temperature windows for NO_x adsorber technology ranges from 200 to 550°C.[197] At the present time, only prototypes of NO_x adsorbtion systems are available, so this technology is not yet commercially available or ready for CARB and/or EPA verification.

LEAN NO_x CATALYSTS (IN DEVELOPMENT)[198]

Lean NO_x catalyst technology can achieve a 10-40% reduction in NO_x emissions.[199]

Lean NOx catalyst in-use reduction numbers	
NO_x	10-40%

This technology is more effective when a supplemental hydrocarbon reductant is injected into the exhaust stream.[200] The hydrocarbons facilitate the conversion of NO_x to nitrogen and water vapor in the catalyst.[201] Lean NO_x catalysts are attractive because the technology requires no core engine modifications or

additional infrastructure and can be used to retrofit older machines.[202]

Like NO_x adsorbtion technology, lean NO_x catalysts require low sulfur fuel; however, this technology has a higher tolerance for sulfur, requiring fuel with a sulfur content of less than 250 ppm versus the less than 15 ppm required for adsorbtion technology.[203] Additionally, this technology imposes a fuel efficiency penalty of 4–7%.[204]

Combinations of different retrofit devices

Retrofit devices as well as fuel additives can be combined to maximize emissions reductions. Some retrofit devices combine, PM, HC, CO with NO_x reduction in one unit.[205] Three examples follow:

SCR SYSTEM COMBINED WITH PM EMISSIONS CONTROL (VERIFIED)[206]

Extengine's ADEC system combines NO_x and PM control technology in one unit. The NO_x is reduced with an SCR system, and the PM control is achieved with a DOC.[207] This technology has been verified by CARB as achieving a 25% reduction in particulate matter emissions, and an 80% reduction in NO_x emissions.[208] The City of Houston has successfully retrofitted two excavators with the ADEC system and has praised the emissions benefits.[209] The ADEC system can also be incorporated with other DPFs for even higher PM reductions, although each individual retrofit application would require evaluation.[210] With a DOC, and SCR with Ammonia Slip Catalyst,[211] the cost of the ADEC System is $14,500 before installation.[212]

ADEC (SCR/DOC system) verified reduction numbers	
NO_x	80%
PM	25%

Johnson Matthey is developing a technology that combines NO_x and PM control technology in one unit, the SCRT™ system (not verified as of February 2005) in which NO_x is reduced with an SCR and PM is reduced with a DPF. The SCRT system virtually eliminates HC and CO emissions and reduces PM and NO_x by 75–90%.[213] To date, approximately 100 SCRTs have been installed on heavy-duty diesel engines for field testing.[214] Johnson Matthey estimates that the SCRT will be commercially available by mid-2005.

Johnson Matthey (SCRT) field-testing reduction numbers (not verified as of February 2005)	
NO_x	75–90%
PM	75–90%
HC	Over 90%
CO	Over 90%

LEAN NO_x CATALYST WITH PM EMISSIONS CONTROL (VERIFIED)[215]

Cleaire Advanced Emission Control's Longview™ diesel emissions control system is a CARB and EPA onroad verified NO_x reducing technology.[216] The Longview system reduces smoke, odors and NO_x by 25%, PM by 85%, and HC and CO by 90%.[217] The Longview system integrates a NO_x reducing catalyst (Lean NO_x Catalyst) and a catalyzed DPF. The Longview is a muffler replacement system. The use of ULSD fuel and an exhaust gas temperature of 260°C for at least 25% of the daily duty cycle are required.[218]

Cleaire's Longview Filter CARB verified reduction numbers	
NO_x	25%
PM	85%
HC	90%
CO	90%

Longview systems have been successfully installed in onroad applications including refuse, transit, school bus, vocational work trucks, delivery trucks and line haul trucks. They have also been installed on nonroad mobile equipment such as motor graders, bucket loaders, agricultural tractors, agricultural water pumps and generators, some dating back to 1988.[219] The Longview needs regular maintenance; the maintenance interval

depends on the number of hours of operation. Cleaire has developed maintenance procedures and equipment that are available through local Cleaire distributors. Pre-installation data logging is typically not required.[220] The cost range[221] is between $18,500-$20,500 (including installation and tax) for 6–11 liter engines and about $21,000 (including installation and tax) for 12–15 liter engines.[222]

Cleaire's Lonestar system achieves about a 25–30% NO_x, a 50–70% PM, and a 40–60% HC and CO emissions reduction.[223] The Lonestar is a combination of a Lean NO_x catalyst and a high-performance DOC.[224] The Lonestar is currently undergoing CARB's verification process[225] and Cleaire is expecting verification by the end of 2005.[226] The Lonestar costs about $12,500 (including tax and installation) for 6–12 liter engines and about $15,000 (including tax and installation) for 12–15 liter engines.[227]

Cleaire's Lonestar system in-use reduction numbers (not verified as of February 2005)	
NO_x	25-30%
PM	50-70%
HC	40-60%
CO	40-60%

LOW PRESSURE EXHAUST GAS RECIRCULATION (IN DEVELOPMENT)[228]

Retrofitting exhaust gas recirculation (EGR) on a diesel engine offers an effective means of reducing NO_x emissions from the engine. Both low-pressure and high-pressure EGR systems exist, but low-pressure EGR is most suitable for retrofit applications because it does not require engine modifications.

As the name implies, EGR involves recirculating a portion of the engine's exhaust back to the charger inlet or intake manifold, in the case of naturally aspirated engines. In most systems, an intercooler lowers the temperature of the recirculated gases. The cooled recirculated gases, which have a higher heat capacity than air and contain less oxygen than air, lower combustion temperature in the engine and reduce NO_x formation. Diesel particulate filters are an integral part of any low-pressure EGR system, ensuring that large amounts of particulate matter are not recirculated to the engine.[229]

EGR systems are capable of achieving NO_x reductions of more than 40%. More than 1,500 EGR systems have been installed worldwide. EGR retrofit systems are now being installed in the U.S. on solid waste collection vehicles, buses and some city-owned vehicles. The cost of retrofitting EGR with a DPF on a typical bus or truck engine is about $13,000–15,000.

Currently, there is one low-pressure EGR system available commercially: STT Emtec's DNOx® system. SST Emtec is currently pursuing CARB onroad verification for this technology, and intends to pursue nonroad verification in the future.[230] STT Emtec has stated that though this technology has "not yet been used with nonroad engines, it can be," and the technology is commercially available for nonroad applications.[231]

Further details of the costs involved in replacing, refueling, and retrofitting diesel vehicles are available from EPA and MECA at http://www.epa.gov/otaq/retrofit/documents/meca1.pdf.

CHAPTER 7
Funding

Using cleaner diesel fuels or pollution control technologies on diesel engines powering construction equipment provides substantial public health benefits and improvements in air quality, but may also require investments in these fuels or technologies. Fortunately, state and local governments, fleet operators and vehicle owners have a number of options for financing cleaner diesel programs. This section of the *Cleaner Diesel Handbook* describes some programs on which state and local governments could model their own funding programs, followed by a discussion of funding available through federal sources.

State and local retrofit financing program models

CARL MOYER MEMORIAL AIR QUALITY STANDARDS ATTAINMENT PROGRAM

Both the state government of California and local air quality management districts play a substantial role in funding California's Carl Moyer Memorial Air Quality Standards Attainment Program (described in detail in the Success Stories section of this handbook). More information on the Carl Moyer Program is available on the California Air Resources Board web site, at: http://www.arb.ca.gov/msprog/moyer/moyer.htm.

In 1998/1999, the years of the program's inception, the legislature and the governor appropriated $25 million in funding for engine projects. Local air quality districts matched every two dollars of state money with a dollar contribution. In the third year of the program, state funding rose to $45 million for engine projects, and the district match was reduced to an average of one dollar per every $3.68 received. "In-kind" contributions, such as administrative costs, comprised up to 15% of match funds.[232]

In 2002, California voters approved Proposition 40, the Clean Water, Clean Air, Safe Neighborhood Parks, and Coastal Protection Act, which included approximately $40 million for Carl Moyer implementation.[233] These funds sustained the program through its fifth and sixth years. Carl Moyer's seventh year funding, approved through the 2004/2005 budget, was approximately $30.5 million.[234] The 2004/2005 budget also authorized an adjustment to Smog Check fees, establishing a continuous source of funding ($61 million/year) for the program.[235]

Assembly Bill 923, approved by the governor in September of 2004, authorized two additional sources of funding for the Carl Moyer program. The first was an increase in funding from tire fees, $25 million in 2005/2006 and $16 million in subsequent years. This brought state funding of the program to a total of approximately $86 million in 2005/2006 and $77 million thereafter.[236] The second increased the allowed surcharge on district-levied motor vehicle registration fees from $4 to $6.[237] Revenue from this program is expected to provide up to $55 million in local funding for Carl Moyer implementation in 2004/2005 and ensuing years.[238] Of the allowed $6 charge, $2 is to be used specifically for the Carl Moyer Program, for the new purchase, retrofit, repower, or add-on of equipment for previously unregulated agricultural sources, for the new purchase of schoolbuses pursuant to the Lower-Emission School Bus Progam, or for accelerated vehicle retirement or repair programs. The remaining $4 will continue to be used to "implement reductions in emissions from

vehicular pollution sources."[239] The district collecting the surcharge may use only 5% of the surcharge for administration of the program. Emissions reductions achieved through this program may not be used to offset emissions reductions obligations, nor are they tradable (i.e. available for sale/purchase) in a marketable pollution permit system. Rather, credits resulting from this funding must be "retired."[240]

NORTH CAROLINA'S MOBILE SOURCE EMISSIONS REDUCTION GRANT PROGRAM

The North Carolina Department of Natural Resources, through its Division of Air Quality, sponsors the Mobile Source Emissions Reduction Grant program in order to provide economic incentives for actual emissions reductions from on and off-road mobile sources. More information on the Mobile Source Emissions Reduction Grant Program is available on the NC Department of Natural Resources web site, at http://daq.state.nc.us/motor/ms_grants/

Funded by a 1/64-cent per gallon tax on gasoline sold in North Carolina, the program has awarded 78 grants totaling $5.74 million statewide since 1995. In 2004, $350,000 was awarded to area school districts to install diesel oxidation catalysts on school buses.[241]

THE TEXAS EMISSIONS REDUCTION PLAN (TERP)

The Texas Emissions Reduction Plan (TERP) combines incentive programs, research, and technology development aimed at improving air quality in Texas. The centerpiece of the program provides grants to eligible projects in nonattainment areas and other, TERP-designated, counties to offset the incremental cost associated with the activities to reduce emissions of NO_x from high-emitting mobile diesel sources.[242] More information on the TERP program is available in the Success Stories section of this handbook, and on the Texas Natural Resources Conservation Commission's web site, at: http://www.tnrcc.state.tx.us/oprd/sips/terp.html.

The Texas Commission on Environmental Quality (TCEQ) administers the TERP program. The Legislature established the TERP in 2001 through Senate Bill 5, and amended it through House Bill 1365 in 2003.[243] Total 2004 revenue was $141.7 million, $127.5 million of which was used for grant programs. The program was extended through 2010 by the Texas Legislature in the 79th regular session.[244]

For more specific information on funding sources, please refer to the "Texas Emissions Reductions Plan: Biennial Report to the Legislature": http://www.tceq.state.tx.us/assets/public/comm_exec/pubs/sfr/079_04.pdf

In addition, your State or local community may have funding available. Fleet owners should contact their local and state air quality and transportation agencies to learn more about available funding.

Federal grant funding

Construction companies, fleet operators or individuals operating construction equipment in states or local communities without funding programs such as those described above may find federal grant programs an option for assisting with the cost of retrofitting vehicles or purchasing clean fuels. EPA and the Diesel Technology Forum have compiled lists of funding sources that may be available in your area. Please visit, http://www.epa.gov/otaq/retrofit/retrofunding.htm and http://www.dieselforum.org/factsheet/programs.html for further details.

CHAPTER 8

Onroad and nonroad EPA/CARB verification

Both EPA and CARB operate onroad and nonroad retrofit technology verification programs. These verification programs test retrofit devices in order to assign PM and/or NO_x emissions reduction values to specific devices. Recently, EPA or CARB have verified new retrofit technologies for the nonroad sector.[245]

There is now a Memorandum of Agreement (MOA) between the Environmental Protection Agency and the California Air Resources Board for coordination and reciprocity in diesel retrofit device verification. This MOA is intended to expedite the verification and introduction of innovative emissions reduction technologies. Additionally, this MOA should reduce the effort needed for retrofit technology manufacturers to complete verification. In the near future, EPA and ARB will provide guidance on how this agreement will be implemented. Please see http://www.epa.gov/otaq/retrofit/documents/epa-arb_moa.pdf for additional detail.

The objective of the EPA Voluntary Diesel Retrofit Program Verification Process is to introduce verified technologies to the market in a cost-effective manner, while providing customers with confidence that verified technologies will provide emissions reductions as advertised.[246] This verification process will evaluate the emissions reduction performance of retrofit technologies, including their durability, and identify engine operating criteria and conditions that must exist for these technologies to achieve those reductions.[247] According to the CARB web site:

> ...the ARB has several programs relating to sale, use, or modification of emission control systems. The programs are specific to the type of device as well as the market for which it was designed. The CARB Verification Procedure provides a way to thoroughly evaluate the PM emission reduction capabilities and durability of a variety of diesel emission control strategies as part of a retrofit in-use program. It ensures that emission reductions achieved by a control strategy are both real and durable and that production units in the field are achieving emission reductions consistent with their verification. The verification procedure requires a minimum PM reduction of at least 25%. Although not a requirement at this time, if a diesel emission control strategy also reduces NO_x emissions by at least 15%, that reduction can also be verified. CARB has established a tiered verification plan which is illustrated in the table below...[248]

In-use testing

In addition to verifying pollution control technologies at certain levels of

TABLE 5
CARB verification classifications for diesel emissions control strategies

Pollutant	Reduction	Classification
PM	< 25%	Not verified
	> 25%	Level 1
	> 50%	Level 2
	> 85%, or ← 0.01 g/bhp-hr	Level 3

Source: http://www.arb.ca.gov/diesel/verdev/background.htm

emissions reductions, it is also very important to have rigorous in-use testing procedures. In-use testing—the process of testing a technology during real world operating conditions—yields the most accurate picture of emissions from a piece of equipment. By using a portable emissions testing system, researchers can get a better understanding of what is happening to emissions throughout the lifecycle of a piece of equipment. This procedure will ensure that technologies are performing at intended levels for the duration of use for a piece of equipment. For more details on EPA in-use testing requirements for manufacturers, please visit: http://www.epa.gov/otaq/retrofit/retrotesting.htm. More information about CARB's verification procedure and in-use compliance requirements is available at: http://www.arb.ca.gov/regact/dieselrv/dieselrv.htm.

Monitoring

While EPA and CARB in-use testing programs are designed for manufacturers of retrofit technologies, Environmental Defense believes that monitoring at a retrofit site can be a valuable part of a retrofit program because it allows all involved to see the actual pollution-control benefits of various retrofit strategies. This type of information can be invaluable to citizens and policy makers advocating on behalf of retrofit programs. We strongly encourage inclusion of good in-use monitoring procedures for all retrofit programs.

CHAPTER 9

Retrofit programs in State Implementation Plans

One way a state may be able to achieve emissions reductions that can be factored into its State Implementation Plan (SIP) is by including a rigorous retrofit program. A State Implementation Plan is a federally enforceable plan that describes a state's strategy for achieving and maintaining the public health based National Ambient Air Quality Standards (NAAQS).[249]

Recent EPA data shows that about half of all Americans live in places that fail to meet public health based standards for ozone and/or fine particulates. On April 15, 2004, EPA found 474 counties—home to 159 million Americans—out of compliance with the health-based eight-hour ozone standard.[250] In December 2004, EPA found that 224 counties in 20 different states are not meeting the nation's first $PM_{2.5}$ air quality standards.[251]

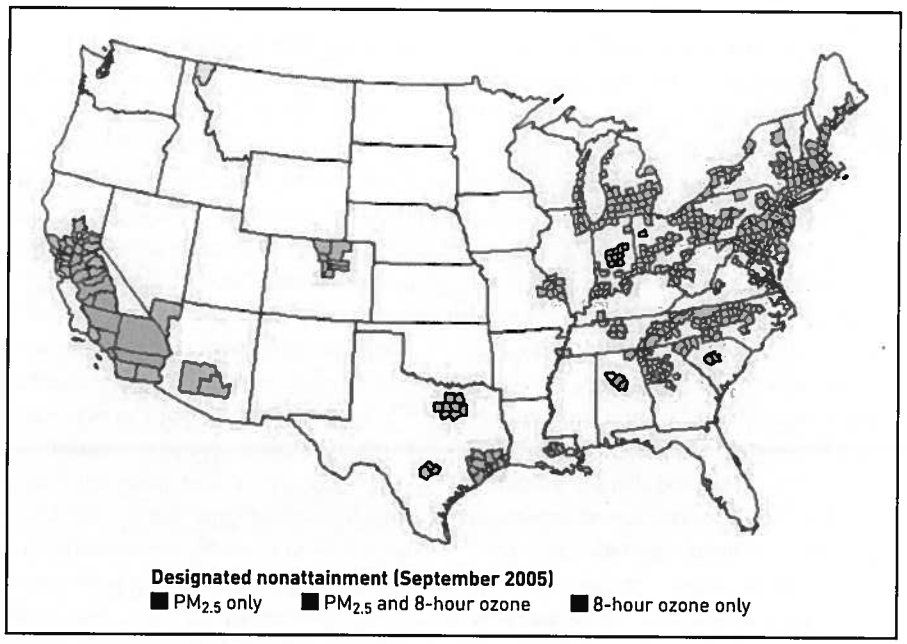
- To find out whether or not you live in a county that is meeting the public health based standards for ozone go to: http://www.epa.gov/ozonedesignations/statedesig.htm.
- To find out whether or not you live in a county that is meeting the federal $PM_{2.5}$ standards go to: http://www.epa.gov/pmdesignations/finaltable.htm.

Because more than half of the U.S. population lives in areas with unhealthy air, Environmental Defense believes that retrofit programs for all diesel equipment currently in use are critical components of any SIP.

If an area does want to quantify the benefits of a retrofit program, it may be able to do so by incorporating the benefits into the SIP, and it may also be able to use the benefits to demonstrate

FIGURE 11

Counties designated nonattainment for $PM_{2.5}$ and/or 8-hour ozone standard



Several counties have only a portion designated nonattainment. These counties are represented as whole counties on the map. Source: http://www.epa.gov/oar/oaqps/greenbk/mappm25o3.html

conformity to its SIP. Areas with large retrofit programs should work with the appropriate EPA Regional Office[252] regarding SIP credits.[253] EPA encourages early consultation between project sponsors, planners, and EPA Regional Offices during the development of a SIP and the calculation of SIP credits. Including a program in a federally enforceable document should be done carefully as legal action can be taken if the program is not carried out as described.

Additionally, project sponsors should work with their state air quality and transportation agencies as well as federal DOT and EPA regarding inclusion of a retrofit program in a SIP or conformity determination and the credits of that program. The state air pollution agency should assume primary responsibility for the calculation of retrofit credits and incorporation into the SIP. With the guidance of the appropriate EPA Regional Office, the state should work with areas, sponsors, planners, fleets, etc. in implementing retrofit projects and programs for this purpose.

To learn more about calculating SIP credits from retrofit projects, please refer to the EPA web page at: http://www.epa.gov/otaq/retrofit/aqsipcalc.htm ("Guidelines For States On Establishing SIP Credits From Heavy-Duty Engine Retrofit Projects"). A NESCAUM report, prepared for EPA in 1999, is a good resource for more information on how these types of calculations are made.[254] EPA is expected to issue additional guidance on how to calculate SIP credits for retrofits in Spring of 2005.[255]

CHAPTER 10

Tools for spurring retrofits

In this section of the handbook, Environmental Defense offers a framework for implementing retrofits and best management practices to help protect public health and ensure clarity for the construction industry and others who wish to reduce the pollution from *existing* diesel construction equipment. Local and state governments seeking to employ clean diesel fuels and technologies in construction projects have a number of options to encourage contractors to retrofit their existing diesel vehicles, use clean fuels or enact other best management practices, such as anti-idling measures. Environmental Defense believes these commitments to cleaner, healthier air can be incorporated in several different ways. The ideas outlined below could be used as: (1) an administrative or legislative commitment; (2) a contract specification, as a preference in the bidding process; (3) in an environmental impact statement, (4) in an executive order; or (5) in a Community Benefit Agreement.

To reduce diesel emissions from existing nonroad vehicles, Environmental Defense recommends both the installation of best available technology and the use of cleaner fuels, including diesel fuel that has 15 ppm of sulfur or less (ULSD). In Environmental Defense's view, "best available" technology is that which achieves maximum emissions reduction of fine particulate matter and NO_x for a given particular engine type and application. Because specific emissions control technologies require different engine performance characteristics (temperature, duty cycles, etc.), each application has to be reviewed to determine the appropriate retrofit technology. Some flexibility and combinations of different technologies will be needed to achieve maximum emissions reductions for each application. Therefore, we suggest a cascading series of emissions-control choices, ranked according to emissions-reduction performance. In this way, states, local agencies, fleet operators and contractors will be able to match best technologies to the specific engine and application, and will be required to achieve the maximum possible clean air benefit.

To begin, there should be an overarching, central commitment to using DPFs in combination with a NO_x control. DPFs can achieve particle reductions of up to 90%. If no NO_x control is available, then the DPF can be used alone. If it is not possible to use a DPF, then Environmental Defense suggests using a DOC or a CWMF in combination with NO_x control. Diesel oxidation catalysts can achieve particle reductions of 20–30%, and CWMFs can reduce PM by more than 50%. If no NO_x control is available, then the DOC or CWMF can be used alone. Lastly, if no pollution control technology can be used, then Environmental Defense suggests using the cleanest possible fuels. Switching from onroad diesel fuel (500 ppm sulfur content) or from nonroad diesel fuel (about 2000-3000 ppm sulfur content) to ULSD (15 ppm sulfur content or less) can reduce particulate matter, smoke and sulfate emissions.[256]

Environmental Defense advises using only technologies that are on or in the queue for EPA's or CARB's verified lists to ensure that you are installing a high quality product on your diesel engine. However, states and local governments should include pilot or demonstration products if they wish to investigate promising new emissions control technologies.

DPF plus NO_x control

▼

If not technologically feasible

▼

DPF without NO_x control

▼

If not technologically feasible

CWMF or DOC plus NO_x control

▼

If not technologically feasible

CWMF or DOC without NO_x control

▼

If not technologically feasible

Cleaner fuels

Sample legislation regarding green contracting (retrofits and clean fuels)

According to the federal Clean Air Act, only EPA may set emissions standards for new nonroad engines and vehicles. EPA sets emissions standards for *new* nonroad engines and *new* nonroad vehicles. In May of 2004, EPA issued a rule setting emissions standards for new nonroad engines as well as regulating the amount of sulfur allowed in diesel fuel for the nonroad sector.[257] For more information on this new nonroad rule, please refer to: http://www.epa.gov/nonroad-diesel/. EPA has addressed new nonroad vehicles, but there are many older vehicles on the road today. Therefore, Environmental Defense recommends that states and local municipalities encourage retrofits and the use of cleaner fuels for *existing* nonroad vehicles. Cleaning up older diesel engines will be an important piece for reducing air pollution while the new nonroad rule phases in.

To encourage retrofits on existing nonroad equipment and the use of cleaner fuels, Environmental Defense suggests that state and local municipalities pass regulations (also sometimes referred to as "green contracting laws") regarding the use of retrofit technology on state/local municipality owned nonroad diesel vehicles as well as nonroad diesel vehicles used when contracting with state/local municipalities. Environmental Defense also suggests including the use of ULSD fuel (15 parts per million of sulfur or less) as one of the contract specifications.

NEW YORK CITY'S LOCAL LAW 77

New York City's Local Law 77 requires the City to use ULSD fuel and retrofits on city-owned nonroad equipment.[258] Local Law 77 also includes use of retrofits and ULSD as a contract specification in public works contracts.

Excerpts from New York City's Local Law 77, Section 1:[259]

b. (1) Any diesel-powered nonroad vehicle that is owned by, operated by or on behalf of, or leased by a city agency shall be powered by ultra low sulfur diesel fuel.

(2) Any diesel-powered nonroad vehicle that is owned by, operated by or on behalf of, or leased by a city agency shall utilize the best available technology for reducing the emission of pollutants.

c. (1) Any solicitation for a public works contract and any contract entered into as result of such solicitation shall include a specification that all contractors in the performance of such contract shall use ultra low sulfur diesel fuel in diesel-powered nonroad vehicles and all contractors in the performance of such contract shall comply with such specification.

(2) Any solicitation for a public works contract and any contract entered into as

a result of such solicitation shall include a specification that all contractors in the performance of such contract shall utilize the best available technology for reducing the emission of pollutants for diesel-powered nonroad vehicles and all contractors in the performance of such contract shall comply with such specification.

NEW YORK STATE ASSEMBLY LAW ON CONSTRUCTION IN LOWER MANHATTAN

The Coordinated Construction Act for Lower Manhattan, passed by both the New York State Senate and Assembly, commits New York State construction projects in lower Manhattan to control emissions by requiring that nonroad vehicles be powered with ULSD and retrofit with technologies such as oxidation catalysts, particulate filters or an emissions control technology that achieves the lowest particulate matter emissions.[260]

Excerpts from Section 4 of the Coordinated Construction Act for Lower Manhattan:

e. Notwithstanding any general, special or local law or rule or regulation to the contrary, a public agency shall require contractors and subcontractors to *use only ultra-low sulfur diesel fuel* to power the diesel-powered non-road vehicles with engine horsepower (HP) rating of 60 HP and above used on lower Manhattan redevelopment projects and, where practicable, to reduce the emission of pollutants by retrofitting such non-road vehicles with oxidation catalysts, particulate filters, or technology with comparable or better effectiveness. (emphasis added)

SACRAMENTO'S OZONE SUMMIT MODEL "GREEN CONTRACTING" ORDINANCE

The Sacramento Ozone Summit, a gathering of agency heads and elected officials from around the Sacramento federally designated Ozone Non-attainment Area, led to the design of a green contracting model ordinance by the Sacramento Metropolitan Air Quality Management District's Mobile Source Division. This ordinance offers a voluntary and flexible approach to reducing construction site emissions that would certify rental firms/construction firms as "green contractors." Being "green" would entail curtailing activities on "spare the air" days, mitigating emissions using ULSD or emulsified fuel, and replacing/retrofitting engines using Carl Moyer incentive funds or Sacramento Emergency Clean Air Transportation Funds (SECATF), which at one point totaled $28 million. "Green contractors" would then receive bidding bonuses that would give them a competitive advantage in the contract bidding process. "Green contractors" would also be subject to detailed monitoring of construction equipment.[261]

Excerpts from Section 3. of the Model "Green Contracting" Ordinance:

Within 90 days of adoption of this Chapter, the *(insert name of local agency)* shall designate a Program Manager *(such as the agency's manager responsible for procurement)* and shall develop and implement a Green Contracting Program. The Green Contracting Program must include a description of the plan to encourage contractors operating within the *(insert name of local agency)* to procure and to operate low-emission vehicles and to obtain low-emission fleet status for off-road equipment fleets and heavy-duty on-road vehicle fleets. The (insert name of local agency)'s Green Contracting Program must focus on fleet owners that have contracts for (insert name of local agency) business.

The (insert name of local agency) must include contract bid language that would

implement the following Green Contracting Program requirements. See (c) for the exception to this requirement.

Sample contract specifications

BOSTON BIG DIG

Excerpt from Section 721.562 of the Big Dig Contract Specifications.

Methods that shall be used by the Contractor to control nuisance odors associated with diesel emissions from construction equipment include:

Turning off diesel combustion engines on construction equipment not in active use and on dump trucks that are idling while waiting to load or unload material for 5 minutes or more.

Establishing a staging zone for trucks that are waiting to load or unload material at the contract area, in a location where the diesel emissions from the trucks will not be noticeable to the public.

Locating combustion engines away from sensitive receptors such as fresh air intakes, air conditioners, and windows. *In addition to the above diesel emission control measures, all off-road diesel powered equipment used for this contract shall contain oxidation catalyst emission control equipment on the exhaust system side of the equipment.* (emphasis added)

Please note that when the Boston Big Dig contract specifications were drafted, ULSD fuel (sulfur content of 15 ppm) was not available in the Boston region. For that reason, DPFs could not be used as retrofit technology and DOCs only were used.

CONNECTICUT I-95 NEW HAVEN HARBOR CROSSING CORRIDOR IMPROVEMENT PROGRAM (NHCC PROJECT)

Connecticut's Department of Transportation (ConnDOT), the Connecticut Department of Environmental Protection, the Connecticut Department of Motor Vehicles, and the Connecticut Construction Industry Association worked together to create a contract specification to improve quality of life during the long-lasting I-95 New Haven Harbor Crossing Corridor Improvement Program.

Notice To Contractors (NTC)—Diesel Vehicle Emission Controls

All diesel powered construction equipment with engine horsepower (HP) ratings of 60 HP and above, that are on the project or are assigned to the contract for a period in excess of 30 days ***shall be retrofitted with Emission Control Devices and/or use Clean Fuels*** in order to reduce diesel emissions. In addition, all motor vehicles and/or construction equipment shall comply withal pertinent State and Federal regulations relative to exhaust emission controls and safety. (emphasis added)

Truck staging zones

The contractor shall establish truck-staging zones that are waiting to load or unload material at the contract area. Such zones shall be located where the diesel emissions from the trucks will have minimum impact on abutters and the general public.

Idling

Idling of delivery and/or dump trucks, or other diesel powered equipment shall not be permitted during periods of non-active use, and it should be limited to three minutes in accordance with the Regulations of Connecticut State Agencies Section 22a-174-18(a)(5).[262]

Environmental performance commitments in environmental impact statements

An Environmental Impact Statement (EIS) is a document required for major

federal actions (or regional, state, or local actions funded with substantial federal monies) that may significantly affect the environment. Describing the positive and negative effects of the major project and citing alternative actions, an EIS serves as a tool for decision-making.

When a governmental agency plans a construction project, Environmental Defense strongly encourages the use of the cleanest possible fuel and pollution control technology in the Environmental Performance Commitments (EPC) section of the project's Environmental Impact Statement (EIS). This puts interested parties on notice that there will probably be future contract specifications that follow the guidelines established in the EIS. Thus, requirements for clean diesel equipment and clean diesel fuel can come out of the EIS and bidding process. Although the following two examples include the type of language that a government seeking cleaner diesel fuel and technology use might include in an Environmental Impact Statement's EPC section, Environmental Defense also recommends that:

- Emissions-reductions steps such as the use of ULSD or best available reductions technologies (BART) should be extended to onroad trucks servicing the construction site and all stationary diesel generators used in connection with construction.
- Emissions standards should cover nonroad vehicles of 50 HP and greater.
- Anti-idling measures include a powerful enforcement plan and mechanism.
- Regular emissions testing be conducted at construction sites, and that the results of these tests be made publicly available, to ensure compliance and accountability.
- Trucks and construction equipment be marked with a label or sticker that certifies that they are using ULSD fuel as well as retrofit technology.
- Truck staging zones should be established for diesel-powered vehicles waiting to load or unload materials. The zones should be located where diesel emissions will have the least impact on abutters and the general public.
- Idling should limited to three minutes for delivery and dump trucks and other diesel-powered equipment (with some exceptions).
- All work should be conducted to ensure that no harmful effects are caused to adjacent sensitive receptors, such as schools, hospitals, and elderly housing.
- Diesel-powered engines should be located away from fresh air intakes, air conditioners, and windows.

New York's Route 9A Draft Supplemental Environmental Impact Statement[263] can serve as a sample for how diesel emissions impacts can be mitigated and addressed in an EIS.

Excerpt from New York's Route 9A Draft Supplemental EIS, page 10:

All diesel construction engines—excluding trucks—would use ultra low-sulfur diesel (ULSD) fuel; where practicable, engines larger that 60 horsepower (HP) would include emissions reduction measures to reduce emissions of PM and volatile organic compounds (VOCs). For the purpose of this study, it was assumed that PM emissions from all such engines would be reduced by 40 percent—the average reduction achieved by using diesel oxidation catalysts (DOC). PM emissions may be further reduced in cases where diesel particle filters (DPF) would be used—85 percent reductions or higher can be achieved with this technology. Since it is uncertain at this time what emission reduction technologies would be most efficient with each equipment type,

and since DOCs reduce more VOCs, which are ozone precursors and are of regional concern, the environmental performance commitments (EPCs) provide the flexibility to utilize either DOC or DPF control technologies. Therefore, the minimum PM emissions reduction of DOCs was assumed for the local impact analyses.[264]

Similarly, the Fulton Street Transit Center Draft EIS[265] also contains language suggesting the use of ULSD fuel and retrofit technology to mitigate the impact of unhealthy diesel emissions.

Excerpts from the Fulton Street Transit Center Draft EIS, page 2:

The Build Alternatives would be implemented with incorporation of Environmental Performance Commitments (EPCs). The EPCs consist of onsite measures that would include the use of ultra-low sulfur diesel (ULSD), with sulfur content less than 15–30 parts per million (ppm) fuel and retrofit technology in heavy-duty engines and off-road construction vehicles operating during the construction of the FSTC, including during year 2005/2006, the peak period of construction. Other EPCs include a dust control plan for the construction site including a soil erosion sediment control plan which would be part of the Construction Environmental Protection Program (CEPP). The dust control plan could include: spraying of a (non-hazardous, biodegradable) suppressing agent on disturbed soil and other surfaces; containment of fugitive dust; and adjustment of work practices to reflect meteorological conditions as appropriate.[266]

Community Benefit Agreements

Community Benefit Agreements (CBAs) can also serve as a tool to improve air quality. CBAs are project-specific contracts between developers of a major project and community organizations. CBAs are safeguards to ensure that local community residents share in the benefits of major developments. They allow community groups to have a voice in shaping a project, press for community benefits that are tailored to their particular needs, and enforce developer's promises.

The CBA process begins with interested members of the community, who identify how a proposed development project can benefit residents and workers. Once a list of potential benefits is determined, community members meet with the developer and/or representatives of the city to negotiate a CBA. Each CBA is unique, reflecting the needs of a particular community.

The first full-fledged CBA came in 2001, when a large coalition of community groups negotiated a far-reaching agreement with the developer of the Staples Center for the Los Angeles Sports and Entertainment District. This was followed by four more CBAs on projects across Los Angeles. A dozen additional projects in Los Angeles have community benefits provisions incorporated into their respective development agreements.

Many communities across the country are now using the community benefits model. In San Jose, two projects have incorporated community benefits provisions into the development agreements, while groups in at least six cities—Denver, Seattle, Milwaukee, Miami, New York and New Haven—are actively pursuing community benefits.[267]

In 2004, community groups, environmental organizations, and labor unions joined together and reached a CBA with Los Angeles World Airports (LAWA), the government entity that operates LAX.

Excerpts from the LAX CBA regarding reducing harmful diesel emissions via cleaner fuels and retrofits:

F. Construction Equipment.
1. Best Available Emissions Control Devices Required. LAWA shall require that all diesel equipment used for construction related to the LAX Master Plan Program be outfitted with the *best available emission control devices primarily to reduce diesel emissions of PM, including fine PM, and secondarily, to reduce emissions of NO_x.* This requirement shall apply to diesel-powered off-road equipment (such as construction machinery), on-road equipment (such as trucks) and stationary diesel engines (such as generators). The emission control devices utilized for the equipment at the LAX Master Plan Program construction shall be: (i) verified or certified for use by CARB for on-road or off-road vehicles or engines; or (ii) verified for use by EPA for on-road or off-road vehicles or engines. Devices certified or verified for mobile engines may be effective for stationary engines and that technology from EPA/CARB on-road verification lists may be used in the off-road context. (emphasis added)

5. ULSD and Other Fuels.
a. ULSD and Other Fuel Requirements. All construction equipment used for construction related to the LAX Master Plan Program *shall use only Ultra-Low Sulfur Diesel fuel (15 ppm or lower), so long as there are adequate supplies of ULSD* in the Southern California area. If adequate supplies of ULSD are not available in the Southern California area, then other fuels may be used, provided that the other fuels do not result in an greater emissions of fine PM or nitrogen oxides than that which would be produced by use of ULSD at 15 ppm or lower. Cost of ULSD shall not be a consideration in determining "adequate supplies." (emphasis added)

For more information on the LAX CBA go to: http://www.environmentaldefense.org/documents/4174_LAX_CBA_Summary.pdf. For the exact language of the LAX CBA go to: http://www.environmentaldefense.org/documents/4201_LAX_CBA_full.pdf.

APPENDIX A

Acronyms

BART Best Available Retrofit Technology

CARB California Air Resources Board

CA/T Project Central Artery Tunnel Project (Big Dig, Boston)

CCIA Connecticut Construction Industries Association

CNG Compressed Natural Gas

CO Carbon monoxide

CIAQC Construction Industry Air Quality Coalition

CPO Catalytic Particulate Oxidizer

CCRT Catalyzed Continuous Regenerating Technology

CRT Continuous Regenerating Technology

CWMF Catalyzed Wire Mesh Filter

DMV Department of Motor Vehicles

DOC Diesel Oxidation Catalyst

DOT Department of Transportation

DPF Diesel Particulate Filter

DTF Diesel Technology Forum

EGR Exhaust Gas Recirculation

EIS Environmental Impact Statement

EPA United States Environmental Protection Agency

EPC Environmental Performance Commitments

FBC Fuel Borne Catalyst

HC Hydrocarbon

LNG Liquefied Natural Gas

LSD Low sulfur diesel fuel (500 ppm)

MECA Manufacturers of Emissions Control Association

MOA Memorandum of Agreement

MTA Massachusetts Turnpike Authority

NAAQS National Ambient Air Quality Standards

NESCAUM Northeast States for Coordinated Air Use Management

NO_x Nitrogen oxides

OEM Original Equipment Manufacturer

OTAQ Office of Transportation and Air Quality

PHA Port of Houston Authority

PM Particulate matter

$PM_{2.5}$ Particulate matter smaller than 2.5 microns

PM_{10} Particulate matter smaller than 10 microns

SCAQMD South Coast Air Quality Management District

SCR Selective Catalytic Reduction

SIP State Implementation Plan

SOF Soluble Organic Fraction

TCEQ Texas Commission on Environmental Quality

TERP Texas Emission Reduction Program

TNRCC Texas Natural Resource Conservation Commission

ULSD Ultra low sulfur diesel fuel (15 ppm)

VOC Volatile organic compound

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APPENDIX B

Retrofit manufacturers contact information

Manufacturer	PM, HC, CO control	NO_x control	Contact information
Argillon LLC http://www.argillon.com	SCR	SCR	Mr. Gary D. Keefe Argillon 5895 Shiloh Rd. Suite 101 Alpharetta, GA 30005 678.341.7532 404.409.3492 (Mobile) 678.341.7509 (Fax) gary.keefe@argillon.com
Caterpillar, Inc. http://www.caterpillar.com EPA Verified Technology for Heavy Duty Highway Use http://www.epa.gov/otaq/retrofit/retroverifiedlist.htm	DOC (CCM: Catalyzed Converter Muffler DPF	SCR	Mr. Steve Hurd Mos 10 PO Box 610 Mossville, IL 61552-0610 309.578.6088 309.578.7152 (Fax) hurd_stephen_s@cat.com
Cleaire Advanced Emission Controls, LLC http://www.cleaire.com Longview® CARB and EPA Verified Technology for Heavy Duty Highway Use	Longview® Lonestar™	Longview® Lonestar™	John Egan 14775 Wicks Blvd. San Leandro, CA 94577 510.347.6163 800.308.2111 510.347.6181 (Fax) john.egan@cleaire.com Tim Taylor Director of Strategic Market Development 916.296.7049 707.220.7260 (Fax) tim.taylor@cleaire.com
Clean Air Power, Inc. www.cleanairpower.com	Catalytic Particulate Oxidizer (CPO)	Mobile SCR DOX SCAT (reduces NO-)	Frits Tan 9837 Whithorn Drive Houston, TX 77095 832-731-7372 (mobile) 281-463-8883 281-463-8951 fax ftan@cleanairpower.com
Clean Diesel Technologies Inc. http://www.cdti.com EPA Verified Technology for Heavy Duty Highway Use[a]	SCR FBC Platinum Plus® Purifier System (fuel borne catalyst plus DOC) FBC Platinum Plus® Purifier System and Catalyzed Wire Mesh Filter (FBC/CWMF) System	SCR	Mr. Glen Reid 300 Atlantic Street, Ste 702 Stamford, CT 06901 203.327.7050 203.323.0461 greid@cdti.com

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Manufacturer	PM, HC, CO control	NO_x control	Contact information
Combustion Components Associates Inc. http://www.combustioncomponents.com	Mobile SCR		Mr. T.J. Tarabulski 884 Main Street Monroe, CT 06468 203.268.3139 203.223.8246 (Mobile) 203.261.7697 (Fax) tarabulski@cca-inc.net
DCL International Inc. http://www.dcl-inc.com	DOC, DPF (active and passive)		Gerry Wilson P.O. Box 90 Concord Ontario, Canada L4K1B2 905.660.6450, ext. 292 gwilson@dcl-inc.com
Donaldson Company, Inc. http://www.donaldson.com EPA Verified Technology for Heavy Duty Highway Use[b]	DOC, DPF (also offers crankcase emissions filtration system)		Mr. Fred Schmidt 1400 West 94th Street Minneapolis, MN 55440 952.887.3835 952.887.3008 (Fax) fschmidt@mail.donaldson.com
Engelhard Corporation http://www.engelhard.com EPA Verified Technology for Heavy Duty Highway Use[c]	DOC, DPF		Mr. Barry Bambo 101 Wood Avenue Iselin, NJ 08830 732.205.7277 732.205.5687 (Fax) Barry.Bambo@engelhard.com
Engine Control Systems, a Division of Lubrizol http://www.lubrizol.com/enginecontrol EPA Verified Technology for Heavy Duty Highway Use[d]	DOC AZ Purimuffler™, DPF Purifilter™		Ms. Michelle Bellamy 165 Pony Drive Newmarket, Ontario L3Y 7V1 800-661-9963 or 905-853-5800 (customer service) 905-853-5801 (Fax) ecs@lubrizol.com
Environmental Solutions Worldwide, Inc. Catalyst Division http://www.cleanerfuture.com/products/ EPA and CARB verification pending	Metallic (high performance— 50% plus PM reduction) DOC[e]		Mr. Frank Haas 571 Chrislea Rd. #5 Woodbridge, Ontario, Canada L4L8A2 905.850.9970 905.850.9925 Fax fhaas@cleanerfuture.com

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Manufacturer	PM, HC, CO control	NO_x control	Contact information
Extengine Transport Systems, LLC http://www.extengine.com/index.html	Mobile and Stationary SCR (ADEC System) DOC Hybrid DPF-C (Diesel Particulate Filter and Catalyst) DPF (passive and active)	Mobile and Stationary SCR (ADEC System)	Mr. Phillip Roberts 1370 S. Acacia Ave Fullerton, CA 92831 714.774.3569 714.774.4036 (Fax) roberts@extengine.com
Fleetguard Emission Solutions	DOC (50% pm reduction), DPF		Western U.S.: Rob Ferguson 2931 Elm Hill Pike Nashville, TN 37214 615.366.9855 812.377.7137 (Fax) rob.r.ferguson@fleetguard.com Eastern U.S.: Jennifer Kain 2931 Elm Hill Pike Nashville, TN 37214 812-377-3132 812-377-7137 (Fax) jennifer.kain@fleetguard.com
International Truck and Engine Corporation http://www.greendieseltechnology.com	DOC, DPX	Green Diesel Technology	Mr. Peter Reba International Truck and Engine Corporation 4201 Winfield Road Warrenville, IL 60555 630-753-6537 (Office) 630-753-6537 (FAX) peter.reba@nav-international.com

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Manufacturer	PM, HC, CO control	NO_x control	Contact information
Johnson Matthey – Environmental Catalysts and Technologies http://www.jmcsd.com/html/crt.html http://www.matthey.com/divisions/catalytic.html EPA Verified Technology for Heavy Duty Highway Use[1]	DOC, DPF (CRT or CCRT) SCRT(tm) systems (SCR+DPF) EGRT(tm) systems (EGR+DPF).	SCR SCRT(tm) systems (SCR+DPF) EGRT(tm) systems (EGR+DPF).	Mr. Brett Alkins 380 Lapp Road Malvern, PA 19355 610.341.8356 484.354.8159 (Mobile) 610.971.3116 (Fax) alkinbd@jmusa.com or Mr. Jim Hale 380 Lapp Road Malvern, PA 19355 610.476.0161 (Mobile) 717.246.6049 (Home Office) 610.971.3116 (Fax) halejr@jmusa.com or Marty Lassen 434 Devon Park Drive Wayne, PA 19087 610.341.3404 610.971.3116 (F) 610.476.0131 (M) lassen@jmusa.com
Nett Technologies, Inc. http://www.nett.ca	DOC: D-Series (low temperature DOC) M-Series (high performance, very low back pressure) NETT Series (standard DOC) DPF: SF Catalyzed SK Catalyzed (lower temperatures) SE Catalyzed (sulfur tolerant) SJ Catalyzed (lower temperature, sulfur tolerant)		For technical information: Mr. Wayne Borean 6707 Goreway Drive Mississauga, Ontario 800.361.6388 905.672.5949 (Fax) sales@nett.ca or Ms. Laura McBurney or Mr. Jorge Santos 800.631.6388
PuriNOx	PuriNOx	PuriNOx	Ron O. Dunfee 29400 Lakeland Blvd. Wickliffe, Ohio 44092 Office: (440) 347-6116 Fax: (440) 347-6978 Cell: (440) 463-2038 Email: rod@lubrizol.com

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Manufacturer	PM, HC, CO control	NO_x control	Contact information
RYPOS Inc. http://www.rypos.com/html/index.html	Regular or catalyzed DPF Active DPF (Rypos Trap™)		Mr. Frank DePetrillo 3 Industrial Park Road Medway, MA 02053 Phone: 508.533-9655 Fax: 508.533-9656 Sales: fd@rypos.com

Engine Manufacturer Contacts
http://www.epa.gov/otaq/retrofit/cont_engmfrs.htm

EPA Verified Retrofit Technologies
http://www.epa.gov/otaq/retrofit/retroverifiedlist.htm

CARB Verified Retrofit Technologies
http://www.arb.ca.gov/diesel/verdev/verdev.htm

[a] EPA, "Verified Products." August 11, 2004. Online resource, available at: http://www.epa.gov/otaq/retrofit/retroverifiedlist.htm Last accessed 03/01/05.
[b] Ibid.
[c] Ibid.
[d] Ibid.
[e] DOC specifically designed for use on small compression ignition engines. Examples of these are small generators and construction equipment such as mixers and concrete floats. Environmental Technology Verification (ETV) Canada Inc. "Current Program Graduates and Licenses." Online resource, available at: http://www.etvcanada.com/English/e_progGrad.htm Last accessed 03/01/05.
[f] EPA, "Verified Products." August 11, 2004. Online resource, available at: http://www.epa.gov/otaq/retrofit/retroverifiedlist.htm Last accessed 03/01/05.

DISCLAIMER: Environmental Defense does not endorse any particular fuel or fuel additive supplier. This is not a comprehensive list of fuel suppliers and is intended to serve only to illustrate that there is a wide variety of choices available. This list was last updated in April 2005.

APPENDIX C

Distributors of ultra low sulfur diesel fuel, emulsified fuels, fuel additives, and synthetic engine oil

Please check with your local Ultra Low Sulfur Diesel (ULSD) fuel distributor whether your fleet needs ULSD fuel No. 1 or No. 2. For example, if a fleet has been using Low Sulfur Diesel (500 ppm) No. 1 then ULSD No. 1 is needed. If only ULSD No. 2 is available and Low Sulfur Diesel No. 1 has been previously used, the engine needs to be tuned accordingly.

1. ULSD Fuel Brokerage

Ultra Low Sulfur Diesel Fuel Brokerage
Ultraco LLC
Mr. Timothy J. Niles
101 Farren Ct, Suite 100
Cary, NC 27511-4559
866.857.3487 or 919.380.0778
http://ultraco.us

2. ULSD Distributors

Northeast

Connecticut, Delaware, Maine, Maryland, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont, Washington, D.C.

Mr. David Wright, ConocoPhillips
600 North Dairy Ashford (77079-1175)
P.O. Box 2197
Houston, TX 77252-2197
Phone 281.293.1544
Fax 281.293.6113
David.W.Wright@conocophillips.com
http://www.conocophillips.com/products/ultralowsulfur/index.htm

or

Mr. Steven J. Levy, Sprague
4 New King Street
White Plains, NY 10604
Phone 914.328.6770 Fax 914.701.2819
914.284.2188 (Pager)
slevy@radenergy.com
www.spragueenergy.com

or

Ms. Debbie McNeal, Sunoco
Ten Penn Center
1801 Market Street
Philadelphia, PA 19103
800.842.0339 Ext. 1
Phone 215.977.3000
Fax 215.246.8119
DLMCNEAL@sunocoinc.com
http://www.sunocoinc.com/

Midwest, West Coast

Oregon, Washington, California, Arizona (Phoenix area), all Midwest States, Chicago area, Detroit area, Toledo area, Cleveland and Columbus area.

Ms. Renee Marchese, BP America Inc.a
28100 Torch Parkway 4th Fl.
Warrenville, IL 60555
Phone: 630.836.5504
Fax 630.836.5500
marcher2@bp.com

Pacific Northwest

Washington State, California.
Mr. David Wright, ConocoPhillips
600 North Dairy Ashford (77079-1175)
P.O. Box 2197
Houston, TX 77252-2197
Phone 281.293.1544
Fax 281.293.6113
David.W.Wright@conocophillips.com
http://www.conocophillips.com/products/ultralowsulfur/index.htm

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South and Southwest

Texas, Colorado, Oklahoma, (southern) California, New Mexico, Kansas, Louisiana, Georgia, and Florida.

Mr. Ray Hernandez
Valero Energy Corporation
One Valero Place
San Antonio, TX 78212
Phone 210.345.2757
Fax 210.345.5930
Raymond.Hernandez@valero.com
http://www.valero.com/About+Valero/

3. Distributors of emulsified fuel

For further information or to purchase emulsified fuel, contact your local fuel distributor.

Mr. Thomas M. Sopko
The Lubrizol Corporation
29400 Lakeland Boulevard
Wickliffe, OH 44092-2298
Phone 440.943.4200
Fax 440.943.5337
tms@lubrizol.com

To purchase PuriNOx™ in the California and Texas area you may also contact:

Mr. Bill Alford
J.A.M. Distributing[b]
711 W.Bay Area Blvd Suite 310
Webster, Texas 77598
800.228.3848
Phone 713.844.7788
Fax 713.844.7789
jam@jamdistributing.com

or

Ms. Debbie McNeal
Sunoco[c]
800.842.0339 Ext. 1
Phone 215.977.3000
Fax 215.246.8119

4. Fuel additives

Mr. Glen Reid
Clean Diesel Technologies, Inc.[d]
300 Atlantic Street, Ste 702
Stamford, CT 06901
Phone 203.327.7050
Fax 203.323.0461
greid@cdti.com

or

Mr. Jim Baumert
AMSOIL Inc.[e]
AMSOIL Building
Superior, WI 54880-1527
Phone 631.587.5896 Fax 715.392.5225
http://www.lubedealer.com/baumert

or

The Stricklin Companies[f]
1415 Stratford Crt.
Del Mar, CA 92014
Phone 858-794-5700 Fax 848-794-2666
stricklin@worldnet.att.net

[a] BP America Inc. offers the users of BP's ULSD fuel (ECD®) risk management solutions enabling construction companies to manage their annual budget while reducing emissions at the same time. Construction companies can set a fixed fuel price over a set time period avoiding the risk of increasing fuel prices. For more information go to: http://www.ecdiesel.com/business/contruction.asp and http://www.bpdirect.com/products/risk.html

[b] J.A.M. Distributing also provides assistance with the installation of filters (EMISSION CONTROL TECHNOLOGY) to help further reduce emissions.

[c] AquaMix(tm) is Sunoco's emulsified fuel which has been verified by the EPA as an emission reduction diesel fuel. AquaMix™ emulsified diesel fuel is blended with Lubrizol's PuriNOx™ additive technology. AquaMix™ has been verified to reduce diesel particulate matter typically by 50% and NO_x emissions by 20%.

[d] Clean Diesel Technologies, Inc. sells a fuel borne catalyst called Platinum Plus.

[e] Amsoil Diesel Fuel Additive. AMSOIL also sells synthetic motor oil for heavy duty diesel engines (SAE 15W-40 or SAE 5W-30). Please contact Mr. Baumert for more information.

[f] Stricklin sells fuel additive called Blue Marble™. Please contact Stricklin for more information.

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APPENDIX D

Summary of retrofit technology status

Status	CARB or EPA verified for onroad use	CARB or EPA verified for nonroad use	In use in nonroad engines*	Known to be pursuing onroad verification	Known to be pursuing nonroad verification	In development
Retrofit technologies						
PM control						
Diesel Particulate Filter (DPF)	●		●	Verified		
Active DPF		●	●		Verified	
Flow-through filters (including CWMF)	●		●	Verified	●	●
Diesel Oxidation Catalyst (DOC)	●	●	●	Verified	Verified	
Closed Crankcase Filter System with DOC—Donaldson Spiracle with DOC Muffler	●	●	●	Verified	Verified	
NO_x control						
Selective Catalytic Reduction (SCR)			●		●	●
NO_x Adsorbers						●
Lean NO_x Catalysts	● (w/ DPF)		●	Verified		
PM and NO_x control						
Low Pressure Exhaust Gas Recirculation (EGR)				●		
SCR System with PM Emission Control		●	●		Verified	
Lean NO_x Catalyst with DPF—Cleaire Longview	●		●	Verified	●	
Lean NO_x Catalyst with DOC—Cleaire Lonestar			●	●		
Retrofit technologies and cleaner fuels						
Fuel Borne Catalyst (FBC) with DOC—Platinum Plus	●		●	Verified	●	
FBC with Catalyzed Wire Mesh Filter (CWMF)—Platinum Plus	●			Verified		
Emulsified Diesel Fuel with DOC		●	●		Verified	
Cleaner fuels and additives						
Emulsified Diesel Fuel—PuriNOx	●	●	●	Verified	Verified	
Biodiesel	●		●	Verified		

*In order for a technology to be considered "in use," it must: 1) be commercially available, and 2) have been used in at least 2 projects with varying locations.

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APPENDIX E

Retrofit technology cost and emissions reductions summary

	Cost (excluding installation)	NO_x	PM	HC	CO
Retrofit technologies and emissions reductions					
PM control					
Diesel Particulate Filter (DPF)	$7,000–$12,000	0%	Up to 90%	Up to 90%	Up to 90%
Active DPF	$10,000–$30,000	0%	85%	0%	0%
Flow-through Filters (including CWMF)	$5,000–$7,000	0-9%	55–76%	75–89%	50–66%
Diesel Oxidation Catalyst (DOC)	$1,200–$2,500	0%	20–30%	50–90%	70–90%
Closed Crankcase Filter System with DOC—Donaldson Spiracle with DOC Muffler	$1,900	0%	25–33%	12–34%	42–52%
NO_x control					
Selective Catalytic Reduction (SCR)	Mobile: $12,500–$15,000 Stationary: up to $80,000	60–80%	25%	50–90%	70–90%
NO_x adsorbers	In development	90% or more	10–30%	90%	90%
Lean NO_x Catalysts	$6,500–$15,000+	10–40%	Up to 80%	0%	0%
PM and NO_x control					
Low Pressure Exhaust Gas Recirculation (EGR)	$13,000–$15,000	40% or more	90% or more	90% or more	90% or more
SCR System with PM Emission Control	$14,500	80%	25%	50–90%	50–90%
Lean NO_x Catalyst with DPF - Cleaire Longview 90%		$18,500–$21,000	25%	85%	90%
Lean NOx Catalyst with DOC—Cleaire Lonestar	$12,500	25–30%	50–70%	40–60%	40–60%
Retrofit technologies and cleaner fuels					
Fuel Borne Catalyst (FBC) with DOC—Platinum Plus	Cost of DOC. Fuel economy gains from use of Platinum Plus are expected to outweigh its incremental cost.	0–5%	25–50%	16–50%	25–50%
FBC with Catalyzed Wire Mesh Filter (CWMF)—Platinum Plus	Cost of CWMF. Fuel economy gains from use of Platinum Plus are expected to outweigh its incremental cost.	0–9%	55–76%	75–89%	50–66%
Emulsified Diesel Fuel with DOC	$0.25 per gallon + $1,500–$2,500	25%	95%	85%	75%
Cleaner fuels and additives					
Emulsified Diesel Fuel—PuriNOx	$0.25 per gallon	9–20%	16.8–58%	(35%)–33%	(20–120%)
Biodiesel (20)	$0.15 per gallon	(2%)	10%	21%	11%
Biodiesel (100)	$0.50 per gallon	(10%)	47%	67%	48%

Emissions reductions data derived from CARB or EPA verified reduction levels where possible.
(Parenthesis denote increase)

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APPENDIX F

Examples of nonroad retrofit technology use

Status	In use in nonroad engines*	Two projects/sites in which the technology/fuel has been used
Retrofit technologies		
PM control		
Diesel Particulate Filter (DPF)	●	1. World Trade Center, NYC, NY—Caterpillar 966 Wheel loaders 2. American Asphalt, CA—Caterpillar 966GII Wheel loader
Active DPF	●	1. World Trade Center, NYC, NY—Rypos trap installed on a diesel 600 kW electrical generator 2. Riverside, CA—three Caterpillar backup generators (100, 225, and 350 kw) retrofit with Rypos trap
Flow-through Filters (including CWMF)	●	1. Nationwide. many non-metal mining applications on Deutz and Caterpillar engines, 100-275 hp 2. World Trade Center Site, NYC, NY—Two cranes retrofit with an ESW particulate reactor
Diesel Oxidation Catalyst (DOC)	●	1. World Trade Center, NYC, NY—Komatsu PC200 5.9 liter engine Excavator 2. Big Dig, Boston, MA—more than 200 pieces of equipment successfully retrofit
Closed Crankcase Filter System with DOC—Donaldson Spiracle with DOC Muffler	●	Between the Port of Los Angeles and the Port of Long Beach in CA, this system has been successfully installed on approximately 400 yard hustlers, top picks/side picks, and rubber tired gantry-cranes.
NO_x control		
Selective Catalytic Reduction (SCR)	●	1. Richmond, CA—Caterpillar modular SCR installed on a gas power module, model G3516B LE 2. Palm Desert, CA—Mobile SCRs installed on seven construction vehicles
NO_x Adsorbers		Not in commercial use for non-road engines
Lean NO_x Catalysts	●	See Lean NO_x Catalyst with DOC, below.
PM and NO_x control		
Low Pressure Exhaust Gas Recirculation (EGR)	●	Not in commercial use for non-road engines
SCR System with PM Emission Control	●	1. Houston, TX—Houston City has retrofit Cummins 6BTA 5.9L engines on 6 Gradall excavators 2. Port of Houston, TX—GR Birdwell has retrofit several pieces of construction equipment
Lean NO_x Catalyst with DPF—Cleaire Longview	●	1. Fresno, CA—Case IH STX 375 wheel lower and a Komatsu WA450 wheel loader 2. CADOT, California - John Deere672 CH motor grader
Lean NO_x Catalyst with DOC—Cleaire Lonestar	●	1. Concord, CA—Onan stationary 300 DGFC generator 2. Sacramento, CA—Caterpillar 8W2517 (16G) motor grader
Retrofit technologies and cleaner fuels		
Fuel Borne Catalyst (FBC) with DOC—Platinum Plus	●	1. Q-Bridge Project, CT—Starr construction excavator, Samsung 280LC 2. New York City, NY—Vergona crane, unknown model
FBC with Catalyzed Wire Mesh Filter (CWMF)—Platinum Plus		Not in commercial use for non-road engines

DISCLAIMER. Environmental Defense does not endorse any particular product on this list. This was last updated in April 2005.

Status	In use in nonroad engines[a]	Two projects/sites in which the technology/fuel has been used
Emulsified Diesel Fuel with DOC	●	Between the Port of Los Angeles and the Port of Long Beach in CA, approximately 250 yard hustlers, top picks/side picks, and rubber tired gantry-cranes, etc have DOCs and use PuriNOx.
Cleaner fuels and additives		
Emulsified Diesel Fuel—PuriNOx	●	1. Port of Houston, TX—approximately 50+ pieces of cargo-handling equipment use PuriNOx 2. Extensive, multi-engine/model testing conducted by USEPA and by Air Improvement Resources
Biodiesel	●	1. Hutchinson Salt Co, KA—uses B100 in all underground diesel machinery, 32,000 gallons/year 2. Pioneer Hi-Bred Intl., Charlotte, NC—uses biodiesel on all farm and tractor equipment

[a]In order for a technology to be considered "in use," it must: 1) be commercially available, and 2(have been used in at least 2 projects with varying locations.

APPENDIX G

Sample action letter

Dear [Decision Maker].

I write to direct your attention to the growing health and environmental impacts associated with diesel engines, and to encourage you to address this problem. Diesel engines, the workhorses of America's economy, are a significant source of air pollution in many communities across the country. Fortunately, cost-effective technology exists to reduce harmful diesel emissions by as much as 90%. Your help is needed to ensure that this technology is taken advantage of.

Emissions from diesel engines contain almost 40 toxic substances and contribute to a laundry list of adverse health effects including: asthma, cardiovascular and respiratory problems, strokes, heart attacks, lung cancer and premature death. Of special concern are two main pollutants: fine particulate matter, which lodges deep in the lung, and oxides of nitrogen (NO_x), which are precursors to smog. Diesel engines are a significant source of fine particulates and NO_x, and recent EPA data shows that about half of all Americans live in places that fail to meet basic health standards for one or both of these pollutants.

Nonroad diesel engines are, quite literally, engines that power vehicles that do not normally operate on roads. They include, for example, locomotives, agricultural equipment (i.e., tractors), construction and mining equipment (i.e., graders and back hoes), and ships. Collectively, nonroad engines discharge more dangerous fine sooty particles than any other source in the transportation sector.

The EPA recently established rigorous emissions standards for new nonroad diesel engines. Unfortunately, the full pollution reduction and public health benefits of the non-road rule will not be realized for decades because they only apply to new nonroad diesel engines and not to older, dirtier diesel engines, which have a long life span. A child born today may still be breathing soot from a backhoe in her neighborhood when she graduates from college—unless that backhoe is replaced with a newer, cleaner one, or is retrofit with emissions controls.

Public and private leadership is needed to ensure that dirty diesel engines in our community are replaced or retrofit to reduce their polluting potential. As a community leader, I am asking you to implement programs to reduce pollution from dangerous diesel engine exhaust from vehicles in use in our community. Environmental Defense's Cleaner Diesel Handbook, available at: www.environmentaldefense.org/go/dieselhandbook, is a good starting point. The handbook shows that there is a cost-effective way to reduce the adverse health effects of diesel pollution.

The Cleaner Diesel Handbook outlines some simple ways to reduce diesel pollution, like enforcing idling laws, using clean fuels (like ultra-low sulfur diesel), and best available retrofit technologies that can reduce diesel emissions by up to 90%. It also offers a variety of methods for implementing successful diesel retrofit programs. With your leadership, these tools can reduce air pollution from diesel engines and protect public health in our community. Thank you.

Sincerely,
[Your name]
[Your address]

Notes

[1] Environmental Defense is a national non-profit environmental organization, head-quartered in New York City, with 400,000 members around the country and over 50,000 members and activists in New York. The Living Cities program at Environmental Defense is focused specifically on actions that will help to improve water and air quality, clean up contaminated lands, support sound transportation investments and will reduce greenhouse gases (GHGs). Environmental Defense is not affiliated with any manufacturer or supplier identified in this handbook, and Environmental Defense does not endorse any particular supplier, retrofit or fuel technology manufacturer. This handbook provides only a general overview of commercialized nonroad retrofit technology and cleaner fuel technology options. We provide information about specific companies or suppliers for informational purposes only, but inclusion in, or omission from, this handbook should not be interpreted as a judgment about a particular technology or company. Questions about specific products, applications, emerging technologies, or next steps should be taken up directly with appropriate private sector companies or consultants.

[2] EPA, "Clean Air Nonroad Diesel Rule Summary." June 8, 2004. Office of Transportation and Air Quality. Online resource, available at: http://www.epa.gov/otaq/regs/nonroad/equip-hd/2004fr/420f04029.htm Last accessed 03/01/05.

[3] EPA, "Press Release: New Clean Diesel Rule Major Step in a Decade of Progress." May 11, 2004. Online resource, available at: http://yosemite.epa.gov/opa/admpress.nsf/b1ab9f485b098972852562e7004dc686/f20d2478833ea3bd85256e91004d8f90?OpenDocument Last accessed 03/01/05.

[4] *Ibid.*

[5] EPA, "8-Hour Ground-level Ozone Designations." 08/13/04. Online resource, available at: www.epa.gov/ozonedesignations Last accessed 03/01/05.

[6] EPA, "Fine Particle (PM 2.5) Designations." Online resource, available at: http://www.epa.gov/pmdesignations/regions/region2desig.htm Last accessed 03/01/05.

[7] Calculated from 1999 EPA National Scale Assessment of Air Toxics data.

Environmental Defense, "Scorecard, 2002." Online resource, available at: http://www.scorecard.org/ Last accessed 03/01/05.

[8] *Ibid.*

[9] *Ibid.*

[10] EPA, "National Emission Inventory (NEI): Air Pollutant Emission Trends." Online resource, available at: http://www.epa.gov/ttn/chief/trends/index.html Last accessed 03/01/05.

[11] California Office of Environmental Health Hazard Assessment, Air Toxicology and Epidemiology Section, "Proposed Identification of Diesel Exhaust as a Toxic Air Contaminant," *Health Risk Assessment for Diesel Exhaust* app. III, part B, as approved by the Scientific Review Panel, April 22, 1998. Online resource, available at: ftp://ftp.arb.ca.gov/carbis/regact/diesltac/partb.pdf Last accessed 03/01/05.

[12] Air Pollution and Birth Weight Among Term Infants in California, PEDIATRICS Vol. 115 No. 1, January 2005, pp. 121–128 Online resource, available at:

http://pediatrics.aappublications.org/cgi/content/abstract/115/1/121?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&author1=Woodruff&fulltext=Birth+weight&andorexactfulltext=and&searchid=1105556093372_12826&stored_search=&FIRSTINDEX=0&sortspec=relevance&resourcetype=1&journalcode=pediatrics Last accessed 03/01/05.

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[15] U.S. Department of Health and Human Services, National Institutes of Health, National Heart, Lung and Blood Institute; Data Fact Sheet: Asthma Statistics; January 1999. See also http://www.environmentaldefense.org/documents/2655_MotorAirPollutionAsthma.pdf

[16] NY State Department of Health and Mental Hygiene, "Asthma Facts." Second Edition, May 2003. Page 7. Online resource, available at: http://nyc.gov/html/doh/pdf/asthma/facts.pdf Last accessed 03/01/05.

[17] Manufacturers of Emissions Controls Association, "Frequently Asked Questions About the Installation of Emission Controls on Existing Diesel Engines." Online resource, available at: http://www.meca.org/jahia/Jahia/engineName/filemanager/pid/224/retrofitFAQ%20%28revised%29.pdf?actionreq=actionFileDownload&fileItem=712 Last accessed 03/01/2005.

[18] Based on email correspondence with Roger Suter of Detroit Diesel, Inc. on August 4, 2004.

[19] EPA Tier 0 standards refer to unregulated diesel engines. Tier 1 standards refer to the nonroad diesel engine emissions control regulations adopted by EPA in 1994. The regulations came into effect for new nonroad diesel engines greater than 37 kilowatts (50 horsepower) between 1996 and 2000. Tier 2 standards refer to stricter regulations that were phased in between 1999 and 2000. Tier 3 standards applied to engines between 37 kilowatts and 560 kilowatts (50 and 750 hp), and will be phased in between 2006 and 2008. Source: EPA, "Reducing Air Pollution From Nonroad Engines." April 2003. Online resource, Last accessed 09/11/05. Available at: http://www.epa.gov/otaq/cleaner-nonroad/f03011.pdf

[20] (Using California's Carl Moyer Program assumptions for an unregulated engine's replacement with a Tier One engine, NO_x emissions would go from 11 grams per brake horsepower-hour (g/bph-hr) to 6.6 g/bph-hr and PM emissions would go from 0.53 g/bph-hr to 0.1 g/bph-hr. For a Tier Two replacement, NMHC + NO_x emissions would decrease to 4.2 g/bph-hr and PM would decrease to 0.1 g/bph-hr.) Based on email correspondence with Stephen Hurd of Caterpillar Inc. on August 30, 2004.

[21] This definition is narrower than the one found in the EPA's "Retrofit Glossary." The EPA glossary is an online resource, available at: http://www.epa.gov/otaq/retrofit/glossary.htm ast accessed 03/01/2005.

[22] EPA, "Voluntary Diesel Retrofit Program: Glossary" Office of Transportation and Air Quality. Online resource, available at http://www.epa.gov/otaq/retrofit/glossary.htm Last accessed 03/01/2005.

[23] Information provided by Alex Kasprak from the Boston Big Dig project and various retrofit manufacturers. The operator of the construction equipment to be retrofitted can typically install the replacement muffler containing the DOC.

[24] Information provided by Johnson Matthey.

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[30] Joe Kubsch. "Retrofit Emission Control Technologies for Diesel Engine." MECA, November 4, 2003. Online resource, available at: http://www.4cleanair.org/JoeKubsh.pdf Last accessed 03/01/2005.

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[32] *Ibid.*

[33] For more information on EPA regulations, please see http://www.epa.gov/otaq/url-fr/fr29jn04.pdf Last accessed 03/01/2005.

[34] For more information on the WTC 7 retrofits, please contact: NESCAUM at 617.259.2000.

[35] Environmental Solutions Worldwide, Inc., "Environmental Solutions Worldwide, Inc.

Puts Diesel Emission Controls to Work at World Trade Center Construction Site." June 1, 2004. Online resource, available at: http://www.cleanerfuture.com/june0104.htm Last accessed 03/23/05.

[36] All information in this section is from a report conducted by M.J. Bradley and Associates, Inc. for the Port Authority of NY/NJ on August 9, 2004. This report is available online at: http://www.mjbradley.com/documents/PANYNJ_WTC_Final_Report-09Aug04.pdf

[37] N.Y. ALS Chapter 259, Assembly Bill 11700. 2004.

[38] New York State Governor's Office. "Press Release: Governor Signs Bill Creating the Coordinated Construction Act for Lower Manhattan." August 10, 2004. Online resource, available at: http://www.state.ny.us/governor/press/year04/aug10_1_04.htm Last accessed 03/02/05.

[39] N.Y. ALS Chapter 259, Assembly Bill 11700. 2004.

[40] Investigation of Diesel Emissions Control Technologies on Off-Road Construction Equipment at the World Trade Center and PATH Re-Development Site" Report prepared for the Port Authority of NY/NJ on August 9, 2004. Pages 39–40. This report is available online at: http://www.mjbradley.com/documents/PANYNJ_WTC_Final_Report-09Aug04.pdf.

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[42] *Ibid.*

[43] New York City's rules Concerning the Use of ULSD and Emissions Control Technology in Nonroad Vehicles Used in City Construction are available online at www.nyc.gov/html/dep/pdf/batrule.pdf

[44] Fulton Street Transit Center Draft Environmental Impact Statement, and Section 4(f) Evaluation, Chapter 12, page 31 (2004).

[45] For more information, please contact: Alex Kasprak via email at akasprak@bigdig.com or via phone at 617-556-2462.

[46] Massachusetts Turnpike Authority, "Big Dig: Project Schedule and Timeline." Online resource, available at: http://www.masspike.com/bigdig/updates/timeline.html Last accessed 03/04/05.

[47] Such small, movable cranes that move on tracks for underground tunnel construction included "nichi lifts" and "mantis cranes." Although stationary cranes can be retrofitted with DOCs, it was decided that those cranes not be retrofitted for the Big Dig project. At the time when the decision to retrofit construction equipment with DOCs was made, it was not clear whether a DOC might affect the stationary crane's heavy lift. Phone conversation with Alex Kasprak, September 8, 2004.

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[49] Alex Kasprak, Environmental Engineer, Massachusetts Turnpike Authority—CA/T Project.

[50] Massachusetts Turnpike Authority, "Big Dig: Controlling Diesel Air Pollution." Online resource, available at: http://www.masspike.com/bigdig/background/airpollution.html Last accessed 03/04/05.

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[52] For example, visit the EPA Region 8 web site at: http://www.epa.gov/Region2/air/8_2000.pdf and the EPA Office of Transportation and Air Quality web site at: http://www.epa.gov/otaq/retrofit/exbigdig.htm

[53] For more information, please contact: Donna Weaver via email at Donna.Weaver@po.state.ct.us or by phone at 860-594-2082.

[54] Connecticut Department of Transportation (DOT). "Connecticut Clean Air Construction Initiative." Online resource, available at: http://www.i95newhaven.com/poverview/environ_init.asp For more information please go to another DOT web site at: http://www.i95newhaven.com/poverview/awma_2002_nhhc.pdf and to the Weaver Presentation on the Clean Fleet USA program's web site at: http://www.cleanfleetsusa.net/highlights/present/weaver_present.pdf Contact person: Donna Weaver, Connecticut Department of Transportation; Phone: 860.594.2082.

[55] For more information on the Port of Houston Authority's use of cleaner diesel fuels and/or technology, please contact:

Shari Baldridge by phone at 713-670-2428 or via email at sbaldridge@poha.com.

[56] EPA, "Region 6: State Designations." Online resource, available at: http://www.epa.gov/ozonedesignations/regions/region6desig.htm Last accessed 09/11/05.

[57] Ibid, Page 20.

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[59] Ibid, Page 24.

[60] Ibid, Page 23.

[61] Ibid, Page 24.

[62] *Ibid.*

[63] Ibid, Page 25.

[64] Environmental Protection Agency. "Port of Houston Pilot Retrofit Program." Online resource, available at: http://www.epa.gov/otaq/retrofit/exporthouston.htm Last accessed 03/02/05.

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[66] Based on a conversation with Paul Carr, of the Puget Sound Clean Air Agency on February 28, 2005.

[67] For a directory of TERP contact information, please visit: http://www.tnrcc.state.tx.us/oprd/sips/contact_info.html

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[76] For more information about CARB, please contact: Scott Rowland, the CARB Manager of its Retrofit Assessment Section via email at srowland@arb.ca.gov or by phone at 626-575-6972.

[77] Based on phone correspondence with Edie Chang of the California Air Resources Board on September 3, 2004. Or CARB, "The Carl Moyer Program Annual Status Report." February 2004. Online resource, available at: http://www.arb.ca.gov/msprog/moyer/moyer_2004_report.pdf Last accessed 03/23/05.

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[94] Information provided by Engine Control Systems (ECS). Numbers are based on the use of PuriNOx and ECS's DPF (Purifilter) and DOC (Purimuffler). EPA has verified that ECS's Purifilter reduces PM emission by 90%, HC emissions by 85% and CO emissions by 75%. EPA has verified that ECS's Purimuffler reduces PM emissions by 20%, HC emissions by 50% and CO emissions by 40%. http://www.epa.gov/otaq/retrofit/retroverifiedlist.htm

[95] For more information regarding different applications and test results of emulsified fuels please refer to reports No. 4576-1 (Emulsified Diesel Fuels: Literature Review and Consolidation of Lubrizol Recommendations), 4576-2 (Emulsified Diesel Emission Testing, Performance Evaluation, and Operational Assessment) and 4576-3 (TxDOT Emulsified Diesel Final Report) listed on the webpage of the Center For Transportation Research. http://www.utexas.edu/research/ctr/pdf_reports/index.html#4177-1

[96] Based on e-mail correspondence with Ron Dunfee, of Lubrizol Corporation, on August 30, 2004.

[97] Number provided by Lubrizol manufacturer of PuriNOx.

[98] Lubrizol, "PuriNOx Questions and Answers." Online resource, available at: http://www.lubrizol.com/purinox/purinoxcd/lzquestions.htm Last accessed 03/01/05.

[99] Based on e-mail correspondence with Ron Dunfee, of Lubrizol Corporation, on August 30, 2004.

[100] *Ibid.*

[101] *Ibid.*

[102] Information taken from a fact sheet about Platinum Plus DFX by Clean Diesel Technologies, Inc.

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[106] United Kingdom Department of Health. "1996 Report of the Committees on Toxicity, Mutagenicity, Carcinogenicity of Chemicals in Food, Consumer Products, and the Environment." January 29, 1998. Online resource, available at: http://www.archive.official-documents.co.uk/document/doh/toxicity/chap-1b.htm Last accessed 03/01/05.

[107] Stricklin Company offers a FBC called Blue Marble(tm). However, Blue Marble(tm) has not yet been EPA verified. According to the Strickling webpage, Blue Marble™ products contain Phosfamid™, an advanced metal treatment that causes metal, according to Stricklin, to become smoother, shinier and resistant to carbon buildup. Distributed by The Stricklin Companies, 1415 Stratford Crt., Del Mar, CA 92014, Ph: 858-794-5700, Fax: 848-794-2666, email: stricklin@worldnet.att.net See also: The Stricklen Companies, "Blue Marble Applications/Engine Test Results." Online resource, available at: http://www.phosfamid.com/html/applications/index.html#HongKongPolytechnicUniversity Last accessed 03/01/05.

[108] National Biodiesel Board. "Biodiesel 2001." 2001. Online resource, available at: http://www.investingdd.com/pdfs/backgrounder.pdf Last accessed 03/01/05.

[109] EPA, "Draft Technical Report: A Comprehensive Analysis of Biodiesel Impacts on Exhaust Emissions." *EPA-420-P-02-001, October 2002.*

[110] In a study of the effects of Biodiesel on greenhouse gas emissions, the U.S. EPA reports: "we cannot confidently conclude the Biodisel increases or decreases CO_2 emissions." Environmental Protection Agency. "A Comprehensive Analysis of Biodiesel Impacts on Exhaust Emissions." *EPA-420-P-02-001*, October 2002. Page 50. Online resource, available at: http://www.epa.gov/otaq/models/analysis/biodsl/p02001.pdf Last accessed 03/01/05.

[111] See also *Ibid.*

[112] EPA, "Retrofit Technologies - Biodiesel." June 10, 2004. Online resource, available at: http://www.epa.gov/otaq/retrofit/techlist-biodiesel.htm Last accessed 03/01/05.

[113] *Ibid*, page 46.

[114] National Biodeisel Board, "Biodeisel Emissions." Online resource, available at: http://www.biodiesel.org/pdf_files/emissions.pdf Last accessed 03/01/05.

[115] *Ibid.*

[116] EPA, "Clean Alternative Fuels: Compressed Natural Gas." EPA 420-F-00-033. March 2002. Online resource, available at: http://www.epa.gov/otaq/consumer/fuels/altfuels/420f00033.pdf Last accessed 03/01/05.

[117] In fact, Waste Management Inc. operates approximately 125 CNG fueled heavy-duty trucks. U.S. Dept. of Energy, "Waste Management, Inc." August 25, 2003. Online resource, available at: http://www.eere.energy.gov/cleancities/progs/new_success_ddown.cgi?110 Last accessed 03/01/05.

[118] U.S. Department of Energy: Alternative Fuel Data Center. Online resource, available at: http://www.eere.energy.gov/afdc/altfuel/natural_gas.html Last accessed 03/01/05.

[119] For example, Waste Management Inc. in California is currently converting old Mack MR trucks to run on LNG and is also buying new LNG-fueled vehicles. Waste Management's fleet includes more than 235 heavy-duty trucks powered by LNG. U.S. Dept. of Energy, "Waste Management, Inc." August 25, 2003. Online resource, available at: http://www.eere.energy.gov/cleancities/progs/new_success_ddown.cgi?110 Last accessed 03/01/05.

[120] EPA, "Clean Alternative Fuels: Propane." March 2002. EPA 420-F-00-039. Online resource, available at: http://www.epa.gov/otaq/consumer/fuels/altfuels/420f00039.pdf Last accessed 03/01/05.

[121] U.S. DOE, "Propane Vehicles." July 21, 2004. Online resource, available at: http://www.eere.energy.gov/afdc/afv/prop_vehicles.html Last accessed 03/04/05.

[122] U.S. Department of Energy: Alternative Fuel Data Center. Online resource, available at: http://www.eere.energy.gov/afdc/altfuel/prop_benefits.html Last accessed 03/01/05.

[123] MECA, "MECA supports U.S. EPA Proposal to Reduce Emissions from Nonroad Diesel Engines and Equipment." April 15, 2003. Online resource, available at: http://www.meca.org/jahia/Jahia/engineName/filemanager/pid/226/EPAnonroadNPRMpr

041503.pdf?actionreq=actionFileDownload &fileItem=500 Last accessed 03/03/05.

[124] *Ibid.*

[125] *Ibid.*

[126] Timothy V. Johnson, "Is there a simple solution for the diesel emission control challenge?" *Environmental Technologies*, January 2004. Volume 25 No. 2. Online resource, available at: http://www.corning.com/environmentaltechnologies/emissions_control_technology_magazine/article2.asp Last accessed 03/03/05.

[127] *Ibid.*

[128] EPA, "Voluntary Diesel Retrofit Program" Office of Transportation and Air Quality. Online resource, available at http://www.epa.gov/otaq/retrofit Last accessed 03/03/05.

[129] For an overview of different retrofit devices, please also refer to: Joe Kubsch. *Retrofit Emission Control Technologies for Diesel Engine*, MECA, November 4, 2003. Online resource, available at: http://www.4cleanair.org/JoeKubsh.pdf Last accessed 08/13/04.

[130] "Verified" means that either the EPA or the California ARB have verified this type of technology. However, please refer to http://www.epa.gov/otaq/retrofit/retroverifiedlist.htm and http://www.arb.ca.gov/diesel/verdev/verdev.htm for detailed information regarding the different types of verified emission control technologies and the different manufacturers whose technologies have been verified.

[131] EPA, "Voluntary Diesel Retrofit Program: Glossary" Office of Transportation and Air Quality. Online resource, available at http://www.epa.gov/otaq/retrofit/glossary.htm Last accessed 03/03/05.

[132] EPA, "Diesel Particulate Matter (PM) Filter Overview." Office of Transportation and Air Quality, February 13, 2004. Online resource, available at: http://www.epa.gov/otaq/retrofit/documents/bigdig_case_08.htm Last accessed 03/03/05.

[133] EPA's verified level of reduction for Johnson Matthey Continuously Regenerating Technology (CRT). EPA, "Verified Products." August 11, 2004. Online resource, available at: http://www.epa.gov/otaq/retrofit/retroverifiedlist.htm Last accessed 03/03/05.

[134] Kodjak et al., Attachment D, "The Clean Air Construction Initiative, Diesel Particulate Filters Technology Description and Overview of Operational Issues"

[135] Information provided by Johnson Matthey.

[136] Joe Kubsch. *Retrofit Emission Control Technologies for Diesel Engine*, MECA, November 4, 2003. Online resource, available at: http://www.4cleanair.org/JoeKubsh.pdf Last accessed 03/03/05.

[137] *Ibid.*

[138] "Verified" means that either the EPA or the California ARB have verified this type of technology. However, please refer to http://www.epa.gov/otaq/retrofit/retroverifiedlist.htm and http://www.arb.ca.gov/diesel/verdev/verdev.htm for detailed information regarding the different types of verified emission control technologies and the different manufacturers whose technologies have been verified.

[139] Block, Michael. *Retrofit Primer—Emission Reduction Technologies and Strategies.* NESCAUM, October 2003. Page 10. Online resource, available at: http://bronze.nescaum.org/retrofitworkshop/folder/Primer.pdf Last accessed 03/03/05.

[140] California Air Resource Board, "Risk Reduction Plan to Reduce Particulate Matter Emissions from Diesel-Fueled Engines and Vehicles", October 2000, p. 19.

[141] Johnson Matthey's CRT and CCRT. For more information, visit the Johnson Matthey Catalyst web site at: http://www.jmcatalysts.com Last accessed 03/03/05.

[142] "Verified" means that either the EPA or the California ARB have verified this type of technology. However, please refer to http://www.epa.gov/otaq/retrofit/retroverifiedlist.htm and http://www.arb.ca.gov/diesel/verdev/verdev.htm for detailed information regarding the different types of verified emission control technologies and the different manufacturers whose technologies have been verified.

[143] Rypos Inc., "Company Info." Online resource, available at: http://www.rypos.com/html/companyinfo.html Last accessed 03/03/05. For examples where Rypos' DPF (Rypos Trap) have been used, visit the Rypos web site at: http://www.rypos.com/html/index.html. DCL International Inc. also sells active DPFs.

[144] Rypos Inc.s' Active DPF does not require the use of ULSD. Online resource, available at: http://www.rypos.com/html/products.html Last accessed 03/03/05.

[145] California Air Resources Board, "Diesel Emission Control Strategies Verification:

Level 3 Verified Technologies." 01.25.2005. Online resource, available at: URL: http://www.arb.ca.gov/diesel/verdev/level3.htm Last accessed 03/03/05.

[146] "Verified" means that either the EPA or the California ARB have verified this type of technology. However, please refer to http://www.epa.gov/otaq/retrofit/retroverifiedlist.htm and http://www.arb.ca.gov/diesel/verdev/verdev.htm for detailed information regarding the different types of verified emission control technologies and the different manufacturers whose technologies have been verified.

[147] FBC called Platinum Plus(r) and CWMF both sold by Clean Diesel Technologies, Inc. Please refer to Appendix A for contact information. EPA, "Verified Products." August 11, 2004. Online resource, available at: http://www.epa.gov/otaq/retrofit/retroverifiedlist.htm Last accessed 08/13/04.

[148] Based on phone conversation with Glen Reid of Clean Diesel Technologies, Inc. on July 6, 2004.

[149] EPA, "Verified Products." June 21, 2005. Online resource, available at: http://www.epa.gov/otaq/retrofit/retroverifiedlist.htm Last accessed 08/03/05.

[150] Based on phone conversation with Glen Reid of Clean Diesel Technologies, Inc. on July 6, 2004.

[151] Based on email correspondence with Glen Reid of Clean Diesel Technologies, Inc. on August 3, 2004.

[152] Based on email correspondence with Glen Reid of Clean Diesel Technologies, Inc. on August 27, 2004.

[153] Sold in the U.S. by Clean Air Power (see Appendix A for contact information).

[154] Based on phone conversation with Clean Air Power. 08/25/04.

[155] The certification was done by AVL, an engine testing center in Sweden. The AVL web site is available at: http://www.mtc.se/eng/content/aboutmtc.htm

[156] The Swiss verification is referred to as "VERT" verification. For more information, please visit: http://www.umwelt-schweiz.ch/buwal/eng/fachgebiete/fg_luft/vorschriften/industrie_gewerbe/filter/index.html

[157] EPA, "Terms of Environment." Online resource, available at: http://www.epa.gov/OCEPAterms/oterms.html Last accessed 03/03/05.

[158] Information provided by Clean Air Power by e-mail.

[159] "Verified" means that either the EPA or the California ARB have verified this type of technology. However, please refer to http://www.epa.gov/otaq/retrofit/retroverifiedlist.htm and http://www.arb.ca.gov/diesel/verdev/verdev.htm for detailed information regarding the different types of verified emission control technologies and the different manufacturers whose technologies have been verified.

[160] Block, Michael. *Retrofit Primer—Emission Reduction Technologies and Strategies.* NESCAUM, October 2003. Page 5. Online resource, available at: http://bronze.nescaum.org/retrofitworkshop/folder/Primer.pdf Last accessed 03/03/05.

[161] Philadelphia Diesel Difference, Diesel Oxidation Catalyst. Online resource, available at: http://www.cleanair.org/dieseldifference/retrofits/ Last accessed 03/03/05.

[162] Diesel Emission Evaluation Program, DEEP. Online resource, available at: http://www.deep.org/reports/sum_gloss.pdf. Last accessed 03/03/05. Also refer to DieselNet. Online resource, available at: http://www.dieselnet.com/gl-s.html Last accessed 03/03/05.

[163] Block, Michael. *Retrofit Primer—Emission Reduction Technologies and Strategies.* NESCAUM, October 2003. Page 5. Online resource, available at: http://bronze.nescaum.org/retrofitworkshop/folder/Primer.pdf Last accessed 03/03/05.

[164] *Ibid.*

[165] *Ibid.*

[166] EPA's verified level of reduction for numerous suppliers of catalyst muffler products. EPA, "Verified Products." August 11, 2004. Online resource, available at: http://www.epa.gov/otaq/retrofit/retroverifiedlist.htm Last accessed 03/03/05.

[167] Joe Kubsch. *Retrofit Emission Control Technologies for Diesel Engine,* MECA, November 4, 2003. Online resource, available at: http://www.4cleanair.org/JoeKubsh.pdf. Last accessed 03/03/05.

[168] Information based on phone conversation with Alex Kasprak of the Big Dig Project on June 18, 2004.

[169] Information based on Donaldson letter to Environmental Defense dated March 25, 2004.

[170] Information based on e-mail correspondence with Fred Schmidt of Donaldson Company, Inc. on November 1, 2004.

[171] EPA, "Verified Products." August 11, 2004. Online resource, available at: http://www.epa.gov/otaq/retrofit/retroverifiedlist.htm Last accessed 03/03/05.

[172] Information provided by Donaldson Brochure for Spiracle Filtration Systems.

[173] Information based on e-mail correspondence with Fred Schmidt, of Donaldson Company, Inc. on October 26, 2004.

[174] California Air Resources Board. "The Carl Moyer Memorial Air Quality Standards Attainment Program Guidelines: Approved Revision 2003." September 30, 2003. Page 6. Online resource, available at: http://www.arb.ca.gov/msprog/moyer/2003moyerguide.pdf Last accessed 03/03/05.

[175] Texas State House of Representatives. "House Bill 1365." §8(a) Effective 06/22/03. Online resource, available at: http://www.capitol.state.tx.us/cgi-bin/tlo/textframe.cmd?LEG=78&SESS=R&CHAMBER=H&BILLTYPE=B&BILLSUFFIX=01365&VERSION=5&TYPE=B Last accessed 03/03/05.

[176] Except for Extengine's ADEC system (see 3.1), no mobile SCR system has been EPA or CARB verified as of February 11, 2005.

[177] A reductant is a substance that is oxidized in the course of reduction. It is a reducing agent that chemically reduces other substances. Here, the reducing agent is urea or ammonia, which chemically reduces NO_x into N_2.

[178] Emissions reduction with use of 30ppm low sulfur fuel. Khair, Magdi. "Integration of EGR, SCR, DPF, and fuel-borne catalyst for NO_x/PM reduction," Oct. 1999. According to Argillon LLC, their SCR reduces 60% of soluble organic fraction of PM and up to 90% NO_x depending on the application (average between 60-80% NO_x reduction).

[179] Block, Michael. *Retrofit Prime—Emission Reduction Technologies and Strategies.* NESCAUM, October 2003. Page 13. Online resource, available at: http://bronze.nescaum.org/retrofitworkshop/folder/Primer.pdf Last accessed 03/03/05.

[180] For example, the Argillon mobile SCR is equipped with such a remote data-recording device.

[181] Information based on phone conversation with T.J. Tarabulski of Combustion Components Associates Inc. on February 11, 2005. Reference is also made to: http://www.extengine.com/index.html Last accessed 03/03/05.

[182] *Retrofit Emission Control Technologies for Diesel Engine*, Joe Kubsh, MECA, November 4, 2003. Joe Kubsch. *Retrofit Emission Control Technologies for Diesel Engine*, MECA, November 4, 2003. Online resource, available at: http://www.4cleanair.org/JoeKubsh.pdf Last accessed 03/03/05.

[183] Combustion Component Association Inc. has installed mobile SCR units in seven big earth moving construction vehicles (four scrapers, one rubber-tire dozer, one motor grader, one waterpull and one watertruck) in Palm Desert, CA). Information provided by Combustion Components Associates Inc.

[184] Based on a phone conversation with T.J. Tarabulski of Combustion Components Associates Inc. on February 11, 2005.

[185] DieselNet, "EMA Releases Urea-SCR Infrastructure Study." Oneline resource, available at: http://www.dieselnet.com/news/0308ema.html Last accessed August 3, 2005.

[186] Combustion Components Associates, Inc, "ELIM-NOx: A Mobile Diesel NO_x Emissions Reduction System." Online resource, available at: http://www.combustioncomponents.com/images/mobilescr/mobilescr.pdf Last accessed 03/03/05.

[187] Based on a phone conversation with T.J. Tarabulski of Combustion Components Associates Inc. on February 11, 2005.

[188] These numbers do not include installation and tax. Installation costs run usually between 20–30% of unit price. NO_x reduction level: 60-90% depending on catalyst volume, baseline NO_x levels and exhaust temperatures. Information provided by Clean Diesel Technologies, Inc. and Argillon LLC.

[189] Information provided by Argillon LLC.

[190] Lexico Publishing, LLC "Dictionary: Adsorb." Online resource, available at: http://dictionary.reference.com/search?q=adsorb. Last accessed 04/05/05.

[191] CARB, "Appendix B: Diesel Engine Emission Control Technologies." Online resource, available at: http://www.arb.ca.gov/regact/dieselrv/appb.doc. Last accessed 04/05/05.

[192] Jim Parks et al., "DeSulfation of NO_x Adsorbers: Studies with the SpaciMS

Technique." 7th Diesel Engine Emissions Reduction Workship. Portsmouth, Virginia. August 5–9, 2001. Online resource, available at: http://www.osti.gov/fcvt/deer2001/parks.pdf Last accessed 03/03/05.

[193] Manufacturers of Emission Controls Association, "Catalyst-Based Diesel Particulate Filters and NO_x Adsorbers: A Summary of the Technologies and the Effects of Fuel Sulfur." August 14, 2000. Online resource, available at: http://www.cleanairnet.org/infopool/1411/articles-35627_catalystbased_diesel.pdf Last accessed 03/03/05.

[194] Bruce Bertelsen, "Reducing Emissions from Existing Diesel Engines: The Critical Role of Diesel Retrofit Technologies: Background Document." Environmental & Energy Technology and Policy Institute. January 15–16, 2004. Online resource, available at: http://embarq.wri.org/documents/hittingtheroad/bertelsen.pdf Last accessed 03/03/05.

[195] Manufacturers of Emission Controls Association, "Catalyst-Based Diesel Particulate Filters and NO_x Adsorbers: A Summary of the Technologies and the Effects of Fuel Sulfur." August 14, 2000. Page 17. Online resource, available at: http://www.cleanairnet.org/infopool/1411/articles-35627_catalystbased_diesel.pdf Last accessed 03/03/05.

[196] Catalytica Energy Systems, "Diesel NO_x Reduction." Online resource, available at: http://www.catalyticaenergy.com/new_technologies/diesel.htm#Retrofit Last accessed 03/03/05.Catalytica is also working to develop NO_x adsorber technology for stationary diesel engines that will produce a 90% reduction in NO_x emissions in both new and retrofitted engines.

[197] Manufacturers of Emission Controls Association, "Catalyst-Based Diesel Particulate Filters and NO_x Adsorbers: A Summary of the Technologies and the Effects of Fuel Sulfur." August 14, 2000. Page 17. Online resource, available at: http://www.cleanairnet.org/infopool/1411/articles-35627_catalystbased_diesel.pdf Last accessed 03/03/05.

[198] "Verified" means that either the EPA or the California ARB have verified this type of technology. However, please refer to http://www.epa.gov/otaq/retrofit/retroverifiedlist.htm and http://www.arb.ca.gov/diesel/verdev/verdev.htm for detailed information regarding the different types of verified emission control technologies and the different manufacturers whose technologies have been verified.

[199] Bruce Bertelsen, "Reducing Emissions from Existing Diesel Engines: The Critical Role of Diesel Retrofit Technologies: Background Document." Environmental & Energy Technology and Policy Institute. January 15–16, 2004. Online resource, available at: http://embarq.wri.org/documents/hittingtheroad/bertelsen.pdf Last accessed 03/03/05.

[200] Paul W. Park, "Correlation Between Catalyst Surface Structure and Catalyst Behavior: Selective Catalytic Reduction with Hydrocarbon." May 21, 2002. EMSL 2002. Richland, Washington. Online resource, available at: http://www.emsl.pnl.gov/new/emsl2002/abstracts/park.doc Last accessed 03/03/05.

[201] Diesel Technology Forum, "Engineering Clean Air: The Continuous Improvement of Diesel Engine Emission Peformance." March, 2001. Page 13. Online resource, available at: http://www.dieselforum.org/whitepaper/downloads/DTF-Continuous Improvement03-01.pdf Last accessed 03/03/05.

[202] Carrie Boyer et al., "Lean NO_x Catalysis: Research and Development." Caterpillar, Inc. Online resource, available at: http://www.orau.gov/deer/DEER2003/presentations/session11/3.%20Endicott%20-%20DEER_2003_Final_Lean-NOx.pdf Last accessed 03/03/05.

[203] EPA, "Technical Summary." Online Resource, available at: http://www.epa.gov/otaq/retrofit/retropotentialtech.htm Last accessed 03/03/05.

[204] *Ibid.*

[205] Cleaire's "Longview" filter reduces 25% NO_x and 85% PM. The Longview filter has been CARB verified for onroad. Cleaire Inc, "Products." Online resource, available at http://www.cleaire.com/site/products/# Last accessed 03/03/05. Extengine's ADEC system reduces PM, HC, CO and NO_x by approx. 75%. CARB nonroad verification is pending (as per August 2004). Extengine, "ADEC Advanced Diesel Emission Control system." Online resource, available at: http://www.extengine.com/adec.html Last accessed 03/03/05.

[206] As of February 11, 2005, only the ADEC system has been verified, Johnson Matthey's SCRT is still in development and undergoing field testing.

[207] Extengine, "ARB Verifies Retrofit System to Reduce Diesel Exhaust on Older Off-Road Equipment." Online resource, available at: http://www.extengine.com/index.html Last accessed 03/03/05.

[208] California Air Resources Board, "Diesel Emission Control Strategies Verification: Level 1 Verified Technologies." 01.27.2005. Online resource, last accessed 02.04.2005. URL: http://www.arb.ca.gov/diesel/verdev/level1.htm

[209] Letter from Steve B. Dornak (Mayor's Office of the City of Houston) to Annette Herbert of CARB, dated July 15, 2004 stating, in part, the following: "Field tests of the Extengine ADEC system were the most impressive. Testing of the ADEC I and II systems produced CO reductions of 76 to 84%, while NO_x reduction of 78 to 82% were observed."

[210] Based on e-mail correspondence with Phillip Roberts, of Extengine, on 01.23.2005.

[211] A Slip Catalyst converts excessive ammonia into nitrogen and water to avoid ammonia being emitted through the exhaust gas. Information based on phone conversation with T.J. Tarabulski of Combustion Components Associates Inc. on February 11, 2005.

[212] *Ibid.*

[213] Johnson Matthey, "Johnson Matthey Introduces the SCRT System." Online resource, available at: http://www.jmcsd.com/scrttm_system.html Last accessed 03/03/05.

[214] Marty Lassen, "EPA Clean Diesel Engine Implementation Workshop." Johnson Matthey, August 6-7, 2003. Online resource, available at: http://www.epa.gov/otaq/regs/hd2007/wrkshop2/lassen.pdf, please see slide 5. Last accessed 03/03/05.

[215] "Verified" means that either the EPA or the California ARB have verified this type of technology. However, please refer to http://www.epa.gov/otaq/retrofit/retroverifiedlist.htm and http://www.arb.ca.gov/diesel/verdev/verdev.htm for detailed information regarding the different types of verified emission control technologies and the different manufacturers whose technologies have been verified.

[216] EPA and CARB have signed a Memorandum of Agreement for the Coordination and Reciprocity in Diesel Retrofit Device Verification.

[217] CARB, "Diesel Emissions Control Strategies Verification: Level 3 Verified Technologies." Online resource, available at: http://www.arb.ca.gov/diesel/verdev/level3.htm Last accessed 03/03/05.

[218] Cleaire Inc, "Products." Online resource, available at http://www.cleaire.com/site/products/# Last accessed 03/03/05.

[219] Longview filters have been installed on motor graders, wheel loaders, backhoe loaders and backup generators.

[220] Only once in a very unusual application could the exhaust gas temperature not be achieved. Information based on phone conversation with Tim Taylor of Cleaire on August 3, 2004.

[221] Pricing can vary depending on the distributor.

[222] These numbers include installation and tax. Numbers provided by Cleaire, Inc.

[223] Information based on e-mail correspondence with Tim Taylor, of Cleaire Advanced Emission Controls, LLC on February 18, 2005.

[224] *Ibid.*

[225] Cleaire Inc, "Products." Online resource, available at http://www.cleaire.com/site/products/# Last accessed 03/03/05.

[226] Information based on e-mail correspondence with Tim Taylor, of Cleaire Advanced Emission Controls, LLC on February 18, 2005.

[227] Numbers include installation and tax. Numbers provided by Cleaire, Inc. However, pricing can vary depending on the distributor.

[228] This section is from Retrofitting Emission Controls On Diesel-Powered Vehicles. MECA, March 2002. Online resource, available at http://www.meca.org/jahia/Jahia/engineName/filemanager/pid/229/dieselretrofitwp.pdf?actionreq=actionFileDownload&fileItem=220 Last accessed 03/03/05.

[229] MECA Diesel Retrofit. Frequently Asked Questions About The Installation Of Emission Controls On Existing Diesel Engines, page 3. Online resource, available at: http://www.meca.org/jahia/Jahia/engineName/filemanager/pid/224/retrofitFAQ%20(revised).pdf?actionreq=actionFileDownload&fileItem=712 Last accessed 03/03/05.

[230] Based on a telephone conversation with Alex Gorrel of SST Emtec on October 5, 2004.

[231] Based on a telephone conversation with Alex Gorrel of SST Emtec on October 5, 2004.

[232] CARB, "Carl Moyer Third Year Status Report." March 26, 2002. Online resource, available at: http://www.arb.ca.gov/msprog/moyer/2002report.pdf Last accessed 03/01/05.

[233] CARB, "The Carl Moyer Program Annual Status Report." February 2004. Online resource, available at: http://www.arb.ca.gov/msprog/moyer/moyer_2004_report.pdf Last accessed 03/01/05

[234] CARB, "Carl Moyer Program Update." January 20, 2005. Online resource, available at: http://www.arb.ca.gov/msprog/moyer/carl_moyer_board_presentation_1_20_05.pdf Last accessed 03/01/05.

[235] *Ibid.*

[236] *Ibid.*

[237] California State Legislature, "Assembly Bill 932, Chapter 707." September 23, 2004. Online resource, available at: http://www.arb.ca.gov/msprog/moyer/ab923/ab923text.pdf Last accessed 03/01/05.

[238] CARB, "Carl Moyer Program Update." January 20, 2005. Online resource, available at: http://www.arb.ca.gov/msprog/moyer/carl_moyer_board_presentation_1_20_05.pdf Last accessed 03/01/05.

[239] California State Legislature, "Assembly Bill 932, Chapter 707." September 23, 2004. Online resource, available at: http://www.arb.ca.gov/msprog/moyer/ab923/ab923text.pdf Last accessed 03/01/05.

[240] *Ibid.*

[241] NCDAQ, "2004 Grant Awards." 09/21/2004. Online resource, available at: http://daq.state.nc.us/motor/ms_grants/grant04.shtml Last accessed 03/01/05.

[242] Texas Natural Resource Conservation Commission (TNRCC). http://www.tnrcc.state.tx.us/oprd/sips/terp.html

[243] TCEQ, "Texas Emissions Reduction Plan: Biennial Report to the Legislature." December 2004. Online resource, available at: http://www.tceq.state.tx.us/assets/public/comm_exec/pubs/sfr/079_04.pdf Last accessed 03/01/05.

[244] Texas Legislature, House Bill 2481, 2005.

[245] For the EPA onroad retrofit technology verification program, visit: http://www.epa.gov/otaq/retrofit/retroverifiedlist.htm Last accessed 08/13/04. For the CARB onraod retrofit technology verification program, visit: http://www.arb.ca.gov/diesel/verdev/background.htm Last accessed 08/13/04.

[246] EPA, "Verified Products." August 11, 2004. Online resource, available at: http://www.epa.gov/otaq/retrofit/retroverifiedlist.htm Last accessed 08/13/04.

[247] *Ibid.*

[248] CARB, "Diesel Emission Control Strategies Verification: Background." April 15, 2003. Online resource, available at: http://www.arb.ca.gov/diesel/verdev/background.htm Last accessed 08/13/04.

[249] EPA, "What is a State Implementation Plan?" Online resource, available at: http://www.epa.gov/region1/topics/air/sips/REVISED_WHAT_IS_A_SIP.pdf Last accessed 03/02/05.

[250] EPA, "8-Hour Ground-level Ozone Designations." March 3, 2005. Online resource, available at: http://www.epa.gov/ozonedesignations Last accessed 03/03/05.

[251] EPA, "EPA Announces Final Designations For First Fine Particle Standards." December 17, 2004. Online resource, available at: http://yosemite.epa.gov/opa/admpress.nsf/b1ab9f485b098972852562e7004dc686/bc63cfdda235542585256f6d005e6738!OpenDocument Last accessed 03/03/05.

[252] EPA, "Regions." Online resource, available at: http://www.epa.gov/epahome/locate2.htm Last accessed 03/03/05.

[253] For Regional EPA Contact Information go to: http://www.epa.gov/otaq/retrofit/cont_eparegions.htm

[254] EPA. *Air and Radiation. Heavy-duty Diesel Emission Reduction Project Retrofit/Rebuild Component.* Prepared by Northeast States for Coordinated Air Use Management. EPA420-R99-014. June 1999.

[255] Based on E-mail correspondence with U.S. EPA, January 26, 2005. Also refer to: Calculating SIP credits. Online resource, available at: http://www.epa.gov/otaq/retrofit/aqsipcalc.htm Last accessed 03/03/05.

[256] EPA Clean Diesel Program. Online resource available, at http://www.epa.gov/diesel/ Last accessed on 03/02/05. See also http://www.dieselforum.org/factsheet/ulsd.html.

[257] Final Rule: "Control of Emissions of Air Pollution from Nonroad Diesel Engines and Fuel" (June 29, 2004): http://www.epa.gov/nonroad-diesel/2004fr.htm#finalrule Last accessed 03/02/05.

[258] New York, NY, Local Law 77, §2(f)(1) (2003). Available online at: http://www.nyccouncil.info/pdf_files/bills/law03077.pdf Last accessed 03/02/05.

[259] *Ibid.*

[260] S. 7652, 227th Leg., (NY. 2004); A. 11716-A, 227th Leg., (NY. 2004).

[261] Sacramento Ozone Summit, "Proactive 'green' contracting by government agencies." Version 13. Online resource, available at: http://airquality.org/modelord/EpisodicModelGreenContractingV13.pdf Last accessed 03/02/05.

[262] The Contract Specification also contin exceptions to idling limits. Those exceptions exist when (a) when a "mobile source" is forced to remain motionless because of traffic conditions or mechanical difficulties over which the "operator" has no control; (b) when it is necessary to operate heating, cooling or auxiliary equipment installed on the "mobile source" when such equipment is necessary to accomplish the intended use of the "mobile source"; (c) to bring the "mobile source" to the manufacturer's recommended operating temperature; (d) when the outdoor temperature is below twenty (20) degrees Fahrenheit; and/or (e) when the "mobile source" is being repaired.

[263] Available online from the NY Department of Transportation's web site, at: http://www.route9a.info/dseis.htm Last accessed 08/25/04.

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California Environmental Protection Agency

Air Resources Board

INITIAL STATEMENT OF REASONS FOR RULEMAKING

STAFF REPORT

PROPOSED IDENTIFICATION OF DIESEL EXHAUST AS A TOXIC AIR CONTAMINANT

Prepared by the Staff of
the Air Resources Board and
the Office of Environmental Health Hazard Assessment

June 1998

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- Volume 1-2: Public Comments - June 1994
- Volume 2-1: ARB and OEHHA Staff Responses to Public Comments - May 1997
- Volume 2-2: Public Comments - May 1997
- Volume 3-1: ARB and OEHHA Staff Responses to Public Comments - February 1998
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INITIAL STATEMENT OF REASONS FOR RULEMAKING

STAFF REPORT

INTRODUCTION

In accordance with California Health and Safety Code sections 39660-39662, the Air Resources Board (ARB or Board) staff is recommending that the Board identify diesel exhaust as a toxic air contaminant (TAC).

This Initial Statement of Reasons for Rulemaking for the Proposed Identification of Diesel Exhaust as a TAC consists of:

1) an ARB Staff Report, which summarizes the scientific basis for the proposed regulation and includes a discussion of the environmental and economic impacts of the proposal;
2) Appendix I (the Proposed Regulation Order);
3) Appendix II (the Findings of the Scientific Review Panel [SRP]); and
4) Appendix III (the SRP-approved version of the Executive Summary and the three-part report that contains the analysis of the exposure and health assessments of diesel exhaust, Parts A, B, and C, as approved on April 22, 1998).

Part A, prepared by the ARB staff, is an evaluation of emissions of, and exposure to, diesel exhaust. Part B, prepared by the Office of Environmental Health Hazard Assessment (OEHHA) staff, assesses the health effects of diesel exhaust. Part C consists of copies of the public comments received on the June 1994, May 1997, and February 1998 draft reports, and the ARB/OEHHA staff responses.

BACKGROUND

1. Definition of a Toxic Air Contaminant

Section 39655 of the California Health and Safety Code defines a TAC as "an air pollutant which may cause or contribute to an increase in mortality or an increase in serious illness, or which may pose a present or potential hazard to human health." California Health and Safety Code section 39013 defines air pollutant as "any discharge, release, or other propagation into the atmosphere and includes, but is not limited to, smoke, charred paper, dust, soot, grime, carbon, fumes, gases, odors, particulate matter, acids, or any combination thereof." In addition, substances which have been listed as federal hazardous air pollutants (HAPs) pursuant to section 7412 of Title 42 of the United States Code have also been identified as TACs under the state's air toxics program pursuant to section 39657(b) of the California Health and Safety Code.

2. The California Program for Identification and Control of Toxic Air Contaminants

This program was established by a California law, Assembly Bill 1807 (AB 1807, Tanner, Chapter 1047, statutes of 1983, Health and Safety Code section 39650 *et seq.*, Food and Agriculture Code section 14021 *et seq.*). AB 1807 created a comprehensive program administered by the ARB to reduce the potential adverse public health impacts caused by emissions of toxic substances to the ambient air.

AB 1807 established a two-phased process which separates risk assessment (identification) from risk management (control). During the identification phase, a report is developed which determines whether there may be potential adverse health effects from substances in consideration of their toxicity, quantities of emissions and human exposure in California. If the Board formally identifies a substance as a TAC, the substance enters the risk management phase. In the risk management phase, the ARB determines the need for and appropriate degree of controls in consideration of cost and potential health benefits. The identification phase and the control phase are open public processes in which the ARB staff actively seeks industry and public participation. (Health and Safety Code section 39660-39666.)

In setting priorities for substances to enter the AB 1807 identification process, the ARB must consider factors relating to: 1) risk of harm to public health; 2) amount or potential amount of emissions; 3) manner of, exposure to, and usage of the substance in California; 4) persistence in the atmosphere; and 5) ambient concentrations in the community. (Health and Safety Code section 39660(f).)

Once a substance is entered into the identification process, the ARB and OEHHA staffs prepare a report that serves as the basis for listing the substance as a TAC. Health and Safety Code section 39660 requires the OEHHA, upon the request of the ARB, to evaluate the health effects of a potential TAC while the ARB evaluates the exposure data associated with it.

The ARB's exposure assessment is based, to the extent available, upon research and monitoring data, emissions inventory data, toxic chemical release data, and information on estimated actual exposures from data on ambient and indoor air environments. (Health and Safety Code section 39660(f).)

The OEHHA's health evaluation includes an assessment of the availability and quality of data on the substance's health effects, including its potency and mode of action. Where it can be established that a threshold of adverse health effects exists, the OEHHA must identify a safe exposure level. If there is no threshold of significant adverse health effects, a range of risk for exposure to the substance is determined. (Health and Safety Code section 39660(c).) In both cases, care is taken by the OEHHA to provide a full explanation of any uncertainties associated with the data.

The report, together with the scientific data on which the report is based, is made available to the public and is formally reviewed by the SRP pursuant to Health and Safety Code section 39661. The SRP is composed of nine members, one each with recognized scientific expertise in the field of oncology, pathology, epidemiology, atmospheric science, biostatistics, occupational medicine, toxicology, and biochemistry (or molecular biology), and one member with relevant scientific experience who is experienced in the operation of scientific review or advisory bodies. The SRP reviews the scientific procedures and methods used to support the data, the data itself, and the conclusions and assessments on which the report is based. The SRP conducts all of its business at noticed meetings which are open to the public.

If the SRP approves the report, it will prepare and adopt formal findings. If the SRP determines that the report is not based on sound scientific knowledge, methods, or practices, it will return the report for revision and resubmittal. Once the SRP has reviewed and approved a report, it transmits the report with the SRP-adopted findings to the ARB. The Board conducts a public hearing to determine, based on the staff's report and the SRP's findings, if a substance should be listed as a TAC. If the Board decides to list the substance as a TAC, it is added to section 93000 of the California Code of Regulations. Health and Safety Code section 39665(a) then requires the ARB to prepare a report which assesses the need for and appropriate degree of control for that substance.

DEVELOPMENT OF THE REPORT ON DIESEL EXHAUST

Diesel exhaust entered the AB 1807 process in October 1989 and has undergone an extensive evaluation. Diesel exhaust was entered into the process because it has potential cancer and noncancer health effects and widespread exposure in California. The International Agency for Research on Cancer (IARC) had listed diesel exhaust as a "probable" human carcinogen and the U.S. Environmental Protection Agency (U.S. EPA) had begun an evaluation of both the cancer and noncancer health effects. The ARB and the OEHHA gave priority to the evaluation of diesel exhaust because it met the TAC program criteria related to potential risk of harm to public health, amount of emissions, exposure and use, and persistence in the atmosphere.

In March 1990, the ARB sponsored a conference on the risk assessment of diesel exhaust. On June 17, 1994, the first draft TAC identification report was released to the public for a six-month comment period. On September 14, 1994, a public workshop was held to discuss the report. On January 29-30, 1996, the OEHHA, the ARB, the Health Effects Institute (HEI), the National Institute for Occupational Safety and Health, the World Health Organization, and the U.S. EPA sponsored a scientific workshop to discuss the application of human health study data in developing quantitative cancer risk estimates for diesel exhaust.

A second draft report, which was revised to incorporate public comments received during the first public comment period (June 1994-December 1994), was released for public comment in May 1997. On July 1, 1997, a third public workshop was held to discuss the revised draft report. SRP members participated in these workshops. On October 16, 1997, the SRP held a meeting to

discuss the comments received on this draft report. A third draft report was released for public comment on February 23, 1998. The SRP held a meeting on March 11, 1998, to hear from invited scientists who have expertise in the study of diesel exhaust. On April 22, 1998, the SRP reviewed and approved the draft report and adopted its findings. Appendix II contains the SRP's findings as adopted at the April 22, 1998, meeting. Throughout this process, the ARB and OEHHA staffs conducted numerous other meetings and conference calls with the affected industries, associations, environmental groups, governmental agencies, and other interested parties.

DIESEL EXHAUST EMISSIONS AND EXPOSURE IN CALIFORNIA

The ARB staff reviewed and evaluated the potential for diesel exhaust exposure in California. The ARB staff considered the estimated emissions inventory and ambient concentrations. The SRP approved the ARB staff's exposure assessment at its April 22, 1998, meeting.

1. Emissions

Diesel exhaust is a complex mixture of inorganic and organic compounds that exist in gaseous, liquid, and solid phases. As with combustion of other fuels, the primary gaseous components are nitrogen, oxygen, carbon dioxide, and water vapor. Diesel exhaust includes over 40 substances that are listed as hazardous air pollutants by the U.S. EPA and by the ARB as TACs. The substances listed below have either been detected or predicted to occur in the exhausts of diesel engines based on observed chemical reactions and/or their presence in the fuel or lubricating oil. Fifteen of these substances are listed by the IARC as carcinogenic to humans, or as a probable or possible human carcinogen. Further research is needed to determine the contribution of many of these substances to atmospheric diesel exhaust exposures.

The combustion of diesel fuel in a compression ignition engine produces diesel exhaust. Approximately 2.1 billion gallons of diesel fuel were burned in such engines in California during 1995. In the future, estimated diesel fuel consumption is predicted to increase in California from current levels up to 2.3 billion gallons in 2000 and to 2.9 billion gallons in 2010.

One of the main characteristics of diesel exhaust emitted from newer diesel engines is the release of particles at a rate of about 20 times greater than from comparable gasoline engines. Diesel exhaust particles carry many of the organics and metals present in the exhaust. Over 90 percent of the mass of these particles are less than 2.5 microns in diameter. Because of their small size, these particles are easily inhaled into the bronchial and alveolar regions of the lung.

There are three groups of sources of diesel exhaust in California: mobile sources (on-road vehicles and other mobile sources), stationary area sources (e.g., oil and gas production facilities, stationary engines, shipyards, repair yards), and stationary point sources (e.g., chemical manufacturing, electric utilities). In 1995, emissions of oxides of nitrogen (NO_x) from diesel fuel use were about 415,000 tons per year (tpy); oxides of sulfur (SO_x) about 28,000 tpy; and reactive

Substances in Diesel Exhaust Listed by the ARB as Toxic Air Contaminants

acetaldehyde	hexane
acrolein	inorganic lead
aniline	manganese compounds
antimony compounds	mercury compounds
arsenic	methanol
benzene	methyl ethyl ketone
beryllium compounds	naphthalene
biphenyl	nickel
bis[2-ethylhexyl]phthalate	4-nitrobiphenyl
1,3-butadiene	phenol
cadmium	phosphorus
chlorine	POM, including PAHs and their derivatives
chlorobenzene	propionaldehyde
chromium compounds	selenium compounds
cobalt compounds	styrene
cresol isomers	toluene
cyanide compounds	xylene isomers and mixtures
dioxins and dibenzofurans	o-xylenes
dibutylphthalate	m-xylenes
ethyl benzene	p-xylenes
formaldehyde	

organic gases (ROG) about 41,000 tpy. Diesel exhaust PM_{10} (particulate matter equal to or less than 10 microns in diameter) and $PM_{2.5}$ (particulate matter equal to or less than 2.5 microns in diameter) emissions during 1995 were estimated to be about 27,000 tpy and 26,000 tpy, respectively. Statewide emission estimates of other substances emitted from diesel exhaust (such as benzene, formaldehyde, and 1,3-butadiene) have not been quantified. Further research is needed to accurately estimate diesel exhaust-associated emissions of these substances.

Over the past 20 years, advances in engine design and fuel formulation have been made as a result of control measures enacted by the ARB and U.S. EPA and, in the case of engine design, to improve efficiency. As a measure of the effectiveness of these standards and regulations, statewide diesel exhaust PM_{10} emissions from on-road mobile sources are expected to be reduced by approximately 60 percent between 1995 and 2010. However, unless further controls are established, emissions are expected to increase by about 10 percent from 2010 through 2020 due to increases in the number of vehicles and usage. Because less stringent standards have been applied to off-road engines, total diesel exhaust emissions from on-road and off-road mobile sources are expected to decrease by about 30 percent between 1995 and 2010.

2. Exposure

Our assessment of population exposure to diesel exhaust focuses on the PM_{10} component because more is known about the particulate matter fraction of diesel exhaust. Diesel exhaust particles contain many of the toxic components of the exhaust. We have a complete emissions inventory and ambient concentration data base for diesel exhaust-derived particulate matter in California. In addition, particulate matter has been associated with approximately 50 to 90 percent of the mutagenic potency of whole diesel exhaust.

However, in our review of the health effects of exposure to diesel exhaust, we are examining the overall toxicity of the exhaust. This is because the exposures experienced in the occupational human health studies have been to the whole exhaust. The IARC, the National Institute for Occupational Safety and Health, and the U.S. EPA have also evaluated diesel exhaust this way. We believe this approach is necessary because it is most consistent with the scientific studies to assess health effects from exposure to diesel exhaust. It is recognized that the compounds of concern are those that are emitted as a result of the incomplete combustion of diesel fuel.

The staff estimated a population-weighted average outdoor diesel exhaust PM_{10} exposure concentration in California in 1995 to be 2.2 micrograms per cubic meter ($\mu g/m^3$) (see Appendix III, Part A). Several independent studies have reported similar outdoor air diesel exhaust PM_{10} concentrations. The 1995 average indoor exposure concentration was estimated to be about 1.47 $\mu g/m^3$, which takes into account building air exchange rates, adult and children's activity patterns, and air concentrations of diesel exhaust particles. The 1995 population time-weighted average total air exposure to diesel exhaust PM_{10} concentrations across all environments (including outdoors) is estimated to be 1.54 $\mu g/m^3$ or, when rounded, 1.5 $\mu g/m^3$. Emission reductions that had occurred by 1995 from adopted new engine emission standards and diesel fuel reformulation were taken into account in calculating these exposure numbers.

Higher level, near-source exposures to diesel exhaust occur near busy roads and intersections where many diesel vehicles are operating. Diesel exhaust PM_{10} concentrations as high as 10 $\mu g/m^3$ over a 24-hour period have been measured near a freeway. This is about five times the 1995 outdoor ambient air concentration of 2.2 $\mu g/m^3$ and about six times the 1995 total air exposure estimate of 1.5 $\mu g/m^3$.

As discussed previously, diesel exhaust is a complex mixture of substances, and each substance will remain in the air or react with other substances according to the substance's individual chemical properties. Diesel particles are typically smaller than 1 micron and are expected to remain in the air for about 10 days, provided that the weather is dry. Diesel particles are effectively removed by precipitation and persist for much shorter periods during these events.

Diesel exhaust emissions can deposit onto water, soil, and vegetation. Exposure by ingestion and dermal absorption can occur through these other media and through airborne exposures to re-entrained dust. In order to assess non-inhalation pathways, substance and site-specific data are

needed. Since the specific parameters for diesel exhaust are not known for these pathways, a multi-pathway assessment for diesel exhaust exposure was not done. Therefore, our estimates of exposure to diesel exhaust are conservative and underestimate the public's actual exposure to diesel exhaust. More research is needed in this area for diesel exhaust.

As a result of the emission reductions described previously, ambient levels of diesel exhaust PM_{10} are expected to be reduced by about 20 percent from 1995 to 2010.

3. Diesel Exhaust Constituents from Pre-1993 Fuel and Post-1993 Fuel Combustion

To address the effects that recent changes in diesel fuel composition may have on the toxic exhaust constituents from newer diesel engines, the ARB funded a study by the College of Engineering, Center for Environmental Research and Technology (CE-CERT) at the University of California, Riverside. The study design included the testing of one heavy-duty diesel engine (that was typical of engines on the market in California) using three fuels (a single fuel that meets specifications of low sulfur fuel required before 1993, a very low aromatic fuel, and a fuel designed to be typical of the fuels in use now). The study design did not produce data that could be used to obtain statistically robust conclusions (due to the use of only one engine and the limited number of data points for each target analyte/fuel combination). Testing was conducted from December 1996 to January 1997 and results became available in spring of 1998.

The results from this study show reductions of criteria pollutants consistent with what was estimated by the ARB staff for the 1988 diesel fuel regulation. The low aromatic and typical in-use fuels produced particulate matter and NO_x exhaust emissions reductions that met the regulation's requirements.

A comparison of the milligram to milligram per brake horsepower-hour emission profiles using the three different fuels showed the presence of the same toxic substances, and a similar distribution of toxic substances in general. The low aromatic and alternative fuels resulted in lower emission rates for some particle- and vapor-phase PAHs including anthracene, benz[a]anthracene, dibenzo[a,h]pyrene, naphthalene, and biphenyl. In addition, higher mutagenic activity was observed in both the particle and vapor phase collected from pre-October 1993 fuel than from the low aromatic and alternative formulation fuels. However, because of the limited testing, it is not possible to determine if the mutagenicity differences are statistically significant.

The CE-CERT study also tested for dioxins with the purpose of identifying and attempting to quantify dioxins for method development. The results show that dioxins are present in exhaust from both the old and the new fuel. However, the results are qualitative only and indicate the need for further method development.

Overall, the results from this study indicate that the diesel exhaust from the new diesel fuel tested contained the same toxic air contaminants as the old fuel, although their concentrations may differ for some compounds. Further research would be necessary to quantify the amounts of

specific compounds emitted from a variety of engine technologies, operating cycles, and fuel to characterize better any differences between old and new fuels and technologies and the potential impact on the toxicity of diesel exhaust.

HEALTH EFFECTS OF DIESEL EXHAUST EXPOSURE

The OEHHA reviewed and evaluated the potential for diesel exhaust to affect human health, and the associated scientific uncertainties. The OEHHA considered acute and chronic noncancer health impacts, and potential cancer health impacts. The SRP approved the OEHHA's health assessment at its April 22, 1998, meeting.

A number of adverse short-term (acute) health effects have been associated with exposures to diesel exhaust. Occupational exposures to diesel exhaust particles have been associated with significant cross-shift decreases in lung function. Increased cough, labored breathing, chest tightness, and wheezing have been associated with exposure to diesel exhaust in bus garage workers. A significant increase in airway resistance and increases in eye and nasal irritation were observed in human volunteers following one-hour chamber exposure to diesel exhaust. In acute and subchronic animal studies, exposure to diesel exhaust particles induced inflammatory airway changes, lung function changes, and increased the animals' susceptibility to infection.

A number of adverse long-term (chronic) noncancer effects have been associated with exposures to diesel exhaust. Occupational studies have shown that there may be a greater incidence of cough, phlegm and chronic bronchitis among those exposed to diesel exhaust than among those not exposed. Histopathological changes in the lung of diesel-exposed test animals reflect inflammation of the lung tissue. Reduced pulmonary function was noted in monkeys during long-term exposure. Reductions in pulmonary function have also been reported following occupational exposures in chronic studies.

Diesel exhaust particles can induce immunological allergic reactions and localized inflammatory responses in humans, as well as acting as an adjuvant for pollen allergy. Intranasal challenge with diesel exhaust particles in human volunteers resulted in an immunological response. Co-exposure to diesel exhaust particles and ragweed pollen resulted in an immune response greater than that following pollen or diesel exhaust particles alone. Effects of intratracheal, intranasal, and inhalation exposures of laboratory animals are supportive of the findings in humans. These effects include allergic reactions and inflammation, increased mucus secretion and respiratory resistance, and airway constriction.

The World Health Organization and the OEHHA have conducted further analyses of the dose-response relationships for several of the non-cancer, adverse effects of chronic exposures to diesel exhaust on the rat lung. These analyses gave a range of health risk guidance values of 2 to 21 $\mu g/m^3$ and support the adoption of 5 $\mu g/m^3$ which is also the 1993 U.S. EPA Reference Concentration. A U.S. EPA Reference Concentration or California Reference Exposure Level (REL) of a chemical is an estimate, with uncertainty spanning perhaps an order of magnitude, of the air concentration below which no noncancer adverse health effects are likely to occur from

lifetime exposure. This estimate takes into consideration persons who may be more sensitive than others to the effects of a chemical. The OEHHA concurs with the U.S. EPA in recommending 5 $\mu g/m^3$ as the chronic REL for diesel exhaust.

Diesel exhaust contains genotoxic compounds in both the vapor phase and the particle phase. Diesel exhaust particles or extracts of diesel exhaust particles are mutagenic in bacteria and in mammalian cell systems, and can induce adverse chromosomal changes. DNA adducts (representing genotoxins bound chemically to DNA) have been shown to increase following inhalation exposure of rodents and monkeys to whole diesel exhaust and have been found in mammalian cells following treatment with diesel exhaust particle extract. Elevated levels of DNA adducts have been associated with occupational exposure to diesel exhaust.

Over 30 human epidemiological studies have investigated the potential carcinogenicity of diesel exhaust. These epidemiological studies provide evidence consistent with a causal relationship between occupational diesel exhaust exposure and lung cancer. These studies, on average, found that long-term occupational exposures to diesel exhaust were associated with a 40 percent increase in the relative risk of lung cancer. The OEHHA analyzed the lung cancer findings for consistency and found that the association was unlikely to be due to bias or chance. Results of inhalation bioassays in the rat, and with less certainty in mice, have demonstrated the carcinogenic potential of diesel exhaust in animals, although the mechanisms by which diesel exhaust induces lung tumors in animals remain uncertain.

Other agencies or scientific bodies have studied the health effects of diesel exhaust. The National Institute of Occupational Safety and Health first recommended that whole diesel exhaust be regarded as a potential occupational carcinogen based upon animal and human evidence in 1988. The IARC concluded that diesel engine exhaust is probably carcinogenic to humans (Group 2A). Based upon the IARC findings, in 1990, the State of California under the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65) identified diesel exhaust as a chemical "known to the State to cause cancer." (Title 22, California Code of Regulations, section 12000.) The 1998 draft U.S. EPA document (Health Assessment Document for Diesel Emissions, Review Draft, February 1998) similarly concluded that diesel exhaust be considered a "probable" human carcinogen (category B1). This conclusion evolves from positive yet "limited" evidence in the human studies, a "sufficient" level of evidence in bioassays, and consideration of the supporting information from mutagenicity and genotoxicity data.

Risk assessments can use carcinogenicity data from either animal or human studies. For diesel exhaust, there are data from human epidemiological studies of occupationally exposed populations which are useful for quantitative risk assessment. On balance, the OEHHA concluded that available human data lend more confidence in the prediction of human risks than the data from the available animal studies because of the uncertainties in the animal studies and of extrapolating from animals to humans. Thus, the OEHHA preferred to derive the range of human risk estimates based only upon the epidemiological findings and not the animal data. Using data from a case-control study and a cohort study, the OEHHA estimated the risk (95 percent upper confidence limit) of lung cancer in the general population due to diesel exhaust. Because of

uncertainties in the actual workplace exposures, the OEHHA developed a variety of exposure scenarios to bracket the exposures that were plausible. Based on these exposure estimates, presented in Table 1-1, the range of resulting estimates of cancer unit risk is 1.3×10^{-4} to 2.4×10^{-3} $(\mu g/m^3)^{-1}$. The unit risk represents the 95 percent upper confidence limit of cancer risk per million people exposed per microgram of diesel exhaust particulate in a cubic meter of air over a 70-year lifetime. The SRP approved the range of risk estimated by the OEHHA. In addition, the SRP concluded that a value of 3×10^{-4} $(\mu g/m^3)^{-1}$ is a reasonable estimate of unit risk expressed in terms of diesel particulate (see Appendix II).

The OEHHA and ARB staffs recognize that the limited exposure information available contributes to the uncertainty of the dose response risk assessment based on the human studies. However, the overall magnitude of uncertainty is not atypical of the types of uncertainty encountered when the Board identified other TACs. The greater than usual uncertainty in the exposure estimates is substantially offset by the much smaller than usual range of extrapolation from the occupational exposures to the ambient air concentrations. Interspecies extrapolation uncertainty is not an issue in this diesel exhaust risk assessment. In addition, there are more than 30 human studies of more than one occupation that show overall an increase in lung cancer from diesel exhaust exposure.

Based on available scientific evidence, a level of diesel exhaust exposure below which no carcinogenic effects are anticipated has not been identified. This finding was approved by the SRP at its meeting on April 22, 1998.

As with other substances evaluated by the SRP and after reviewing the field of published peer reviewed research studies on diesel exhaust, the SRP indicated that additional research is appropriate to further clarify the health effects of diesel exhaust. The OEHHA and ARB staffs recognize that diesel exhaust health studies will continue. For example, the HEI, which is jointly funded by industry and the U.S. EPA, has started a five-year study to review key epidemiologic studies and make recommendations for the design of new studies. The OEHHA and ARB staffs will follow these efforts closely, and will provide support to the extent resources are available. If the outcome of this, or other future health studies, ultimately reduces uncertainties or improves the scientific basis for estimating diesel exhaust risk, the OEHHA and ARB staffs would consider such information. When research results become available, the TAC program has a process in place for further evaluation of new scientific evidence pertaining to a previously completed TAC risk assessment. The process specifically addresses the evaluation and response to submittals of new scientific information as evidence for review of a TAC risk assessment.

Table 1-1. Summary of Cancer Unit Risks According to Study, Exposure Assumptions, and Modeling Approaches.

		95% UCL Cancer Unit Risk ($\mu g/m^3)^{-1}$	95% Upper Confidence Limit of Cancer Risk per Million per Microgram of Diesel Exhaust Particulate in a Cubic Meter of Air Exposure Over a 70-year Lifetime
Garshick *et al.* (1987a) Case Control[1]			
Scenario[2]			
	A	2.4×10^{-3}	2400
	B	1.8×10^{-3}	1800
	C	1.0×10^{-3}	1000
	D	6.6×10^{-4}	660
	E	3.6×10^{-4}	360
Garshick *et al.* (1988) Cohort Study (Chapter 7)[3]			
Scenario			
	A	1.8×10^{-3}	1800
	B	1.4×10^{-3}	1400
	C	8.2×10^{-4}	820
	D	5.1×10^{-4}	510
	E	2.8×10^{-4}	280
Garshick *et al.* (1988) Cohort Study (Appendix D)[4]			
Scenario A			
	general multiplicative model	1.9×10^{-3}	1900
	biologically based [5]	3.8×10^{-4}	380
Scenario C			
	general multiplicative model	7.2×10^{-4}	720
	biologically based [5]	1.3×10^{-4}	130
	biologically based [6]	1.5×10^{-4}	150

EVALUATION OF NEED AND APPROPRIATE DEGREE OF CONTROL FOR DIESEL

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[1] ***Using published slope coefficient for hazard on years to diesel exhaust as described in Appendix III (Part B, Section 7.3.3).***

[2] ***A Ramp pattern of exposure plateauing in 1959 at the 1980 exposure level of 50 $\mu g/m^3$***

B Roof pattern of exposure peaking in 1959 at twice the 1980 exposure level of 40 $\mu g/m^3$

C Roof pattern of exposure peaking in 1959 at 3-fold the 1980 exposure level of 50 $\mu g/m^3$

D Roof pattern of exposure peaking in 1959 at 3-fold the 1980 exposure level of 80 $\mu g/m^3$

E Roof pattern of exposure peaking in 1959 at 10-fold the 1980 exposure level of 50 $\mu g/m^3$

[3] ***Using individual data to obtain a slope for hazard on years of exposure to diesel exhaust as described in Appendix III (Part B, Section 7.3.4).***

[4] ***Applying time varying concentrations to individual data to obtain a slope of hazard on exposure as described in Appendix III (Part B, Appendix D).***

[5] ***6th/7 stage model.***

[6] ***7th/7 stage model.***

EXHAUST

If the Board votes to formally identify diesel exhaust as a TAC, the staff will begin an analysis to determine what if any further regulatory action to reduce exposures to diesel exhaust is necessary. A report will be prepared, in consultation with the local districts, affected industries, and the public, on the need and appropriate degree of control (the "needs assessment") for diesel exhaust. The report is required by Health and Safety Code section 39665(a) and must include the following information: present and potential future emissions and associated potential risks; atmospheric persistence; number and categories of emission sources; available control technologies; costs for reducing emissions; alternative sources of emission reductions; and the potential adverse health, safety, or environmental impacts associated with the implementation of a control measure.

In its assessment, staff will focus on technological opportunities, beyond those already in place, to reduce further public exposures to emissions from diesel engines. Staff's focus will be on reducing emissions of those components of diesel exhaust that are emitted as a result of the incomplete combustion of diesel fuel. We anticipate that our focus will be on the particulate matter component, and potentially the volatile organic component, of diesel exhaust. We believe this approach to be consistent with the identification of whole diesel exhaust because we know there are toxic constituents on the particle and in the vapor phase. Staff will not be considering a ban on the use of diesel fuel or diesel engines, because such a strategy would not be technically and economically feasible.

If this needs assessment identifies additional technically feasible and cost-effective opportunities for reducing exposures to diesel emissions within the authority of the ARB or air pollution control districts, the ARB would then design specific control measures in an open regulatory process with full public involvement.

To ensure full opportunity for public consultation and participation in the needs assessment process, the ARB staff intends to create a diesel exhaust risk management working group (working group). Invitations to participate would be sent to interested industries, associations, environmental groups, other governmental agencies such as the U.S. EPA and air districts, and other interested parties.

The working group would advise the ARB staff and serve as a forum for on-going communication, cooperation, and coordination in the identification of additional opportunities to reduce further emissions from diesel engines. Meetings of the group would be publicly noticed and the meetings would be open to all. We intend to hold an initial organizational meeting of the working group this fall.

Over the past 20 years, a number of regulations have been adopted by the ARB and the

U.S. EPA that have resulted in or will result in significant reductions in emissions of pollutants such as NO_x, SO_x, and particulate matter from diesel engines. These include:

- a requirement for low sulfur/low aromatic diesel fuel that reduces particulate matter, NO_x, and SO_x emissions (effective 1993);
- emission standards that restrict the amount of particulate matter emitted by new diesel cars, trucks, urban buses, and heavy-duty trucks (phased-in from 1982 through 1996);
- emission standards for NO_x emissions from diesel vehicles, heavy-duty trucks, and urban buses (phased in from 1984 through 2004);
- the roadside testing of heavy-duty diesel vehicles for excessive particulate matter emissions (effective 1991) and a requirement for fleet inspection and maintenance of heavy-duty diesel vehicles (anticipated to begin in summer 1998);
- emission standards that restrict the amount of particulate matter and NO_x that can be emitted from many 1995 and newer small off-road diesel engines (<25 hp) (effective 1995);
- emission standards for particulate matter and NO_x from heavy-duty off-road diesel equipment (>175 hp) (effective 1996); and
- a requirement that portable diesel engines registered in the Statewide Portable Equipment Program must satisfy, by 2010, the above emission standards for heavy-duty off-road diesel equipment (>175 hp) and federal standards for particulate matter and NO_x from heavy-duty off-road diesel equipment (>50 hp) (effective 1997).

Significant progress has been made as a result of the above emissions standards and fuel regulations. For example, since 1988, particulate matter emissions from new heavy-duty diesel truck engines have been reduced by over 85 percent, and from urban bus engines by over 90 percent. Emissions of NO_x from heavy-duty diesel truck engines have also been reduced since the mid-1980s by over 20 percent. SO_x emissions have also decreased due to the reduction of sulfur content in fuels by over 80 percent in 1993.

In addition, the ARB staff is working on the following measures to reduce emissions from diesel engines:

- fuel specifications for locomotives;
- more stringent standards for light- and medium-duty diesel vehicles;
- more stringent standards (in conjunction with U.S. EPA) for all off-road diesel equipment;
- more stringent standards (in conjunction with U.S. EPA) for locomotives operating in the

South Coast Air Basin in 2010 and beyond;

- incentive measures for new and in-use on-road diesel vehicles and off-road diesel engines that could provide a boost for alternative fuel engine introduction.

Part of the effort of the working group would be to assess whether additional control measures are needed in light of the impact of existing and planned regulations on diesel exhaust emission trends and exposures. Technical work already planned in connection with new federal fine particulate matter standards will help quantify the sources of diesel particulate matter and the effect of the ARB's current control program. If a need for further control is found, the ARB staff would examine strategies such as tighter emission standards for new vehicles; further reformulation of diesel fuel; maintaining low emissions in-use; and incentive programs to promote accelerated turnover of in-use diesel engines and alternative engine and fuel technologies in urban areas where the vast majority of population exposure to diesel exhaust occurs. An incentive program, such as that proposed by the Governor for the 1998-1999 budget, could provide a boost for alternative fuel engine introduction and engine replacement with cleaner engines.

ENVIRONMENTAL IMPACT ASSESSMENT

The identification of diesel exhaust as a TAC is not expected to result in any adverse impact on the environment. The Board's identification of diesel exhaust as a TAC and the subsequent analysis of the need to control emissions in the AB 1807 risk management program may result in the adoption of control measures pursuant to Health and Safety Code sections 39665 and 39666. When considering the adoption of control measures, the ARB will consider all potential impacts of the measures on human health, as well as the potential benefits to public health by reducing diesel exhaust emissions. Therefore, the identification of diesel exhaust as a TAC may ultimately result in control measures that will result in environmental benefits. Adverse environmental impacts identified with respect to specific control measures will be included in the consideration of such control measures pursuant to Health and Safety Code sections 39665 and 39666.

ECONOMIC IMPACT ASSESSMENT

The identification of diesel exhaust as a TAC will not directly have any economic impact on mobile sources of diesel exhaust because the act of identifying a TAC does not mandate any specific risk management action. Once a substance is identified, the ARB is required to assess the need and appropriate degree of control for that substance. Potential control measures for both mobile and stationary sources will be assessed and developed in a full public forum in which the impact of these measures on businesses would be fully assessed.

While most of the diesel exhaust emitted to California's atmosphere is a result of the incomplete combustion of diesel fuel in mobile sources, diesel exhaust emissions also occur from

stationary facilities using diesel fuel. Identifying diesel exhaust as a TAC could have an economic impact on these types of stationary sources as they comply with district rules and permit requirements. Districts have the authority to require that public exposure to particular toxic substances not exceed levels deemed by the district to be protective of public health. Some districts' permitting requirements specify that no new or modified facilities exceed a specific risk level based on the SRP-approved cancer risk numbers for specific toxic substances. These requirements may result in facility operators needing to purchase control equipment or being denied a permit.

Districts are required to implement the AB 2588 Air Toxics Hot Spots Information and Assessment Act of 1987 (AB 2588; Health and Safety Code sections 44300-44384.) This Act establishes a program to inventory emissions of toxic air pollutants and to assess the risk to public health caused by these emissions. Under this program, districts prioritize, require risk assessments, and determine which facilities must notify the public of potential health risks posed by emissions of toxic substances that are on the Hot Spots toxic substances list. If a facility's emissions present a significant health risk, it must develop an Audit and Plan for reducing the risk. The program is supported by fees paid by the affected industries. The fees are specified by state and district regulations which are updated each year through a public process, including public workshops and public hearings.

Diesel exhaust is already on the Hot Spots toxic substances list, and qualified facilities have been required to report their emissions of diesel exhaust and pay program fees. However, the health impacts of diesel exhaust have not been evaluated or quantified under the Program up to this point due to lack of a cancer potency value. The diesel exhaust TAC identification report includes a range of cancer potency values that districts could use to evaluate the cancer risk from sources emitting diesel exhaust. Some facilities may have to prepare risk assessments and, depending on the results, may be required by the districts to notify nearby residents of their emissions. Facilities with large numbers of engines, or with very large engines, and which are located close to populated areas might be affected by these requirements. For example, a stationary diesel engine of approximately 300 horsepower, operating 24 hours per day, 365 days per year, with an emission release point 9 feet above the ground, may exceed a risk of 10 per million. This is only a rough estimate, as the estimated risk will vary with site-specific meteorological conditions, hours of operation, stack height, and control equipment.

There may be Hot Spots fee increases if a facility's potential cancer health risk is equal to or greater than 10 per million. Facilities having a potential cancer risk equal to or greater than 100 per million may need to purchase control equipment or change their operations to reduce exposures to nearby residents.

Some districts include substances listed in the AB 2588 Air Toxics Hot Spots program in their list of sources and substances affected by permitting rules. Other districts may add diesel exhaust upon its identification as a TAC. If districts add facilities that emit diesel exhaust to their permit programs, the affected facilities may be required to pay additional permitting fees. Districts must

conduct socioeconomic analyses, as well as public workshops and hearings, before identified TACs are added to their programs.

Health and Safety Code section 42311 authorizes local air pollution control districts to assess permit fees to recover the cost of district programs required or authorized by state law. Most districts charge facilities fees to cover the cost of developing and implementing the controls required by Health and Safety Code section 39666. The amount of these fees is generally determined by the district resources needed to implement the control requirements. The fees are established by district rulemaking action, and districts must conduct socioeconomic impact analyses, workshops and public hearings before adopting or revising any fee rule.

STAFF RECOMMENDATION AND PLAIN ENGLISH SUMMARY OF THE PROPOSED REGULATION

Based on the information available on diesel exhaust-induced noncancer and cancer health effects and the results of the risk assessment, and the findings of the SRP, we conclude that diesel exhaust meets the definition of a TAC which is an air pollutant "which may cause or contribute to an increase in mortality and serious illness, or which may pose a present or potential hazard to human health" (Health and Safety Code section 39655). Therefore, staff recommends that the Board adopt the proposed regulation shown in Appendix I identifying diesel exhaust as a TAC with no identified level of exposure below which no carcinogenic effects are anticipated. Staff further recommends that the Board direct staff to begin the risk management phase of the program for diesel exhaust and form a diesel exhaust risk management working group to coordinate efforts with the U.S. EPA, industry, environmental groups, and other interested parties.

APPENDIX I

PROPOSED REGULATION ORDER

PROPOSED REGULATION ORDER

Amend Titles 17 and 26, California Code of Regulations, Section 93000 to read as follows:

93000. Substances Identified as Toxic Air Contaminants.
Each substance identified in this section has been determined by the State Board to be a toxic air contaminant as defined in Health and Safety Code Section 39655. If the State Board has found there to be a threshold exposure level below which no significant adverse health effects are anticipated from exposure to the identified substance, that level is specified as the threshold determination. If the Board has found there to be no threshold exposure level below which no significant adverse health effects are anticipated from exposure to the identified substance, a determination of "no threshold" is specified. If the Board has found that there is not sufficient available scientific evidence to support the identification of a threshold exposure level, the "Threshold" column specifies "None identified."

Substance	Threshold Determination
Benzene (C_6H_6)	None identified
Ethylene Dibromide ($BrCH_2CH_2Br$; 1,2-dibromoethane)	None identified
Ethylene Dichloride ($ClCH_2CH_2Cl$; 1,2-dichloroethane)	None identified
Hexavalent Chromium [Cr(VI)]	None identified
Asbestos [asbestiform varieties of serpentine (chrysotile) riebeckite (crocidolite) cummingtonite-grunerite (amosite), tremolite, actinolite, and anthophyllite]	None identified
Dibenzo-p-dioxins and Dibenzofurans chlorinated in the 2,3,7 and 8 positions and containing 4,5,6, or 7 chlorine atoms	None identified
Cadmium (metallic cadmium and cadmium compounds)	None identified
Carbon Tetrachloride (CCl_4; tetrachloromethane)	None identified
Ethylene Oxide (1,2-epoxyethane)	None identified
Methylene Chloride (CH_2Cl_2; Dichloromethane)	None identified
Trichloroethylene	None identified

Chloroform ($CHCl_3$)	None identified
Vinyl Chloride (C_2H_3Cl; Chloroethylene)	None identified
Inorganic Arsenic	None identified
Nickel	None identified
Perchloroethylene (C_2Cl_4; Tetrachloroethylene)	None identified
Formaldehyde (HCHO)	None identified
1,3-Butadiene (C_4H_6)	None identified
Inorganic Lead	None identified
Diesel Exhaust	None identified

NOTE: Authority cited: Sections 39600, 39601, and 39662, Health and Safety Code. Reference: Sections 39650, 39660, 39661, and 39662, Health and Safety Code.

APPENDIX II

FINDINGS OF THE SCIENTIFIC REVIEW PANEL

May 27, 1998

Mr. John D. Dunlap, III
Chairman
Air Resources Board
2020 L Street
Sacramento, California 95814

Dear Chairman Dunlap:

I am pleased to forward to you the Scientific Review Panel's (SRP/Panel) Findings (enclosure) for the Proposed Identification of Diesel Exhaust as a Toxic Air Contaminant Report as adopted unanimously at the Panel's April 22, 1998 meeting.

The data, developed and reviewed by OEHHA and ARB, in the scientific risk assessment on exposure to diesel exhaust (Part A) and its health effects (Part B), are extensive and scientifically sound. The SRP notes the report documents the fact that diesel exhaust includes over 40 substances listed by the U.S. Environmental Protection Agency as hazardous air pollutants and by the ARB as toxic air contaminants.

The exposure estimate in the report may underestimate many Californians' actual total exposure because it excludes elevated exposures near roadways, railroad tracks, and inside vehicles. Other routes of exposure to diesel exhaust, such as ingestion and dermal absorption are also excluded.

Development of this report began in 1989, and this compound has the most human epidemiological studies (over 30) than any of the previous 21 toxic air contaminant reports the Panel has reviewed. These studies have investigated the relationship between occupational diesel exhaust exposure and lung cancer, and the epidemiological evidence indicates exposure to diesel exhaust increases the risk of lung cancer. It is noted that in 1990 the State of California, pursuant to Proposition 65, identified diesel exhaust as a chemical "known to the State to cause cancer."

There are a number of adverse long-term noncancer effects associated with exposure to diesel exhaust. These effects include chronic bronchitis, inflammation of lung tissue, thickening of the alveolar walls, immunological allergic reactions, and airway constriction. As new quantitative data emerge from research on adverse noncancer effects from diesel exhaust, the Reference Exposure Level may require adjustment.

The Panel believes there is still more to be learned about the adverse health effects associated with exposure to diesel exhaust. The Panel is concerned that some technological advances may result in greater total particulate exposure, particularly of fine particles that penetrate deeper into the lungs, but some controls and fuels may reduce overall particulate level. The Panel encourages further research to quantify the amounts of specific compounds emitted from a variety of engine technologies, operating cycles, and fuel to characterize better any differences between old and new fuels and technologies.

The Panel recognizes that diesel exhaust is a mixture of compounds and the potency factor may change as a result of new engine technologies and "cleaner" fuel. Accordingly, the unit risk factor may change as a result of new peer reviewed research.

We welcome any opportunity to provide additional information helpful to you or that would facilitate the process of identification.

We would appreciate our Findings and this transmittal letter being made a part of the final report.

Sincerely,

/s/

John R. Froines, Ph.D.
Acting Chairman
Scientific Review Panel

Enclosure

cc: Scientific Review Panel Members
Michael Kenny, ARB
Bill Lockett, ARB

Findings of the Scientific Review Panel on
THE REPORT ON DIESEL EXHAUST
as adopted at the Panel's April 22, 1998, Meeting

Pursuant to Health and Safety Code section 39661, the Scientific Review Panel (SRP/Panel) has reviewed the report *Proposed Identification of Diesel Exhaust as a Toxic Air Contaminant* by the staffs of the California Air Resources Board (ARB or Board) and the Office of Environmental Health Hazard Assessment (OEHHA) describing the public exposure to, and health effects of, diesel exhaust. The Panel members also reviewed the public comments received on this report.

Panel members participated in workshops devoted to discussion of the exposure and health issues associated with diesel exhaust in September 1994, January 1996, July 1997, and March 1998. The SRP reviewed the issues at its meetings in October 1997 and April 1998. A special meeting of the SRP was held on March 11, 1998, to hear testimony on health issues including the quantitative risk assessment from highly respected scientists invited by the Panel. Based on these reviews and information provided at scientific workshops and meetings, the SRP makes the following findings pursuant to Health and Safety Code section 39661:

Exposure related conclusions

1. Diesel exhaust is a complex mixture of gases and fine particles emitted by a diesel-fueled internal combustion engine.

2. The gaseous fraction is composed of typical combustion gases such as nitrogen, oxygen, carbon dioxide, and water vapor. However, as a result of incomplete combustion, the gaseous fraction also contains air pollutants such as carbon monoxide, sulfur oxides, nitrogen oxides, volatile organics, alkenes, aromatic hydrocarbons, and aldehydes, such as formaldehyde and 1,3-butadiene and low-molecular weight polycyclic aromatic hydrocarbons (PAH) and PAH-derivatives.

3. One of the main characteristics of diesel exhaust is the release of particles at a markedly greater rate than from gasoline-fueled vehicles, on an equivalent fuel energy basis. The particles are mainly aggregates of spherical carbon particles coated with inorganic and organic substances. The inorganic fraction primarily consists of small solid carbon (or elemental carbon) particles ranging from 0.01 to 0.08 microns in diameter. The organic fraction consists of soluble organic compounds such as aldehydes, alkanes and alkenes, and high-molecular weight PAH and PAH-derivatives, such as nitro-PAHs. Many of these PAHs and PAH-derivatives, especially nitro-PAHs, have been found to be potent mutagens and carcinogens. Nitro-PAH compounds can also be formed during transport through the atmosphere by reactions of adsorbed PAH with nitric acid and by gas-phase radical-initiated reactions in the presence of oxides of nitrogen.

4. Diesel exhaust includes over 40 substances that are listed by the United States Environmental Protection Agency (U.S. EPA) as hazardous air pollutants and by the ARB as toxic air contaminants. Fifteen of these substances are listed by the International Agency for Research on Cancer (IARC) as carcinogenic to humans, or as a probable or possible human carcinogen. Some of these substances are: acetaldehyde; antimony compounds; arsenic; benzene; beryllium compounds; bis(2-ethylhexyl)phthalate; dioxins and dibenzofurans; formaldehyde; inorganic lead; mercury compounds; nickel; POM (including PAHs); and styrene.

5. Almost all of the diesel particle mass is in the fine particle range of 10 microns or less in diameter (PM_{10}). Approximately 94 percent of the mass of these particles are less than 2.5 microns in diameter. Because of their small size, these particles can be inhaled and a portion will eventually become trapped within the small airways and alveolar regions of the lung.

6. The estimated population-weighted average outdoor diesel exhaust PM_{10} concentration in California for 1995 is 2.2 microgram per cubic meter ($\mu g/m^3$). Several independent studies have reported similar outdoor air diesel exhaust PM_{10} concentrations. The 1995 estimated average indoor exposure concentration is approximately 1.5 $\mu g/m^3$.

7. The population time-weighted average total air exposure to diesel exhaust particle concentrations across all environments (including outdoors) is estimated to be 1.5 $\mu g/m^3$ in 1995. This total exposure estimate may underestimate many Californians' actual total exposure because it excludes elevated exposures near roadways, railroad tracks, and inside vehicles. Near-source exposures to diesel exhaust may be as much as five times higher than the 1995 population time-weighted average total air exposure. It also excludes other routes of exposure to diesel exhaust, such as ingestion and dermal absorption.

8. Diesel engine exhaust contains small carbonaceous particles and a large number of chemicals that are adsorbed onto these particles or present as vapors. These particles have been the subject of many studies because of their adverse effects on human health and the environment. A recent study conducted for the Health Effects Institute showed that, despite a substantial reduction in the weight of the total particulate matter, the total number of particles from a 1991-model engine was 15 to 35 times greater than the number of particles from a 1988 engine when both engines were operated without emission control devices. This suggests that more fine particles, a potential health concern, could be formed as a result of new technologies. Further study is needed since the extent of these findings only measured exhaust from two engines and engine technologies.

9. The major sources of diesel exhaust in ambient outdoor air are estimated to emit approximately 27,000 tons per year in 1995. On-road mobile sources (heavy-duty trucks, buses, light-duty cars and trucks) contribute the majority of total diesel exhaust PM_{10} emissions in California. Other mobile sources (mobile equipment, ships, trains, and boats) and stationary sources contribute the remaining emissions.

10. Significant progress has been made as a result of federal and state regulations that have addressed particulate matter levels from diesel engines. Emissions of on-road mobile source diesel exhaust PM_{10} in California are expected to decline by approximately 85 percent from 1990 to 2010 as a result of mobile source regulations already adopted by the ARB.

11. The results of a study funded by the ARB at the University of California, Riverside, indicate that the diesel exhaust from the new fuel tested contained the same toxic air contaminants as the old fuel, although their concentrations and other components may differ. Further research would be helpful to quantify the amounts of specific compounds emitted from a variety of engine technologies, operating cycles, and fuel to characterize better any differences between old and new fuels and technologies.

Health effects associated with diesel exhaust

12. A number of adverse short-term health effects have been associated with exposures to diesel exhaust. Occupational exposures to diesel exhaust particles have been associated with significant cross-shift decreases in lung function. Increased cough, labored breathing, chest tightness, and wheezing have been associated with exposure to diesel exhaust in bus garage workers. A significant increase in airway resistance and increases in eye and nasal irritation were observed in human volunteers following one-hour chamber exposure to diesel exhaust. In acute or subchronic animal studies, exposure to diesel exhaust particles induced inflammatory airway changes, lung function changes, and increased the animals' susceptibility to infection.

13. A number of adverse long-term noncancer effects have been associated with exposure to diesel exhaust. Occupational studies have shown that there may be a greater incidence of cough, phlegm and chronic bronchitis among those exposed to diesel exhaust than among those not exposed. Reductions in pulmonary function have also been reported following occupational exposures in chronic studies. Reduced pulmonary function was noted in monkeys during long-term exposure. Histopathological changes in the lung of diesel-exposed test animals reflect inflammation of the lung tissue. These changes include dose-dependent proliferations of type II epithelial cells, marked infiltration of macrophages, plasma cells and fibroblasts into the alveolar septa, thickening of the alveolar walls, alveolar proteinosis, and focal fibrosis.

14. Studies have shown that diesel exhaust particles can induce immunological reactions and localized inflammatory responses in humans, as well as acting as an adjuvant for pollen allergy. Intranasal challenge with diesel exhaust particles in human volunteers resulted in increased nasal IgE antibody production and a significant increase in mRNA for pro-inflammatory cytokines. Co-exposure to diesel exhaust particles and ragweed pollen resulted in a nasal IgE response greater than that following pollen or diesel exhaust particles alone. Effects of intratracheal, intranasal, and inhalation exposures of laboratory animals are supportive of the findings in humans. These effects include eosinophilic

infiltration into bronchi and bronchioles, elevated IgE response, increased mucus secretion and respiratory resistance, and airway constriction.

15. Based on the animal studies, the U.S. EPA determined a chronic inhalation Reference Concentration value of 5 $\mu g/m^3$ for noncancer effects of diesel exhaust. This estimate takes into consideration persons who may be more sensitive than others to the effects of diesel exhaust. The report supports the recommendation of 5 $\mu g/m^3$ as the California Reference Exposure Level (REL) (Table 1). It should be noted that this REL may need to be lowered further as more data emerge on potential adverse noncancer effects from diesel exhaust.

16. Diesel exhaust contains genotoxic compounds in both the vapor phase and the particle phase. Diesel exhaust particles or extracts of diesel exhaust particles are mutagenic in bacteria and in mammalian cell systems, and can induce chromosomal aberrations, aneuploidy, and sister chromatid exchange in rodents and in human cells *in vitro*. Diesel exhaust particles induced unscheduled DNA synthesis *in vitro* in mammalian cells. DNA adducts have been isolated from calf thymus DNA *in vitro* following treatment with diesel exhaust particle extracts. DNA adducts have been shown to increase following inhalation exposure of rodents and monkeys to whole diesel exhaust. Elevated levels of DNA adducts have been associated with occupational exposure to diesel exhaust. Results of inhalation bioassays in the rat, and with lesser certainty in mice, have demonstrated the carcinogenicity of diesel exhaust in test animals, although the mechanisms by which diesel exhaust induces lung tumors in animals remains uncertain.

17. Over 30 human epidemiological studies have investigated the potential carcinogenicity of diesel exhaust. These studies, on average, found that long-term occupational exposures to diesel exhaust were associated with a 40 percent increase in the relative risk of lung cancer. The lung cancer findings are consistent and the association is unlikely to be due to chance. These epidemiological studies strongly suggest a causal relationship between occupational diesel exhaust exposure and lung cancer.

18. Other agencies or scientific bodies have evaluated the health effects of diesel exhaust. The National Institute of Occupational Safety and Health first recommended in 1988 that whole diesel exhaust be regarded as a potential occupational carcinogen based upon animal and human evidence. The International Agency for Research on Cancer (IARC) concluded that diesel engine exhaust is probably carcinogenic to humans and classified diesel exhaust in Group 2A. Based upon the IARC findings, in 1990, the State of California under the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65) identified diesel exhaust as a chemical "known to the State to cause cancer." The U.S. EPA has proposed a conclusion similar to IARC in their draft documents. The 1998 draft U.S. EPA document concluded similarly that there was sufficient animal evidence of carcinogenicity and that the human evidence was limited.

19. There are data from human epidemiological studies of occupationally exposed populations which are useful for quantitative risk assessment. The estimated range of lung cancer risk (upper 95% confidence interval) based on human epidemiological data is 1.3×10^{-4} to 2.4

x 10^{-3} ($\mu g/m^3$)$^{-1}$ (Table 2). After considering the results of the meta-analysis of human studies, as well as the detailed analysis of railroad workers, the SRP concludes that 3 x 10^{-4} ($\mu g/m^3$)$^{-1}$ is a reasonable estimate of unit risk expressed in terms of diesel particulate. Thus this unit risk value was derived from two separate approaches which yield similar results. A comparison of estimates of risk can be found in Table 3.

20. Based on available scientific information, a level of diesel exhaust exposure below which no carcinogenic effects are anticipated has not been identified.

21. Based on available scientific evidence, as well as the results of the risk assessment, we conclude that diesel exhaust be identified as a Toxic Air Contaminant.

22. As with other substances evaluated by this Panel and after reviewing the field of published peer reviewed research studies on diesel exhaust, additional research is appropriate to clarify further the health effects of diesel exhaust. This research may have significance for estimating the unit risk value.

23. The Panel, after careful review of the February 1998 draft SRP version of the ARB report, *Proposed Identification of Diesel Exhaust as a Toxic Air Contaminant*, as well as the scientific procedures and methods used to support the data, the data itself, and the conclusions and assessments on which the Report is based, finds this report with the changes specified during our October 16, 1997, meeting and as a result of comments made at the March 11, 1998, meeting, is based upon sound scientific knowledge, methods, and practices and represents a complete and balanced assessment of our current scientific understanding.

For these reasons, we agree with the science presented in Part A by ARB and Part B by OEHHA in the report on diesel exhaust and the ARB staff recommendation to its Board that diesel exhaust be listed by the ARB as a Toxic Air Contaminant.

I certify that the above is a true and correct copy of the findings adopted by the Scientific Review Panel on April 22, 1998.

/s/

_____

John R. Froines, Ph.D
Acting Chairman,
Scientific Review Panel

TABLE 1

NONCANCER HEALTH VALUES APPROVED BY THE SCIENTIFIC REVIEW PANEL 1998

Compound	Health Value	Endpoint
Acetaldehyde	9 $\mu g/m^3$	Respiratory System
Diesel Exhaust	**5 $\mu g/m^3$**	**Respiratory System**
Inorganic Lead	4.6×10^{-4} $(\mu g/m^3)^{-1}$	Cardiovascular Mortality
Perchloroethylene	35 $\mu g/m^3$	Alimentary System (Liver)

$\mu g/m^3$: microgram per cubic meter

TABLE 2

CANCER POTENCIES APPROVED BY THE SCIENTIFIC REVIEW PANEL FROM 1984 TO 1998
(in order of cancer potency)

Compound	Unit Risk $(\mu g/m^3)^{-1}$	Range $(\mu g/m^3)^{-1}$
Dioxins	3.8×10^{1}	2.4×10^{1} to 3.8×10^{1}
Chromium VI	1.5×10^{-1}	1.2×10^{-2} to 1.5×10^{-1}
Cadmium	4.2×10^{-3}	2.0×10^{-3} to 1.2×10^{-2}
Inorganic Arsenic	3.3×10^{-3}	6.3×10^{-4} to 1.3×10^{-2}
Benzo[a]pyrene	1.1×10^{-3}	1.1×10^{-3} to 3.3×10^{-3}
Diesel Exhaust	**3×10^{-4}**	**1.3×10^{-4} to 2.4×10^{-3}**
Nickel	2.6×10^{-4}	2.1×10^{-4} to 3.7×10^{-3}
1,3-Butadiene	1.7×10^{-4}	4.4×10^{-6} to 3.6×10^{-4}
Ethylene Oxide	8.8×10^{-5}	6.1×10^{-5} to 8.8×10^{-5}
Vinyl Chloride	7.8×10^{-5}	9.8×10^{-6} to 7.8×10^{-5}
Ethylene Dibromide	7.1×10^{-5}	1.3×10^{-5} to 7.1×10^{-5}
Carbon Tetrachloride	4.2×10^{-5}	1.0×10^{-5} to 4.2×10^{-5}
Benzene	2.9×10^{-5}	7.5×10^{-6} to 5.3×10^{-5}
Ethylene Dichloride	2.2×10^{-5}	1.3×10^{-5} to 2.2×10^{-5}
Inorganic Lead	1.2×10^{-5}	1.2×10^{-5} to 6.5×10^{-5}
Perchloroethylene	5.9×10^{-6}	3.0×10^{-7} to 1.1×10^{-5}
Formaldehyde	6.0×10^{-6}	2.5×10^{-7} to 3.3×10^{-5}
Chloroform	5.3×10^{-6}	6.0×10^{-7} to 2.0×10^{-5}
Acetaldehyde	2.7×10^{-6}	9.7×10^{-7} to 2.7×10^{-5}
Trichloroethylene	2.0×10^{-6}	8.0×10^{-7} to 1.0×10^{-5}
Methylene Chloride	1.0×10^{-6}	3.0×10^{-7} to 3.0×10^{-6}
Asbestos	1.9×10^{-4} (per 100fiber/m^3)	Lung: $11 - 110 \times 10^{-6}$ (per 100 fiber/m^3) Mesothelioma: $38 - 190 \times 10^{-6}$ (per 100 fiber/m^3)

$\mu g/m^3$: microgram per cubic meter

TABLE 3

Comparison of Other Organizations' Estimated 95% Upper Confidence Limits of Lifetime Risk per $\mu g/m^3$ Diesel Particulate Matter from Risk Assessments Based on Epidemiologic Data with OEHHA Estimates

Method	Unit Risk/Range	Basis of Assessment	Reference
Epidemiologic analysis	3×10^{-4}	based on smoking-adjusted pooled RR	Smith, 1998
Epidemiologic analysis[b]	**3.6×10^{-4} to 2.4×10^{-3}**	**case-control study of Garshick et al., 1987**	**OEHHA, Part B, Section 7.3.3**
Epidemiologic analysis	**2.8×10^{-4} to 1.8×10^{-3}**	**cohort study of Garshick et al., 1988**	**OEHHA, Part B, Section 7.3.4**
Epidemiologic analysis	**1.3 to 7.2×10^{-4}**	**cohort study, time varying conc., roof (3,50) pattern**	**OEHHA, Part B, Appendix D**
Epidemiologic analysis	**3.8×10^{-4} to 1.9×10^{-3}**	**cohort study, time varying conc., ramp (1,50) pattern**	**OEHHA, Part B, Appendix D**
Epidemiologic analysis	1.4×10^{-3}	London transport study[c]	Harris, 1983
Epidemiologic analysis	2×10^{-3}	epidemiologic data of Garshick (top end of U.S. EPA's range)	U.S. EPA, 1998;
Epidemiologic analysis	1.3×10^{-4} to 1.3×10^{-2}	using smoking adjusted RR and exposures of 5 or 500 $\mu g/m^3$	OEHHA, Part B, Section 7.3; bracketed risk bounds

a) Bolded values are included in OEHHA's range of risk.
b) Obtained by applying Harris' slope of 5×10^{-4} $(\mu g/m^3 \times yr)^{-1}$ to California life table.

Comment Letter I14

United States
Environmental Protection
Agency

Health Assessment Document For Diesel Engine Exhaust

Comment Letter I14

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Health Assessment Document for Diesel Engine Exhaust

National Center for Environmental Assessment
Office of Research and Development
U.S. Environmental Protection Agency
Washington, DC

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ABSTRACT

This assessment examined information regarding the possible health hazards associated with exposure to diesel engine exhaust (DE), which is a mixture of gases and particles. The assessment concludes that long-term (i.e., chronic) inhalation exposure is likely to pose a lung cancer hazard to humans, as well as damage the lung in other ways depending on exposure. Short-term (i.e., acute) exposures can cause irritation and inflammatory symptoms of a transient nature, these being highly variable across the population. The assessment also indicates that evidence for exacerbation of existing allergies and asthma symptoms is emerging. The assessment recognizes that DE emissions, as a mixture of many constituents, also contribute to ambient concentrations of several criteria air pollutants including nitrogen oxides and fine particles, as well as other air toxics. The assessment's health hazard conclusions are based on exposure to exhaust from diesel engines built prior to the mid-1990s. The health hazard conclusions, in general, are applicable to engines currently in use, which include many older engines. As new diesel engines with cleaner exhaust emissions replace existing engines, the applicability of the conclusions in this Health Assessment Document will need to be reevaluated.

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FOREWORD

The diesel engine has been a vital workhorse in the United States, powering many of its large trucks, buses, and farm, railroad, marine, and construction equipment. Expectations are that diesel engine use in these areas will increase due to the superior performance characteristics of the engine. Diesel engine exhaust (DE), however, contains harmful pollutants in a complex mixture of gases and particulates. Human exposure to this exhaust comes from both highway uses (on-road) as well as nonroad uses of the diesel engine.

EPA started evaluating and regulating the gaseous emissions from the heavy-duty highway use of diesel engines in the 1970s and particle emissions in the 1980s. The reduction of harmful exhaust emissions has taken a large step forward because of standards issued in 2000 which will bring about very large reductions in exhaust emissions for model year 2007 heavy-duty engines used in trucks, buses, and other on-road uses. A draft of this assessment, along with the peer review comments of the Clean Air Scientific Advisory Committee, was part of the scientific basis for EPA's regulation of heavy-duty highway engines completed in December 2000. The information provided by this assessment was useful in developing EPA's understanding of the public health implications of exposure to DE and the public health benefits of taking regulatory action to control exhaust emissions. EPA anticipates developing similarly stringent regulations for other diesel engine uses, including those used in nonroad applications.

Until these regulations take effect, EPA is partnering with state and local agencies to retrofit older, dirtier, engines to make them run cleaner and to develop model programs to reduce emissions from idling engines. In addition, EPA and local authorities are working to ensure early introduction of effective technologies for particulate matter control and the availability of low- sulfur fuel where possible in advance of the 2007 requirements. Today, at least one engine manufacturer is producing new engines with particulate traps that, when coupled with low-sulfur fuel, meet 2007 particulate emission levels. The Agency expects significant environmental and public health benefits as the environmental performance of diesel engines and diesel fuels improves.

The health assessment concludes that long-term (i.e., chronic) exposure to DE is likely to pose a lung cancer hazard as well as damage the lung in other ways depending on exposure. The health assessment's conclusions are based on exposure to exhaust from diesel engines built prior to the mid-1990s. Short-term (i.e., acute) exposures can cause transient irritation and inflammatory symptoms, although the nature and extent of these symptoms are highly variable across the population. The assessment also states that evidence is emerging that diesel exhaust

exacerbates existing allergies and asthma symptoms. The assessment recognizes that DE emissions, as a mixture of many constituents, also contribute to ambient concentrations of several criteria air pollutants including nitrogen oxides, sulfur oxides, and fine particles, as well as other hazardous air pollutants.

The particulate fraction of DE and its composition is a key element in EPA's present understanding of the health issues and formulation of the conclusions in the health assessment. The amount of exhaust particulate from on-road engines has been decreasing in recent years and is expected to decrease 90% from today's levels with the engines designed to meet the 2007 regulations. The composition of the exhaust particulates and the gases also will change. While EPA believes that the assessment's conclusions apply to the general use of diesel engines today, as cleaner diesel engines replace a substantial number of existing engines, the general applicability of the conclusions in this health assessment document will need to be reevaluated.

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PREFACE

This document is the U.S. Environmental Protection Agency's science-based *Health Assessment Document for Diesel Engine Exhaust.* The assessment was prepared by the National Center for Environmental Assessment which is the health risk assessment program in EPA's Office of Research and Development. The assessment broadly supports activities authorized in the 1990 Clean Air Act. This assessment was specifically prepared for EPA's Office of Transportation and Air Quality which requested information regarding the potential health hazards associated with diesel engine exhaust (DE) exposure. As DE emissions also contribute to urban air toxics and ambient particulate matter, other EPA air programs also have an interest in this assessment.

This document was preceded by five earlier drafts: a Workshop Review Draft (EPA/600/8-90/057A, July 1990), an External Review Draft (EPA/600/8-90/057B, December 1994), an SAB Review Draft (EPA/600/8-90/057C, February 1998), an SAB Review Draft (EPA/600/8-90/057D, November 1999), and an SAB Review Draft (EPA/600/8-90/057E, July 2000). There was an SAB Environmental Health Committee Review in 1990 of the July 1990 draft. The Science Advisory Board's Clean Air Scientific Advisory Committee (CASAC) reviewed the 1994 draft in public sessions in May 1995, the 1998 draft in May 1998, the 1999 draft in December 1999, and the July 2000 draft in October 2000. Public comment periods also were conducted concurrently with the CASAC reviews. In addition many reviewers, both within and outside the Agency, provided assistance at various review stages. This is the final version of the assessment which was prepared in response to CASAC advice and public comments received on the 2000 draft.

The scientific literature search for this assessment is generally current through January 2000, although a few later publications have been included.

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The authors wish to thank all those who sought to improve the quality of this report with their comments and are particularly grateful to the CASAC for its advice.

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1. EXECUTIVE SUMMARY

1.1. INTRODUCTION

This Health Assessment Document for Diesel Engine Exhaust (DE) represents EPA's first comprehensive review of the potential health effects from ambient exposure to exhaust from diesel engines. The assessment was developed to provide information about the potential for DE to pose environmental health hazards, information that would be useful in evaluating regulatory needs under provisions of the Clean Air Act. The assessment identifies and characterizes the potential human health hazards of DE (i.e, hazard assessment) and seeks to estimate the relationship between exposure and disease response for the key health effects (i.e., dose-response assessment). A full exposure assessment and risk characterization, the other two components of a complete risk assessment, are beyond the scope of this document.

The report has nine chapters and three appendices. Chapter 2 provides a characterization of diesel emissions, atmospheric transformation, and human exposures to provide a context for the hazard evaluation of DE. Chapters 3, 4, 5, and 7 provide a review of relevant information for the evaluation of potential health hazards of DE, including dosimetry (Chapter 3), mutagenicity (Chapter 4), noncancer effects (Chapter 5), and carcinogenic effects (Chapter 7). Chapters 6 and 8 contain dose-response analyses to provide insight about the significance of the key noncancer and cancer hazards. Chapter 9 summarizes and characterizes the overall nature of the health hazard potential in the environment and the overall confidence and/or uncertainties associated with the conclusions.

1.2. COMPOSITION OF DIESEL EXHAUST

DE is a complex mixture of hundreds of constituents in either a gas or particle form. Gaseous components of DE include carbon dioxide, oxygen, nitrogen, water vapor, carbon monoxide, nitrogen compounds, sulfur compounds, and numerous low-molecular-weight hydrocarbons. Among the gaseous hydrocarbon components of DE that are individually known to be of toxicologic relevance are the aldehydes (e.g., formaldehyde, acetaldehyde, acrolein), benzene, 1,3-butadiene, and polycyclic aromatic hydrocarbons (PAHs) and nitro-PAHs.

The particles present in DE (i.e., diesel particulate matter [DPM]) are composed of a center core of elemental carbon and adsorbed organic compounds, as well as small amounts of sulfate, nitrate, metals, and other trace elements. DPM consists of fine particles (fine particles have a diameter <2.5 μm), including a subgroup with a large number of ultrafine particles (ultrafine particles have a diameter <0.1 μm). Collectively, these particles have a large surface area which makes them an excellent medium for adsorbing organics. Also, their small size makes them highly respirable and able to reach the deep lung. A number of potentially

toxicologically relevant organic compounds are on the particles. The organics, in general, range from about 20% to 40 % of the particle weight, though higher and lower percentages are also reported. Many of the organic compounds present on the particle and in the gases are individually known to have mutagenic and carcinogenic properties. For example, PAHs, nitro-PAHs, and oxidized PAH derivatives are present on the diesel particles, with the PAHs and their derivatives comprising about 1% or less of the DPM mass.

DE emissions vary significantly in chemical composition and particle sizes between different engine types (heavy-duty, light-duty), engine operating conditions (idle, accelerate, decelerate), and fuel formulations (high/low sulfur fuel). Also, there are emission differences between on-road and nonroad engines simply because the nonroad engines to date are generally of older technology. The mass of particles emitted and the organic components on the particles from on-road diesel engines have been reduced over the years. Available data for on-road engines indicate that toxicologically relevant organic components of DE (e.g., PAHs, nitro-PAHs) emitted from older vehicle engines are still present in emissions from newer engines, though relative amounts have decreased. There is currently insufficient information to characterize the changes in the composition of DE from nonroad diesel engines over time.

1.3. DIESEL EXHAUST AS A COMPONENT OF AMBIENT PARTICULATE MATTER

DE is emitted from "on-road" diesel engines (vehicle engines) or "nonroad" diesel engines (e.g., locomotives, marine vessels, heavy-duty equipment, etc.). Nationwide, data in 1998 indicated that DE as measured by DPM made up about 6% of the total ambient $PM_{2.5}$ inventory (i.e., particles with aerodynamic diameter of 2.5 micrometers or less) and about 23% of the inventory, if natural and miscellaneous sources of $PM_{2.5}$ are excluded. Estimates of the DPM percentage of the total inventory in urban centers are higher. For example, estimates range from 10% to 36% in some urban areas in California, Colorado, and Arizona. Available data also indicate that over the years there have been significant reductions in DPM emissions from the exhaust of on-road diesel engines, whereas limited data suggest that exhaust emissions from nonroad engines have increased.

1.4. ATMOSPHERIC TRANSFORMATION OF DIESEL EXHAUST

After emission from the tailpipe, DE undergoes dilution and chemical and physical transformations in the atmosphere, as well as dispersion and transport in the atmosphere. The atmospheric lifetime for some compounds present in DE ranges from hours to days. DPM is directly emitted from diesel-powered engines (primary particulate matter) and can be formed from the gaseous compounds emitted by diesel engines (secondary particulate matter). Limited information is available about the physical and chemical transformation of DE in the

atmosphere. It is not clear what the overall toxicological consequences of DE's transformations are because some compounds in the DE mixture are altered to more toxic forms while others are made less toxic.

1.5. EXPOSURE TO DIESEL EXHAUST

DPM mass (expressed as μg DPM/m^3) has historically been used as a surrogate measure of exposure for whole DE. Although uncertainty exists as to whether DPM is the most appropriate parameter to correlate with human health effects, it is considered a reasonable choice until more definitive information about the mechanisms of toxicity or mode(s) of action of DE becomes available. In the ambient environment, human exposure to DE comes from both on-road and nonroad engine exhaust. A large percentage of the U.S. population also is exposed to ambient $PM_{2.5}$, of which DPM is typically a significant constituent. Although this document does not provide an exposure assessment, DE exposure information is included to provide a context for the health effects information. Exposure estimates for the early to mid-1990s suggest that national annual average DE exposure from on-road engines alone was in the range of about 0.5 to 0.8 μg DPM/m^3 of inhaled air in many rural and urban areas, respectively. Exposures could be higher if there is a nonroad DE source that adds to the exposure from on-road vehicles. For example, preliminary estimates show that, on a national average basis, accounting for nonroad DE emissions adds another twofold to the on-road exposure. For localized urban areas where people spend a large portion of their time outdoors, the exposures are higher and, for example, may range up to 4.0 μg DPM/m^3 of inhaled air.

1.6. HEALTH EFFECTS OF DIESEL EXHAUST

Available evidence indicates that there are human health hazards associated with exposure to DE. The hazards include acute exposure-related symptoms, chronic exposure-related noncancer respiratory effects, and lung cancer. The health hazard conclusions are based on exhaust emissions from diesel engines built prior to the mid-1990s. With current engine use including some new and many more older engines (engines typically stay in service for a long time), the health hazard conclusions, in general, are applicable to engines currently in use. As new and cleaner diesel engines, together with different diesel fuels, replace a substantial number of existing engines, the general applicability of the health hazard conclusions will need to be re-evaluated. With new engine and fuel technology expected to produce significantly cleaner engine exhaust by 2007 (e.g., in response to new federal heavy duty engine regulations), significant reductions in public health hazards are expected for those engine uses affected by the regulations.

1.6.1. Acute (Short-Term Exposure) Effects

Information is limited for characterizing the potential health effects associated with acute or short-term exposure. However, on the basis of available human and animal evidence, it is concluded that acute or short-term (e.g., episodic) exposure to DE can cause acute irritation (e.g., eye, throat, bronchial), neurophysiological symptoms (e.g., lightheadedness, nausea), and respiratory symptoms (cough, phlegm). There also is evidence for an immunologic effect–the exacerbation of allergenic responses to known allergens and asthma-like symptoms. The lack of adequate exposure-response information in the acute health effect studies precludes the development of recommendations about levels of exposure that would be presumed safe for these effects.

1.6.2. Chronic (Long-Term Exposure) Noncancer Respiratory Effects

Information from the available human studies is inadequate for a definitive evaluation of possible noncancer health effects from chronic exposure to DE. However, on the basis of extensive animal evidence, DE is judged to pose a chronic respiratory hazard to humans. Chronic-exposure, animal inhalation studies show a spectrum of dose-dependent inflammation and histopathological changes in the lung in several animal species including rats, mice, hamsters, and monkeys.

This assessment provides an estimate of inhalation exposure of DE (as measured by DPM) to which humans may be exposed throughout their lifetime without being likely to experience adverse noncancer respiratory effects. This exposure level, known as the reference concentration (RfC) for DE of 5 $\mu g/m^3$ of DPM was derived on the basis of dose-response data on inflammatory and histopathological changes in the lung from rat inhalation studies. In recognition of the presence of DPM in ambient $PM_{2.5}$, it also is appropriate to consider the wealth of $PM_{2.5}$ human health effects data. In this regard, the 1997 National Ambient Air Quality Standard for $PM_{2.5}$ of 15 $\mu g/m^3$ (annual average concentration) also would be expected to provide a measure of protection from DPM, reflecting DPM's current approximate proportion to $PM_{2.5}$.

1.6.3. Chronic (Long-Term Exposure) Carcinogenic Effects

This assessment concludes that DE is "likely to be carcinogenic to humans by inhalation" and that this hazard applies to environmental exposures. This conclusion is based on the totality of evidence from human, animal, and other supporting studies. There is considerable evidence demonstrating an association between DE exposure and increased lung cancer risk among workers in varied occupations where diesel engines historically have been used. The human evidence from occupational studies is considered strongly supportive of a finding that DE

exposure is causally associated with lung cancer, though the evidence is less than that needed to definitively conclude that DE is carcinogenic to humans. There is some uncertainty about the degree to which confounders are having an influence on the observed cancer risk in the occupational studies, and there is uncertainty evolving from the lack of actual DE exposure data for the workers. In addition to the human evidence, there is supporting evidence of DPM's carcinogenicity and associated DPM organic compound extracts in rats and mice by noninhalation routes of exposure. Other supporting evidence includes the demonstrated mutagenic and chromosomal effects of DE and its organic constituents, and the suggestive evidence for bioavailability of the DPM organics in humans and animals. Although high-exposure chronic rat inhalation studies show a significant lung cancer response, this is not thought predictive of a human hazard at lower environmental exposures. The rat response is considered to result from an overload of particles in the lung resulting from the high exposure, and such an overload is not expected to occur in humans at environmental exposures.

Although the available human evidence shows a lung cancer hazard to be present at occupational exposures that are generally higher than environmental levels, it is reasonable to presume that the hazard extends to environmental exposure levels. While there is an incomplete understanding of the mode of action for DE-induced lung cancer that may occur in humans, there is the potential for a nonthreshold mutagenic mode of action stemming from the organics in the DE mixture. A case for an environmental hazard also is shown by the simple observation that the estimated higher environmental exposure levels are close to, if not overlapping, the lower range of occupational exposures for which lung cancer increases are reported. These considerations taken together support the prudent public health choice of presuming a cancer hazard for DE at environmental levels of exposure. Overall, the evidence for a potential cancer hazard to humans resulting from chronic inhalation exposure to DE is persuasive, even though assumptions and uncertainties are involved. While the hazard evidence is persuasive, this does not lead to similar confidence in understanding the exposure/dose-response relationship.

Given a carcinogenicity hazard, EPA typically performs a dose-response assessment of the human or animal data to develop a cancer unit risk estimate that can be used with exposure information to characterize the potential cancer disease impact on an exposed population. The DE human exposure-response data are considered too uncertain to derive a confident quantitative estimate of cancer unit risk, and with the chronic rat inhalation studies not being predictive for environmental levels of exposure, EPA has not developed a quantitative estimate of cancer unit risk.

In the absence of a cancer unit risk, simple exploratory analyses were used to provide a perspective of the range of possible lung cancer risk from environmental exposure to DE. The analyses make use of reported lung cancer risk increases in occupational epidemiologic studies,

and the differences between occupational and environmental exposure. The purpose of having a risk perspective is to illustrate and have a sense of the possible significance of the lung cancer hazard from environmental exposure. The risk perspective cannot be viewed as a definitive quantitative characterization of cancer risk nor is it suitable for estimation of exposure-specific population risks.

1.7. SOURCES OF UNCERTAINTY

Even though the overall evidence for potential human health effects of DE is persuasive, many uncertainties exist because of the use of assumptions to bridge data and knowledge gaps about human exposures to DE and the general lack of understanding about underlying mechanisms by which DE causes observed toxicities in humans and animals. A notable uncertainty of this assessment is whether the health hazards identified from studies using emissions from older engines can be applied to present-day environmental emissions and related exposures, as some physical and chemical characteristics of the emissions from certain sources have changed over time. Available data are not sufficient to provide definitive answers to this question because changes in DE composition over time cannot be confidently quantified, and the relationship between the DE components and the mode(s) of action for DE toxicity is/are unclear. While recognizing the uncertainty, for this assessment a judgment is made that prior-year toxicologic and epidemiologic findings can be applied to more current exposures, both of which use DPM mass in air as the measure of DE exposure.

Other uncertainties include the assumptions that health effects observed at high doses may be applicable to low doses, and that toxicologic findings in laboratory animals generally are predictive of human responses. In the absence of a more complete understanding of how DE may cause adverse health effects in humans and laboratory animals, related assumptions (i.e., the presence of a biological threshold for chronic respiratory effects based on cumulative dosage and absence of a threshold for lung cancer stemming from subtle and irreversible effects) are considered reasonable and prudent.

Although parts of this assessment, particularly the noncancer RfC estimate, have been derived with a generic consideration of sensitive subgroups within the population, the actual spectrum of the population that may have a greater susceptibility to DE is unknown and cannot be better characterized until more information is available regarding the adverse effects of DPM in humans. Increased susceptibility, for example, could result from above-average increases in DE deposition and retention in the respiratory system or intrinsic differences in respiratory system tissue sensitivity. There is no DE-specific information that provides direct insight to the question of differential human susceptibility. Given the nature of DE's noncancer effects on the respiratory system it would be reasonable, for example, to consider possible vulnerable

subgroups to include infants/children, the elderly, or individuals with preexisting health conditions, particularly respiratory conditions.

In developing a perspective on the possible significance of the environmental cancer hazard of DE, this assessment uses information about the differences in the magnitude of DE exposures between the occupational and environmental settings. Although an appreciation for differences in exposure is needed only at an order-of-magnitude level for this assessment, one should recognize that individual exposure is a function of both the variable concentrations in the environment and the related breathing and particle retention patterns of the individual. Because of variations in these factors across the population, different subgroups could receive lower or higher exposure to DE than those groups mentioned in this assessment.

Lastly, this assessment considers only potential heath effects from exposures to DE alone. Effects of DE exposure could be additive to or synergistic with concurrent exposures to many other air pollutants. However, in the absence of more definitive data demonstrating interactive effects (e.g., potentiation of allergenicity effects, potentiation of DPM toxicity by ambient ozone and oxides of nitrogen) from combined exposures to DE and other pollutants, it is not possible to address this issue. Further research is needed to improve the knowledge and data on DE exposures and potential human health effects, and thereby reduce uncertainties of future assessments of the DE health effects data.

2. DIESEL EXHAUST EMISSIONS CHARACTERIZATION, ATMOSPHERIC TRANSFORMATION, AND EXPOSURES

2.1. INTRODUCTION

This chapter provides background information relating to the diesel engine, the pollutants it emits, the history of its use in highway vehicles and railroad locomotives, diesel exhaust composition and emissions trends, and air pollution regulatory standards for diesel engines in the United States. The chapter also provides specific information about the physical and chemical composition of diesel exhaust, descriptions of its atmospheric transformations, observations of measured and modeled ambient concentrations (considered alone and as a component of atmospheric particles in general), some estimates of population exposures as well as a comparison of DPM with ambient fine particulate matter ($PM_{2.5}$). In addition, this chapter gives background information that is used in conjunction with toxicology and epidemiology data to formulate conclusions about human health hazards that are discussed in later chapters of this document. The exposure information does not represent a formal or rigorous exposure assessment; it is intended only to provide a context for the health effects data and health hazard findings.

For the purposes of this document, carbonaceous matter, diesel exhaust, diesel particulate matter, elemental carbon, organic carbon, soluble organic fraction, and soot are defined below.

Carbonaceous matter: Carbon-containing compounds that are associated with particulate matter in diesel exhaust. In this document, the term carbonaceous matter includes all organic and elemental carbon-containing compounds that are found in the particle phase. In other documents, this term is sometimes used interchangeably to refer to the insoluble fraction of diesel particulate matter or the soot fraction.

Diesel engine exhaust (DE): Gaseous and particle-phase emissions resulting from the combustion of diesel fuel in an internal-combustion, compression-ignition engine. DE includes emissions from a diesel engine or diesel vehicle (inclusive of aftertreatment devices), but does not include emissions from brake and tire wear.

Diesel particulate matter (DPM): The particle-phase compounds emitted in DE. DPM can refer to both primary emissions and secondary particles that are formed by atmospheric processes. In this document, DPM refers to primary particles. Primary diesel particles are considered fresh after being emitted and aged after

undergoing oxidation, nitration, or other chemical and physical changes in the atmosphere. As used in this document, DPM refers to both fresh and aged DPM unless a distinction is made.

Elemental carbon (EC): Carbon that has undergone pyrolysis (i.e., has been stripped of hydrogen). In pure form, EC contains only carbon atoms, although EC as it exists in combustion particulate matter is likely to contain some hydrogen atoms.

Organic carbon (OC): Carbon- and hydrogen-containing molecules emitted in DE largely as the result of unburned diesel fuel and, to a lesser extent, from engine lubrication oil. OC compounds also can contain oxygen, nitrogen, and sulfur, as well as other elements in small quantities.

Soluble organic fraction (SOF): The organic portion of DPM that can be extracted from the particle matrix into solution. Extraction solutions and procedures vary and are described in Section 2.2.8.1.

Soot: Agglomerations of EC and OC particles. Soot also is often characterized as the insoluble portion of DPM, and is therefore considered to be mainly EC by some investigators.

This chapter begins with a history of dieselization for on-road vehicles and locomotives, followed by an introductory discussion of the formation of primary diesel emissions to assist the reader in understanding the complex factors that influence the formation of particulate matter (PM) and other DE emissions. The next section is a summary of EPA emission standards for on-road and locomotive diesel engines and a description of the national trends in emissions from on-road and nonroad diesel engine sources based on inventory modeling. The chapter continues with a discussion of diesel fuel use and the impact of fuel properties on emissions. The chronological assessment of emissions factors is presented in summaries of chassis and engine dynamometer testing and tunnel tests. This is followed by a description of engine technologies and their effect on emissions, and a description of the chemical and physical nature of emissions. The data describing the important atmospheric transformations of DE are summarized. The chapter concludes with a summary of the available literature regarding atmospheric concentrations of DPM and exposures to DE. EPA has assessed national and urban-area annual average exposure to DPM using the Hazardous Air Pollutant Exposure Model, and this assessment is presented in Section 2.4.3. A full exposure assessment would include the

distribution of ambient DE exposures in different geographic regions and among different demographic groups, the most highly exposed (90th percentile), exposures in microenvironments for short and long durations, the maximum exposure range (98th percentile), and the number of maximum-exposed individuals. However, such an assessment is not currently available. EPA is developing tools to provide a more complete exposure assessment.

2.2. PRIMARY DIESEL EXHAUST EMISSIONS

2.2.1. History of Dieselization

The diesel engine was patented in1892 by Rudolf Diesel, who conceived it as a prime mover that would provide much improved fuel efficiency compared with spark-ignition (SI) engines. To the present day, the diesel engine's excellent fuel economy remains one of its strongest selling points. In the United States, the diesel engine is used mainly in trucks, buses, agricultural and other nonroad equipment, locomotives, and ships.

The chief advantages of the diesel engine over the gasoline engine are its fuel economy and durability. Diesel engines, however, emit more PM per mile driven compared with gasoline engines of a similar weight. Over the past decade, modifications of engine components have substantially reduced particle emissions from both diesel and gasoline engines (Hammerle et al., 1994; Sawyer and Johnson, 1995).

The diesel engine compresses air to high pressure and temperature. Fuel, when injected into this compressed air, autoignites, releasing its chemical energy. The expanding combustion gases do work on the piston before being exhausted to the atmosphere. Power output is controlled by the amount of injected fuel rather than by throttling the air intake. Compared to its SI counterpart, the diesel engine's superior efficiency derives from a higher compression ratio and no part-load throttling. To ensure structural integrity for prolonged reliable operation at the higher peak pressures brought about by a higher compression ratio and autoignition, the structure of a diesel engine generally is more massive than its SI counterpart.

Diesel engines (also called compression-ignition) may be broadly identified as being either two- or four-stroke cycle, injected directly or indirectly, and naturally aspirated or supercharged. They also are classified according to service requirements such as light-duty (LD) or heavy-duty (HD) automotive/truck, small or large industrial, and rail or marine.

All diesel engines use hydraulic fuel injection in one form or another. The fuel system must meet four objectives if a diesel engine is to function properly over its entire operating range. It must: (1) meter the correct quantity of fuel, (2) distribute the fuel to the correct cylinder, (3) inject the fuel at the correct time, and (4) inject the fuel so that it is atomized and mixes well with the in-cylinder air. The first two objectives are functions of a well-designed injection pump, and the last two are mostly functions of the injection nozzle. Fuel injection

systems are moving toward the use of electronic components for more flexible control than is available with purely mechanical systems to obtain lower exhaust emissions without diminishing fuel efficiency.

Both the fuel and the lubricants that service diesel engines are highly finished petroleum-based products combined with chemical additives. Diesel fuel is a mixture of many different hydrocarbon molecules from about C_7 to about C_{35}, with a boiling range from roughly 350 °F to 650 °F. Many of the fuel and oil properties, such as specific energy content (which is higher than gasoline), ignition quality, and specific gravity, are related to hydrocarbon composition. Therefore, fuel and lubricant composition affect many aspects of engine performance, including fuel economy and exhaust emissions.

Complete and incomplete combustion of fuel in the diesel engine results in the formation of a complex mixture of gaseous (gas-phase hydrocarbons, CO, CO_2, NO, NO_2, SO_2) and particulate exhaust (carbonaceous matter, sulfate, and trace elements). Because of concerns over health effects associated with DE, EPA began regulating emissions from diesel engines in 1970 (for smoke) and then added regulations for gaseous emissions. EPA first regulated particulate emissions from HD diesels in 1988.

2.2.1.1. *Dieselization of the On-Road Fleet*

Because of their durability and fuel economy, the use of diesel engines, particularly in long-distance applications, has increased over the years. The Census of Transportation, Truck Inventory and Use Survey (TIUS) indicates that among Class 3-8 trucks, diesel engine use has increased more rapidly than gasoline engine use in the past 20 years. Truck classes are defined by gross vehicle weight as described in Table 2-1. Dieselization first occurred among Class 7 and 8 trucks. The TIUS indicates that 81.5% of diesel trucks on the road in 1963 were Class 7 or 8 trucks (Table 2-2). Class 7 sales became predominantly (>50%) diesel in the 1970s and Class 8 sales became predominantly diesel in the 1960s. Diesels did not make up a majority of class 5 and 6 sales until the 1990s (Figures 2-1 and 2-2). HD trucks have historically constituted the majority of diesel sales and mileage. However, an increasing number of LD diesel trucks have been sold domestically in recent years. In the 1990s, approximately one in three diesel trucks sold was a Class 1 or Class 2 vehicle. Diesel trucks have historically been driven more miles per truck than gasoline trucks. For example, the TIUS indicates that 59% of diesel trucks were driven more than 50,000 miles in 1963, compared with 3% of gasoline trucks.

Table 2-1. Vehicle classification and weights for on-road trucks

Class	Gross vehicle weight (lb)
1	<6,000
2	6,001–10,000
3	10,001–14,000
4	14,001–16,000
5	16,001–19,500
6	19,501–26,000
7	26,001–33,000
8A[a]	33,001–60,000
8B[a]	>60,000
Medium duty (MD)	10,001–19,500 (same as Classes 3–5)
Light-heavy duty (LHD)	19,501–26,000 (same as Class 6)
Heavy-heavy duty (HHD)	>26,001 (same as Class 7–8)

[a]Class 8A and Class 8B are often considered together.

Table 2-2. Total (gas and diesel) diesel trucks in the fleet in 1992

Truck class	1992 gas and diesel trucks	1992 diesel trucks	% Diesels
Class 1 and 2 (Light duty)	55,193,300	1,387,600	3
Class 3, 4, and 5 (Medium duty)	1,258,500	326,300	26
Class 6 (Light heavy-duty)	732,300	273,800	37
Class 7 and 8 (Heavy heavy-duty)	2,016,600	1,725,300	86

Source: Census of Transportation, 1995.

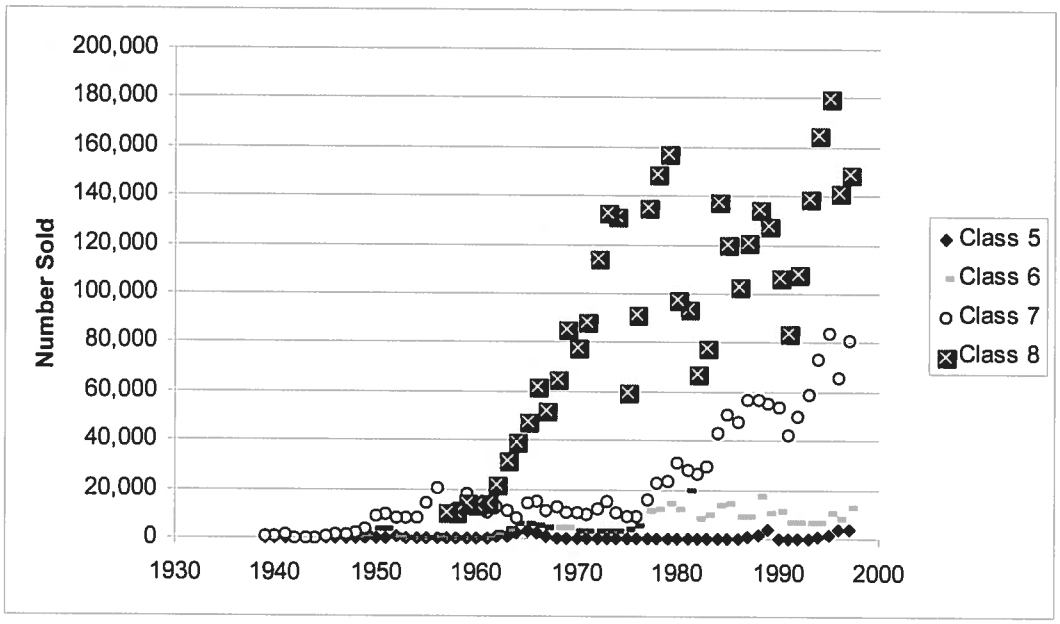


Figure 2-1. Diesel truck sales (domestic) for the years 1939-1997.
Source: AAMA, 1927-1974 and 1975-1998.

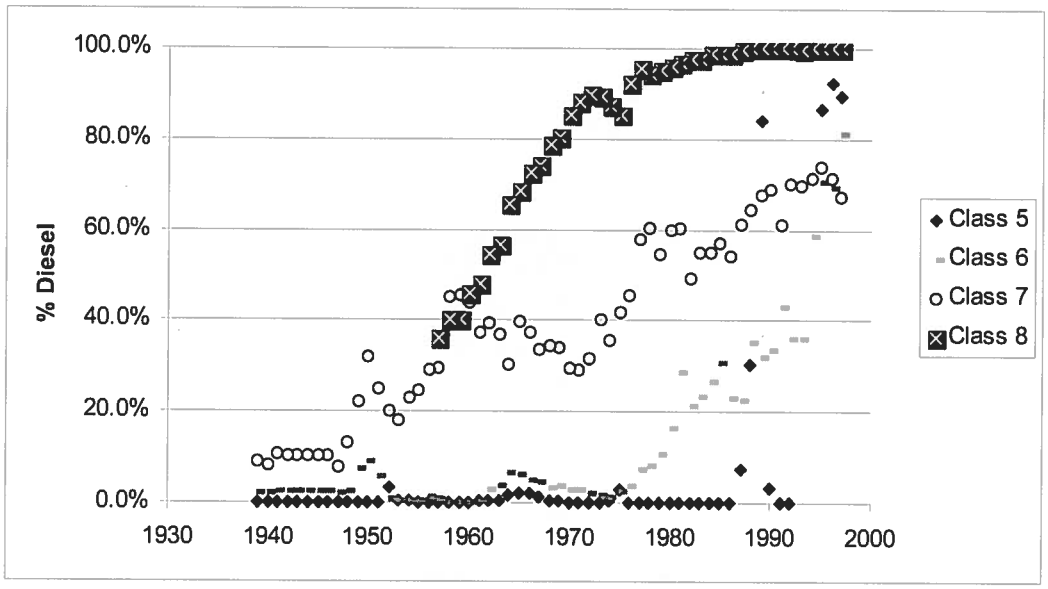
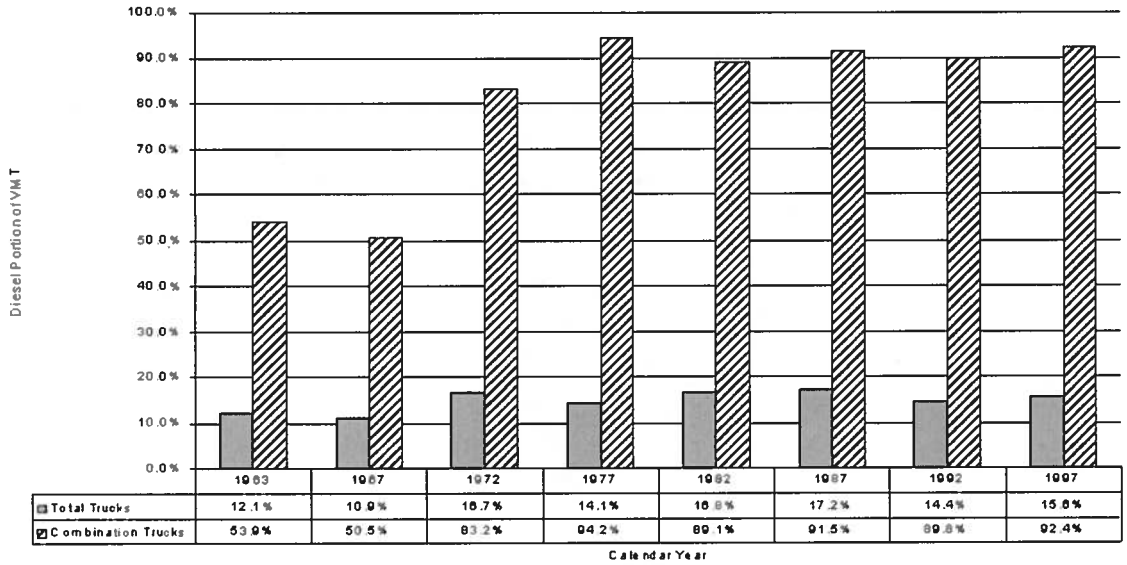


Figure 2-2. Diesel truck sales as a percentage of total truck sales for the years 1939-1997.
Source: AAMA, 1927-1974 and 1975-1998.

Among combination trucks, consisting of tractor-trailers and single-unit trucks with trailers, diesel vehicles have driven a majority of the miles since at least 1963, the first year in which TIUS was conducted (Figure 2-3).



	1963	1967	1972	1977	1982	1987	1992	1997
Total Trucks	12.1%	10.9%	16.7%	14.1%	16.8%	17.2%	14.4%	15.6%
Combination Trucks	53.9%	50.5%	83.2%	94.2%	89.1%	91.5%	89.8%	92.4%

Figure 2-3. Percentage of truck miles attributable to diesel trucks. VMT= vehicle miles traveled.
Source: U.S. Bureau of the Census, 1999b.

The longevity of diesel trucks is an important factor to understand past, current, and projected exposures to DE because older vehicles are subject to less stringent regulations and may remain in use for several decades after their manufacture. American Automobile Manufacturers Association publications (AAMA, 1927-1997) indicate that 53% of trucks from model years 1947-1956 were still on the road after 14 years. The proportion of trucks in use after 14 years was 63% for model years 1974-1983, suggesting that the lifespan of trucks built in later years is longer. According to the 1997 TIUS, vehicles older than 10 years made up 40% of Class 7 and 8 trucks and 16% of Class 7-8 vehicle miles traveled (VMT) (Figures 2-4 and 2-5). Almost all Class 7 and 8 trucks were diesel vehicles in the period 1982-1997 (93% in 1982 and 99% in 1997).

2.2.1.2. *Dieselization of Railroad Locomotive Engines*

Early in the 20th century the political and economic pressure on the railroads to replace steam locomotives was substantial. Railroads were losing business to other forms of transport. The diesel-electric locomotive provided 90% in-service time, compared with only 50% for steam locomotives, and had three times the thermal efficiency (Klein, 1991; Kirkland, 1983).

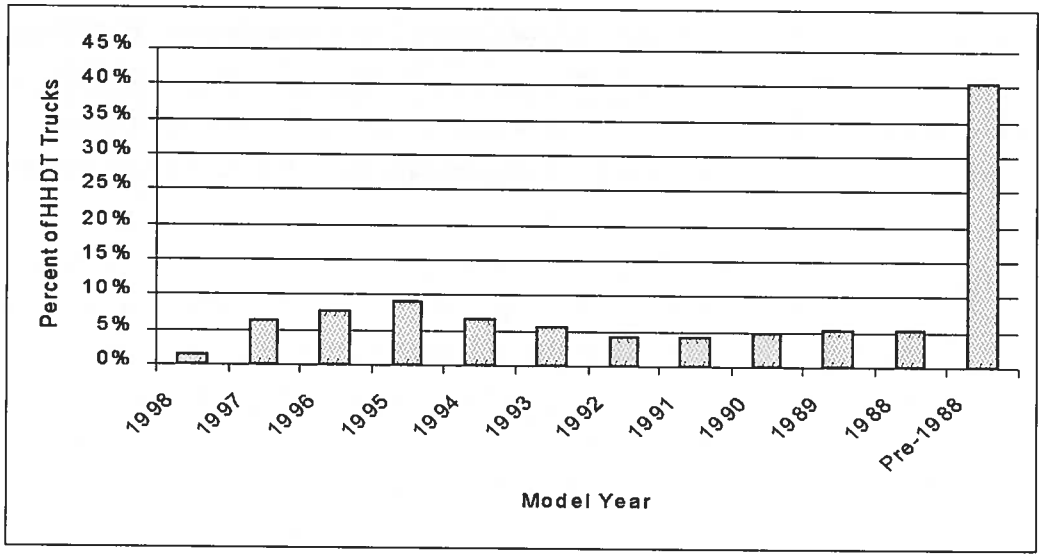


Figure 2-4. Model year distribution of in-use HD truck fleet in 1997.
Source: U.S. Bureau of the Census, 1999b.

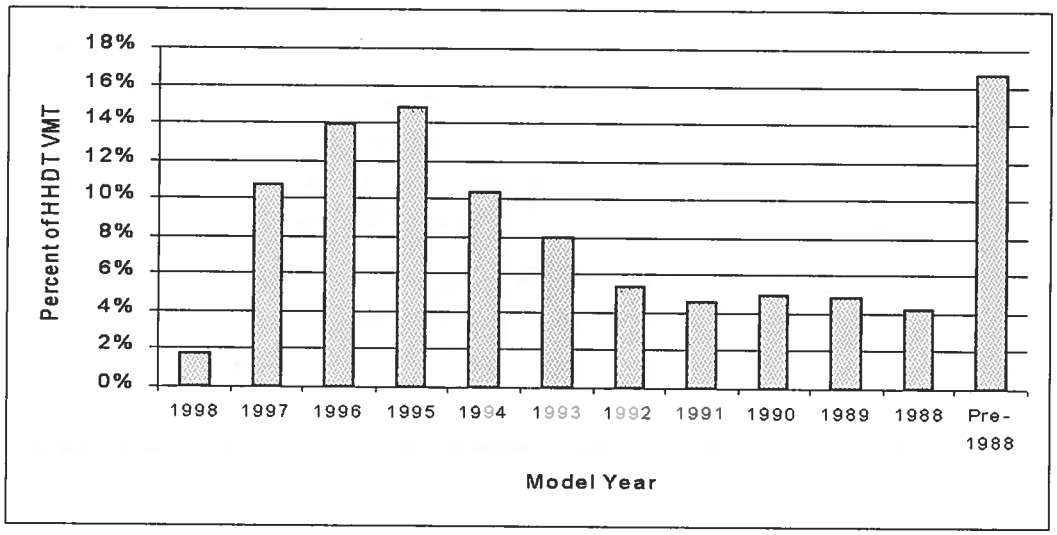


Figure 2-5. Model year distribution of vehicle miles traveled by the in-use HD truck fleet in 1997.
Source: U.S. Bureau of Census, 1999b.

Additionally, several cities had passed laws barring steam locomotives within the city limits because the large quantities of smoke obscured visibility, creating a safety hazard. The first prototype diesel locomotive was completed in 1917. By 1924 General Electric (GE) was producing a standard line of switching locomotives on a production basis. Electro-Motive Corporation was founded the same year to produce diesel locomotives in competition with GE. This company was purchased in 1929 by General Motors (GM) and became the Electro-Motive Division. After this acquisition, GM began to develop the two-stroke engine for this application. Up to this time, all locomotive diesel engines were four-stroke. Two-strokes offered a much higher power-to-weight ratio, and GM's strategy was to get a large increase in power by moving to the two-stroke cycle. The first true high-speed, two-stroke, diesel-electric locomotives were produced by GM in 1935. However, because of the economic climate of the Great Depression, few of these were sold until after the Second World War. At the end of the war, most locomotives were still steam-driven but were more than 15 years old, and the railroads were ready to replace the entire locomotive fleet. Few, if any, steam locomotives were sold after 1945 because the entire fleet was converted to diesel (Coifman, 1994).

The locomotive fleet has included significant percentages of both two- and four-stroke engines. The four-stroke diesel engines were naturally aspirated in the 1940s and 1950s. It is unlikely that any of the two-stroke engines used in locomotive applications were strictly naturally aspirated. Nearly all two-stroke diesel locomotive engines are uniflow scavenged, with a positive-displacement blower for scavenging assistance. In 1975, it was estimated that 75% of the locomotives in service were two-stroke, of which about one-half used one or more turbochargers in addition to the existing positive-displacement blower for additional intake boost pressure.

Almost all of the four-stroke locomotive engines were naturally aspirated in 1975. Electronic fuel injection for locomotive engines was first offered in the 1994 model year (U.S. EPA, 1998b). All locomotive engines manufactured in recent years are turbocharged, aftercooled or intercooled four-stroke engines. In part, this is because of the somewhat greater durability of four-strokes, although impending emissions regulations may have also been a factor in this shift. The typical lifespan of a locomotive has been estimated to be more than 40 years (U.S. EPA, 1998b). Many of the smaller railroads are still using engines built in the 1940s, although the engines may have been rebuilt several times since their original manufacture.

2.2.2. Diesel Combustion and Formation of Primary Emissions

A basic understanding of diesel combustion processes can assist in understanding the complex factors that influence the formation of DPM and other DE emissions. Unlike SI combustion, diesel combustion is a fairly nonhomogenous process. Fuel is sprayed at high

pressure into the compressed cylinder contents (primarily air with some residual combustion products) as the piston nears the top of the compression stroke. The turbulent mixing of fuel and air that takes place is enhanced by injection pressure, the orientation of the intake ports (inducement of intake-swirl tangential to the cylinder wall), piston motion, and piston bowl shape. In some cases, fuel and air mixing is induced via injection of the fuel into a turbulence-generating pre-chamber or swirl chamber located adjacent to the main chamber (primarily in older, higher speed engines and some LD diesels). Examples of typical direct injection and indirect injection combustion systems are compared in Figure 2-6. Diesel combustion can be considered to consist of the following phases (Heywood, 1988; Watson and Janota, 1982):

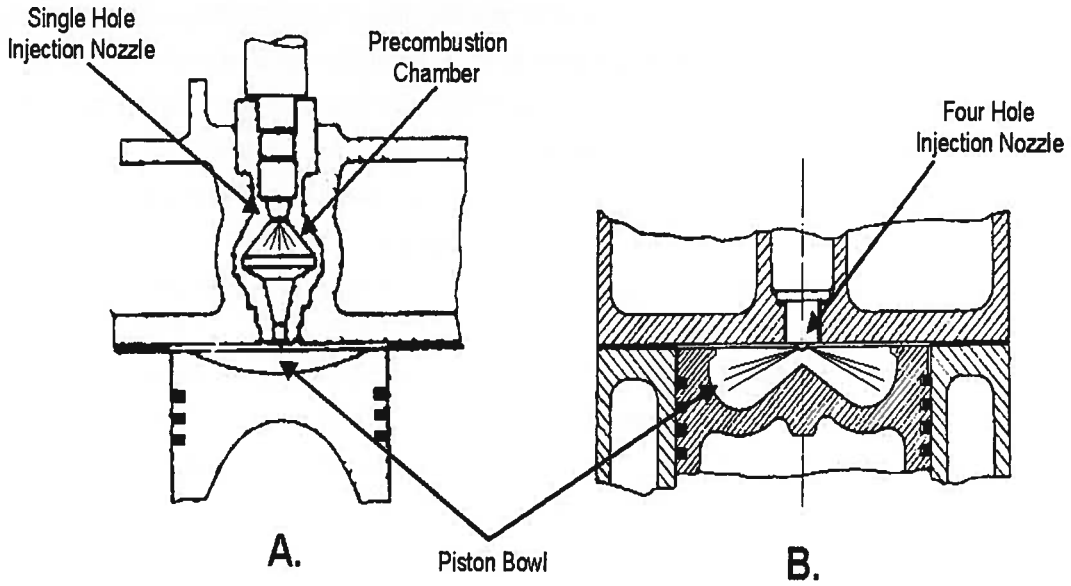


Figure 2-6. A comparison of IDI (A) and DI (B) combustion systems of high-speed HD diesel truck engines. DI engines almost completely replaced IDI engines for these applications by the early 1980s. (IDI = indirect injection, DI=direct injection)

- An ignition delay period, which starts after the initial injection of fuel and continues until the initiation of combustion. The delay period is governed by the rate of fuel and air mixing, diffusion, turbulence, heat transfer, chemical kinetics, fuel vaporization, and fuel composition. Fuel cetane rating is an indication of ignition delay.
- Rapid, premixed burning of the fuel and air mixture from the ignition delay period.
- Diffusion-controlled burning, where the fuel burns as it is injected and diffuses into the cylinder.
- A very small amount of rate-controlled burning during the expansion stroke, after the end of injection.

Engine speed and load are controlled by the quantity of fuel injected. Thus, the overall fuel-to-air ratio varies greatly as engine speed and load vary. On a macro scale, the cylinder contents are always fuel-lean. Depending on the time available for combustion and the proximity of oxygen, the fuel droplets are either completely or partially oxidized. At temperatures above 1,300 K, much of the unburned fuel that is not oxidized is pyrolized (stripped of hydrogen) to form EC (Dec and Espey, 1995). In addition to EC, other carbonaceous matter is present, largely from unburned fuel. The agglomeration of elemental and OC forms particles that are frequently referred to as "soot" particles. In this document, the terms "EC" and "OC" are used to refer to the carbon-containing components of DPM, and collectively, they are referred to as the carbonaceous fraction of a diesel particle.

Carbonaceous particle formation occurs primarily during the diffusion-burn phase of combustion, and is highest during high load and other conditions consistent with high fuel-air ratios. Most of the carbonaceous matter formed (80% to 98%) is oxidized during combustion, most likely by hydroxyl radicals (Kittelson et al., 1986; Foster and Tree, 1994).

DPM is defined by the measurement procedures summarized in the Code of Federal Regulations, Title 40 CFR, Part 86, Subpart N (CFR 40:86.N). These procedures define DPM emissions as the mass of material collected on a filter at a temperature of 52 °C or less after dilution of the exhaust with air. DPM is formed by a number of physical processes acting in concert as the exhaust is cooled and diluted. These are nucleation, coagulation, condensation, and adsorption. The core DE particles are formed by nucleation and coagulation from primary spherical particles consisting of solid carbonaceous (EC) material and ash (trace metals and other elements). To these, through coagulation, adsorption, and condensation, are added organic and sulfur compounds (sulfate) combined with other condensed material (Figure 2-7). Because of

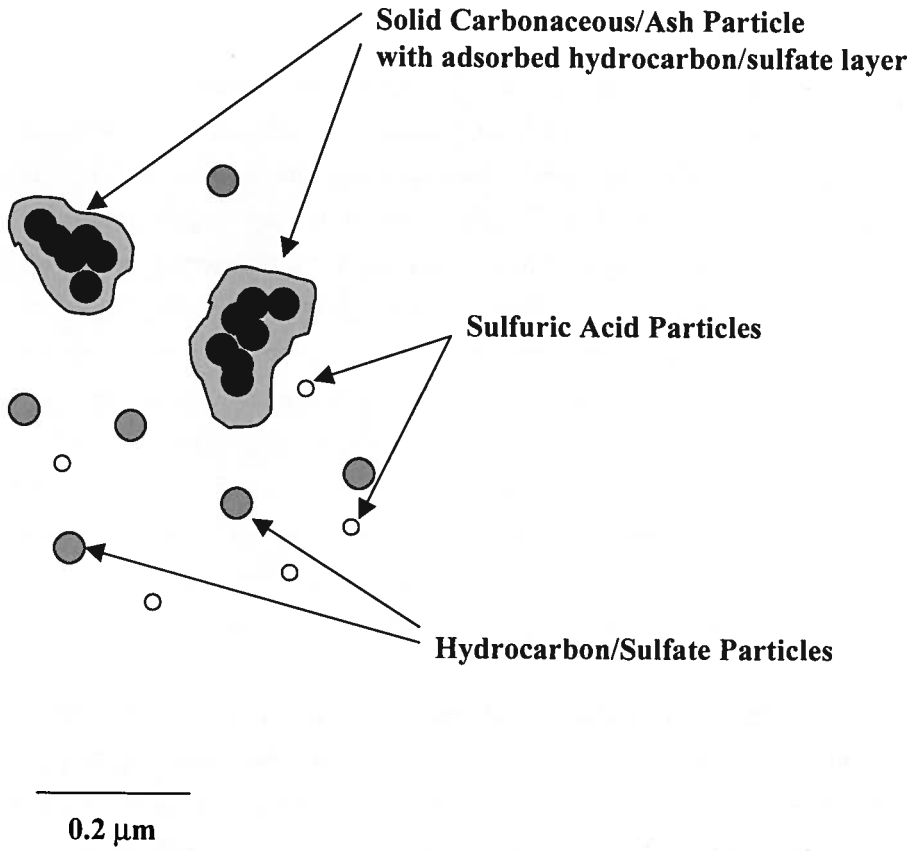


Figure 2-7. Schematic diagram of diesel engine exhaust particles.

Source: Modified from Kittelson, 1998.

their size, <0.5 mm, these particles have a very large surface area per gram of mass, which makes them able to adsorb large quantities of ash, organic compounds, and sulfate. The specific surface area of the EC core has been measured to be approximately 30–50 m^2/g (Frey and Corn, 1967). Pierson and Brachaczek (1976) report that after the extraction of adsorbed organic material, the surface area of the diesel particle core is approximately 90 m^2/g.

The organic material associated with diesel particles originates from unburned fuel, engine lubrication oil, and small quantities of partial combustion and pyrolysis products. This is frequently quantified as the SOF, which is discussed in much more detail in Section 2.2.7. The formation of sulfate in DE depends primarily on fuel sulfur content. During combustion, sulfur compounds present in the fuel are oxidized to sulfur dioxide (SO_2). Approximately 1% to 4% of fuel sulfur is oxidized to form sulfuric acid (H_2SO_4) (Wall et al., 1987; Khatri et al., 1978; Baranescu, 1988; Barry et al., 1985). Upon cooling, sulfuric acid and water condense into an aerosol that is nonvolatile under ambient conditions. The mass of sulfuric acid DPM is more than doubled by the mass of water associated with the sulfuric acid under typical DPM measurement conditions (50% relative humidity, 20–25 °C) (Wall et al., 1987).

Emissions from combustion engines produce oxide of nitrogen (NO_x) primarily (at least initially) as of NO. High combustion temperatures cause reactions between oxygen and nitrogen to form NO and some NO_2. Most NO_2 formed during combustion is rapidly decomposed. NO can also decompose to N_2 and O_2, but the rate of decomposition is very slow (Heywood, 1988; Watson and Janota, 1982). Thus, almost all of the NO_x emitted is NO.

Some organic compounds from unburned fuel and from lubricating oil consumed by the engine can be trapped in crevices or cool spots within the cylinder and thus are not sufficiently available to conditions that would lead to their oxidation or pyrolysis. These compounds are emitted from the engine and either contribute to gas-phase organic emissions or to DPM emissions, depending on their volatility. Within the exhaust system, temperatures are sufficiently high that these compounds are entirely present within the gas phase (Johnson and Kittelson, 1996). Upon cooling and mixing with ambient air in the exhaust plume, some of the less volatile organic compounds can adsorb to the surfaces of the EC agglomerate particles. Lacking sufficient EC adsorption sites, the organic compounds may condense on sulfuric acid nuclei to form a heterogeneously nucleated organic aerosol (Abdul-Khalek et al., 1999).

Although not unique to DE, the high content of EC associated with typical DPM emissions has long been used by some investigators to distinguish diesel engine sources of this particle from other combustion aerosols. Diesel particles from newer HD engines are typically composed of ~75% EC (EC can range from 33% to 90%), ~20% OC (OC can range from 7% to 49%), and small amounts of sulfate, nitrate, trace elements, water, and unidentified components (Figure 2-8). Metallic compounds from engine component wear, and from compounds in the fuel and lubricant, contribute to DPM mass. Ash from oil combustion also contributes trace amounts.

Ambient $PM_{2.5}$ measured in the eastern United States is dominated by sulfate (34%), whereas ambient $PM_{2.5}$ in the western United States is dominated by OC (39%) (Table 2-3) (U.S. EPA, 1999a). Many sources contribute to ambient $PM_{2.5}$, and these sources and their relative contribution to ambient $PM_{2.5}$ can be identified on the basis of the chemical species present. The OC fraction of DPM is increasingly being used to assist investigators in identifying the contribution of diesel engine emissions to ambient $PM_{2.5}$. In particular, hopane and sterane compounds (aromatic compounds, $>C_{30}$) have been used in addition to other polycyclic aromatic hydrocarbons (PAHs) and long-chain alkanes to distinguish DPM from other mobile source PM and from ambient PM (Schauer et al., 1996; Fujita et al., 1998). Although PAH compounds make up 1% or less of DPM mass, diesel emissions have been observed to have elevated concentrations of methylated naphthalenes and methylated phenanthrene isomers compared to other combustion aerosols (Benner et al., 1989; Lowenthal et al., 1994; Rogge et al., 1993). Enrichment of benzo[*a*]anthracene and benzo[*a*]pyrene (B[*a*]P) in DPM has also been

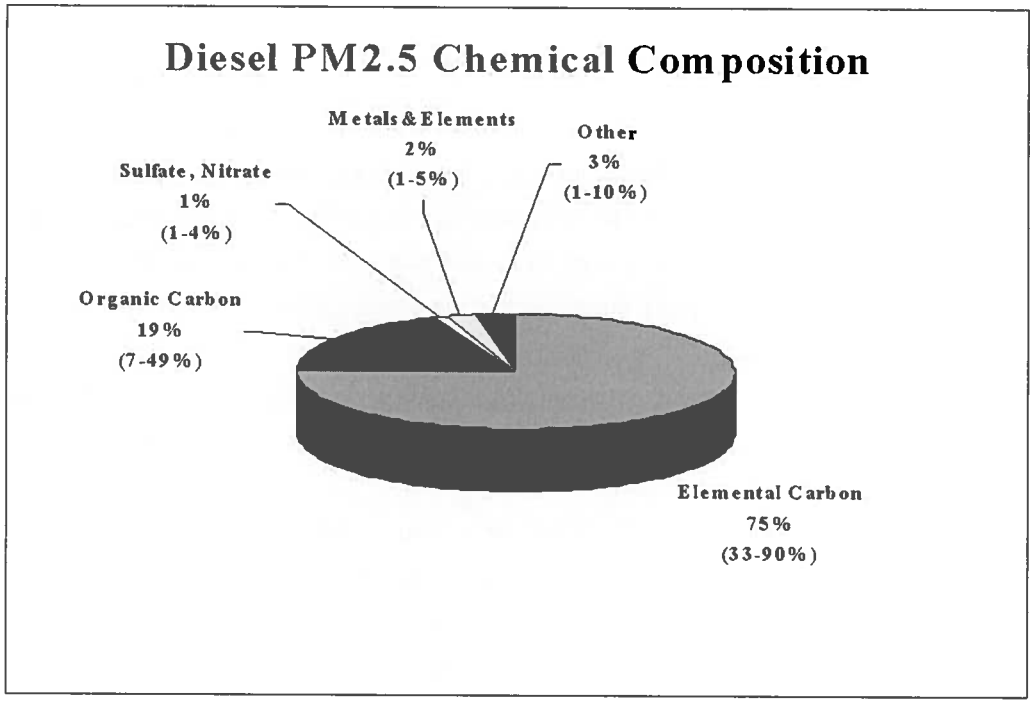


Figure 2-8. Typical chemical composition for diesel particulate matter ($PM_{2.5}$) from new (post-1990) HD diesel vehicle exhaust.

Table 2-3. Typical chemical composition of fine particulate matter

	Eastern U.S.	Western U.S.	Diesel $PM_{2.5}$
Elemental carbon	4%	15%	75%
OC	21%	39%	19%
Sulfate, nitrate, ammonium	48%	35%	1%
Minerals	4%	15%	2%
Unknown	23%	–	3%

Source: U.S. EPA, 1999a.

observed under some conditions and has been used to assess the relative contribution of DE to ambient PM.

Although specific OC species are being used to help distinguish DPM aerosols from other combustion aerosols, up to 90% of the organic fraction associated with DPM is currently classified as unresolvable complex material. Ultrafine DPM (5–50 nm) accounts for the majority (50% to 90%) of the number of particles but only 1% to 20% of the mass of DPM. A study conducted by Gertler (1999) in the Tuscarora Mountain tunnel demonstrated an increase in 20 nm diameter particles as the fraction of diesel vehicles in the tunnel increased from 13% to 78%. The contribution of nuclei-mode particles from a freeway on an ambient aerosol size distribution was reported by Whitby and Sverdrup (1980).

In summary, four main characteristics of DPM are (1) the high proportion of EC, (2) the large surface area associated with the carbonaceous particles in the 0.2 μm size range, (3) enrichment of certain polycyclic organic compounds, and (4) 50%–90% of the number of DPM particles in diesel engine exhaust are in the nuclei-mode size range, with a mode of 20 nm.

2.2.3. Diesel Emission Standards and Emission Trends Inventory

EPA set a smoke standard for on-road HD diesel engines beginning with the 1970 model year and added a carbon monoxide (CO) standard and a combined hydrocarbon (HC) and NO_x standard for the 1974 model year (Table 2-4). Beginning in the 1979 model year, EPA added a HC standard while retaining the combined HC and NO_x standard. All of the testing for HC, CO, and NO_x was completed using a steady-state test procedure. Beginning in the 1985 model year,EPA added a NO_x standard (10.7 g/bhp-hr), dropped the combined HC and NO_x standard, and converted from steady-state to transient testing for HC, CO, and NO_x emissions. EPA introduced a particulate standard for 1988 model year diesel engines using the transient test (0.6 g/bhp-hr). Transient testing involves running an engine on a dynamometer over a range of load and speed set points.

Since the 1985 model year, only the NO_x and particulate standards have been tightened for on-road diesel engines. For truck and bus engines, the particulate standard was reduced to 0.25 g/bhp-hr in 1991, and it was reduced again in 1994 for truck engines to 0.1 g/bhp-hr. For urban bus engines, the particulate standard was reduced in 1994 to 0.07 g/bhp-hr and again in 1996 to 0.05 g/bhp-hr. The NO_x standard was reduced to 4.0 g/bhp-hr in 1998 for all on-road diesel engines (bus and truck engines). The standards for nonmethane hydrocarbon (NMHC) and NO_x combined were further lowered in a 1997 rulemaking, to take effect in 2004. EPA has recently finalized a regulation that will further reduce NO_x, NMHC, and PM emissions from diesel engines starting in 2007.

Table 2-4. U.S. emission standards: HD highway diesel engines

Model year	Pollutant (g/bhp-hr)					Smoke[a]
	HC	CO	NO_x	HC + NO_x	Particulate (PM) t=truck, b=bus, ub=urban bus	
1970	—	—	—	—	—	A:40%; L:20%
1974	—	40	—	16[b]	—	A:20%; L:15%; P:50%
1979	1.5	25	—	10[b]	—	A:20%; L:15%; P:50%
1985[c]	1.3	15.5	10.7	—	—	A:20%; L:15%; P:50%
1988	1.3	15.5	10.7	—	0.60	A:20%; L:15%; P:50%
1990	1.3	15.5	6.0	—	0.60	A:20%; L:15%; P:50%
1991	1.3	15.5	5.0	—	0.25	A:20%; L:15%; P:50%
1993	1.3	15.5	5.0	—	0.25 t, 0.10 b	A:20%; L:15%; P:50%
1994	1.3	15.5	5.0	—	0.10 t, 0.07 ub	A:20%; L:15%; P:50%
1996	1.3	15.5	5.0	—	0.10 t, 0.05 ub	A:20%; L:15%; P:50%
1998	1.3	15.5	4.0	—	0.10 t, 0.05 ub	A:20%; L:15%; P:50%
2004	1.3	15.5	—	2.4 NMHC[d]	0.10 t, 0.05 ub	A:20%; L:15%; P:50%
2007		15.5	0.2	0.14 NMHC	0.01	A:20%; L:15%; P:50%

[a]Emissions measured in percent opacity during different operating modes: A=acceleration; L=lug; P=peaks during either mode.

[b]Total HC.

[c]In 1985, test cycle changed from steady-state to transient operation for HC, CO, and NO_x measurement and in 1988 for PM.

[d]Or 2.5 plus a limit of 0.5 nonmethane hydrocarbon (NMHC).

In December 1997, EPA adopted emission standards for NO_x, HC, CO, PM, and smoke for newly manufactured and remanufactured railroad locomotives and locomotive engines. The rulemaking, which took effect in the year 2000, applies to locomotives originally manufactured in 1973 or after, and any time they are manufactured or remanufactured (locomotives originally manufactured before 1973 are not regulated). Three sets of emission standards have been adopted (Tier 0, 1, and 2); they apply to locomotives and locomotive engines originally manufactured from 1973 through 2001 (Tier 0), from 2002 through 2004 (Tier 1), and in 2005 and later (Tier 2) (Table 2-5; see EPA web page at http://www.epa.gov/omswww/ or http://www.dieselnet.com/standards/ for current information on mobile source emission standards). The emissions are measured over two steady-state test cycles that represent two

Table 2-5. U.S. emission standards: locomotives (g/bhp-hr)

	Year[a]	CO	HC	NO_x	PM
Line-haul	1973-2001 (Tier 0)	5.0	1.0	9.5	0.6
Switch	1973-2001 (Tier 0)	8.0	2.1	14.0	0.72
Line-haul	2002-2004 (Tier 1)	2.2	0.55	7.4	0.45
Switch	2002-2004 (Tier 1)	2.5	1.2	11.0	0.54
Line-haul	2005 + (Tier 2)	1.5	0.3	5.5	0.20
Switch	2005 + (Tier 2)	2.4	0.6	8.1	0.24

[a]Date of engine manufacture.

different types of service, including line-haul (long-distance transport) and switch (involved in all transfer and switching operations in switchyards) locomotives.

Emission standards for nonroad equipment are not as stringent as current standards for on-road equipment and are being phased in within the next decade. Currently, Federal PM standards exist for nonroad equipment of several horsepower ratings. For equipment between 175 and 750 horsepower, the PM standard was set at 0.4 g/bhp-hr in 1996 and will decrease to 0.15 g/bhp-hr between 2001 and 2003 depending on the power rating (Table 2-6). This equipment includes construction, agricultural, and industrial such as bulldozers, graders, cranes, and tractors. The current PM standard for this equipment is only slightly lower than the 0.6 g/bhp-hr PM standard in place for on-road HD diesel engines in the late 1980s.

The EPA emission trends report (U.S. EPA, 2000a) provides emission inventories for criteria pollutants (PM_{10}, $PM_{2.5}$, SO_2, NO_x, volatile organic compounds [VOC], CO, Pb, and NH_3) from point, area, and mobile sources, which indicate how emissions have changed from 1970 to 1998. The emission trends are based on the EPA mobile source inventory models MOBILE, PART5, and the draft NONROAD model. PART5 derives particulate emission rates for HD diesel vehicles using data generated for new engine certification purposes. PART5 is currently being modified to account for deterioration, in-use emissions, poor maintenance, and tampering effects, all of which would increase emission factors. PM, SO_2, NO_x, and VOC emissions trends from the report are discussed below. Ambient urban/suburban PM samples rarely reflect the large fraction of natural and miscellaneous sources suggested by the national inventory, owing to removal of a large portion of these emissions close to their sources as well as dispersion from these sources to urban/suburban sites. The removal of natural and miscellaneous PM_{10} (largely fugitive dust) near their source is a result of the lack of inherent thermal buoyancy, low release height, and interaction with their surroundings (impaction and filtration by vegetation).

Table 2-6. U.S. emission standards for nonroad diesel equipment (g/bhp-hr)

Power rating	Model year	Pollutant (g/bhp-hr)					Smoke %[a]
		HC	CO	NO_x	NMHC + NO_x	PM	
11 < hp	2000	—	6.0	—	7.8 (ABT)	0.74 (ABT)	
	2005+	—	6.0	—	5.6 (ABT)	0.60 (ABT)	
11≤ hp < 25	2000	—	4.9	—	7.0 (ABT)	0.60 (ABT)	
	2005+	—	4.9	—	5.6 (ABT)	0.60 (ABT)	
25≤ hp < 50	2000	—	4.1	—	7.0 (ABT)	0.60 (ABT)	
	2005+	—	4.1	—	5.6 (ABT)	0.44 (ABT)	
50≤ hp <100	1998+	—	—	6.9 (ABT)	—	—	20/15/50
	2004	—	3.7		5.6 (ABT)	0.30 (ABT)	
	2008+	—	3.7		3.5 (ABT)	—	
100≤ hp <175	1997+	—	—	6.9 (ABT)	—	—	20/15/50
	2003	—	3.7	—	4.9 (ABT)	0.22 (ABT)	
	2007+	—	3.7	—	3.0 (ABT)	—	
175≤ hp < 750	1996+	1.0	8.5	6.9 (ABT)	—	0.4	20/15/50
175≤ hp < 300	2003	—	2.6	—	4.9 (ABT)	0.15 (ABT)	
	2006+	—	2.6	—	3.0 (ABT)	—	
300≤ hp < 600	2001	—	2.6	—	4.8 (ABT)	0.15 (ABT)	
	2006+	—	2.6	—	3.0 (ABT)	—	
600≤ hp < 750	2002	—	2.6	—	4.8 (ABT)	0.15 (ABT)	
	2006+	—	2.6	—	3.0 (ABT)	—	
≥750 hp	2000+	1.0	8.5	6.9 (ABT)	—	0.4	20/15/50
	2006+	—	2.6	—	4.8 (ABT)	0.15 (ABT)	

[a]Emissions measured in percent opacity during different operating modes: acceleration/lug/peaks during either mode.
ABT=average banking and trading.

Note: The standards for engines less than 50 hp also apply to diesel marine engines.

For the summaries presented here, natural and miscellaneous sources are excluded from the national PM and NO_x inventories.

From 1970 to 1998, PM_{10} emissions decreased from slightly over 12,200,000 tons to just over 2,800,000 tons (Figure 2-9). PM_{10} emissions from on-road and nonroad diesel engines increased from 320,000 tons to more than 521,000 tons during this same period, so that in 1970 diesel engine emissions were 3% of the PM_{10} inventory whereas in 1998, diesel engine emissions were 18% of the PM_{10} inventory. Diesel engines also contribute to secondary PM formation from NO_x and SO_2 emissions that are converted to nitrate and sulfate. VOCs from diesel engines also contribute to secondary organic particle formation. The contribution of secondary PM is not included in the national trends inventories cited here.

Mobile sources of PM include both gasoline- and diesel-powered on-road vehicles and a variety of nonroad equipment. Nonroad diesel engine sources include construction equipment, agricultural equipment, marine vessels, locomotives, and other sources. The EPA emission trends report (U.S. EPA, 2000a) indicates that, excluding natural and miscellaneous sources, mobile sources were responsible for 25% of PM_{10} emissions in 1998. Diesel engines (on-road and nonroad combined) were estimated to contribute 72% of mobile-source PM_{10} emissions.

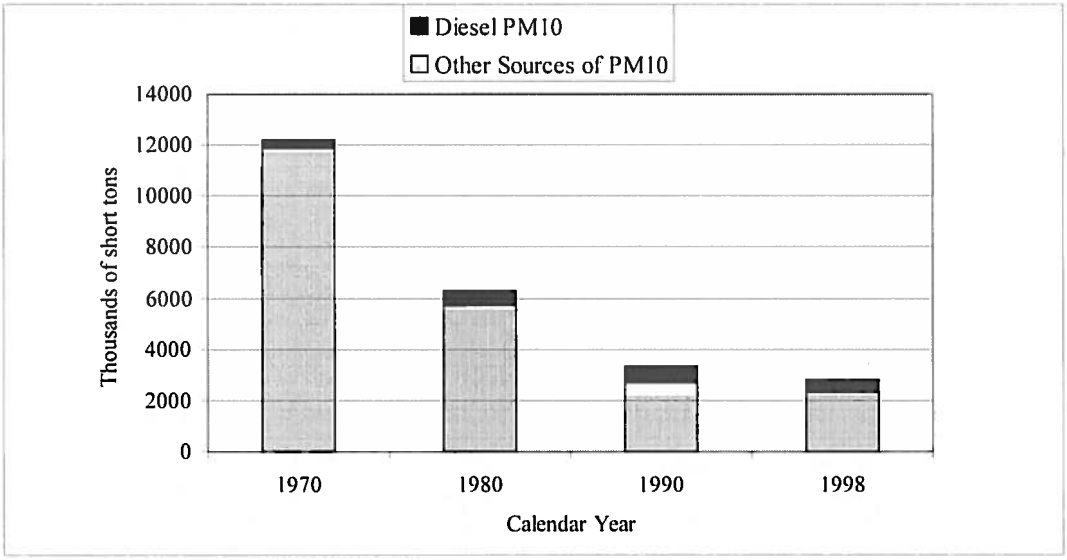


Figure 2-9. Trends in PM_{10} emissions from on-road and nonroad engines combined and other anthropogenic sources of PM_{10} from 1970 to 1998 (excludes miscellaneous and natural sources).

Source: U.S. EPA, 2000a, National Air Pollutant Emission Trends, 1900-1998.

Because of the high concentration of fine particles in engine emissions, diesel engines (on-road and nonroad combined) were estimated to contribute 77% of mobile-source $PM_{2.5}$ emissions and 23% of total $PM_{2.5}$ in 1998 (excluding natural and miscellaneous emissions). If natural and miscellaneous $PM_{2.5}$ sources are included in the inventory, diesel $PM_{2.5}$ contributes 6% to the national inventory.

Gram per mile particulate emissions from diesel vehicles are much greater than those from gasoline-fueled vehicles, accounting for the large contribution of diesel engine emissions to the national inventory in spite of the smaller number of diesel engines in use. Particulate emissions (PM_{10}) from gasoline-fueled engines decreased dramatically in 1975 with the widespread introduction of unleaded gasoline. Particulate emissions from diesel highway vehicles have decreased recently because of EPA emission standards for new model year HD diesel trucks that were first implemented in 1988 and became increasingly stringent in 1991, 1994, and 2000, as presented in Table 2-4. A decrease in on-road HD DPM emissions since the mid-1980s is confirmed by in-use vehicle testing, as described in Section 2.2.5. Because of the implementation of existing regulations, DPM emissions from on-road sources are expected to decrease 37% from 1998 to 2007; however, nonroad DPM emissions are expected to increase 15% in the same period (Figure 2-10).

The EPA emission trends report (U.S. EPA, 2000a) indicates that annual on-road vehicle PM_{10} emissions decreased from 397,200 tons to 257,080 tons from 1980 to 1998.[1] Passenger car particulate emissions decreased 53% (from 119,000 to 56,000 tons) in this timeframe, while on-road diesel vehicle PM_{10} emissions decreased 27% (from 208,000 to 152,000 tons) (Figure 2-10). Nonroad diesel engine PM_{10} emissions increased 17% (from 314,000 tons in 1980 to 69,000 tons in 1998). Emissions data for $PM_{2.5}$ are available only for the period from 1990 to 1998. Between 1990 and 1998, $PM_{2.5}$ emissions from mobile sources decreased by 14%, largely as the result of decreased on-road emissions.

From 1970 to 1998, NO_x emissions increased from 20,598,000 tons to 24,126,000 tons (Figure 2-11). NO_x emissions from on-road and nonroad diesel engines increased from 1,748,000 tons to 4,753,000 tons during this same period, so that in 1970 diesel engine emissions were 8% of the NO_x inventory while in 1998, diesel engine emissions were 20% of the NO_x

[1]Exhaust emissions constitute the majority of PM emissions from mobile sources, with tire and brake wear contributing the remainder. To compare trends estimates from past years with future projections (which are provided for exhaust emissions only), the fraction of brake and tire wear would need to be omitted from these estimates as reported in the emission trends report (U.S. EPA, 2000a). On average in the late 1990s 39% and 64% of gasoline vehicle particulate emissions originated from exhaust and 95% and 98% of on-road diesel emissions originated from exhaust for PM_{10} and $PM_{2.5}$, respectively.

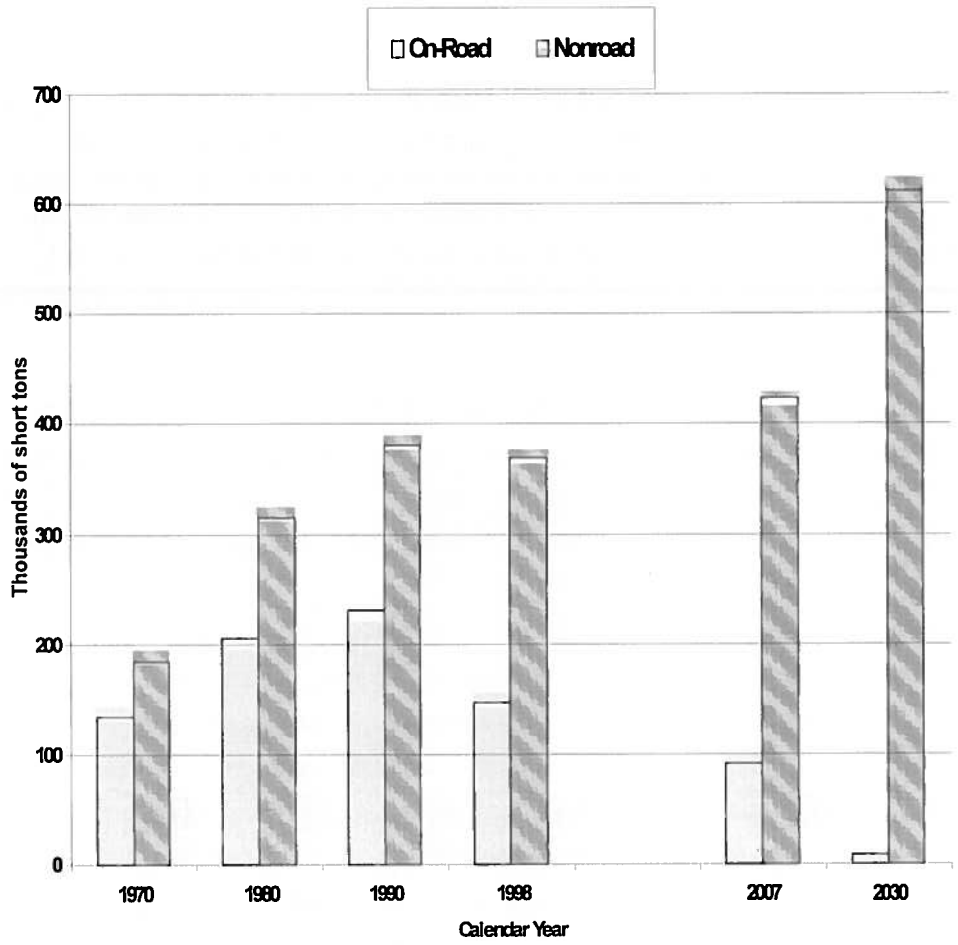


Figure 2-10. Trends in PM_{10} emissions from on-road and nonroad diesel engines from 1970 to 1998 and projections of emissions to 2007 and 2030*.

Source: U.S. EPA, 2000a, National Air Pollutant Emission Trends, 1900-1998.
*Projection to 2030 includes implementation of the recently finalized regulation "Control of Air Pollution from New Motor Vehicles: Heavy-Duty Engine and Vehicle Standards and Highway Diesel Fuel Sulfur Control Requirements" U.S. EPA, 2000b.

inventory. As mentioned above, some of this NO_x will be converted to particulate nitrate in the atmosphere, and this contribution to ambient PM is not quantified in national inventories.

In 1998, 53% of total emitted NO_x came from mobile sources, with diesels responsible for 57% of the mobile-source contribution. Overall, NO_x emissions from mobile sources have remained relatively constant over time, increasing an estimated 7% from 1980 to 1998. Whereas

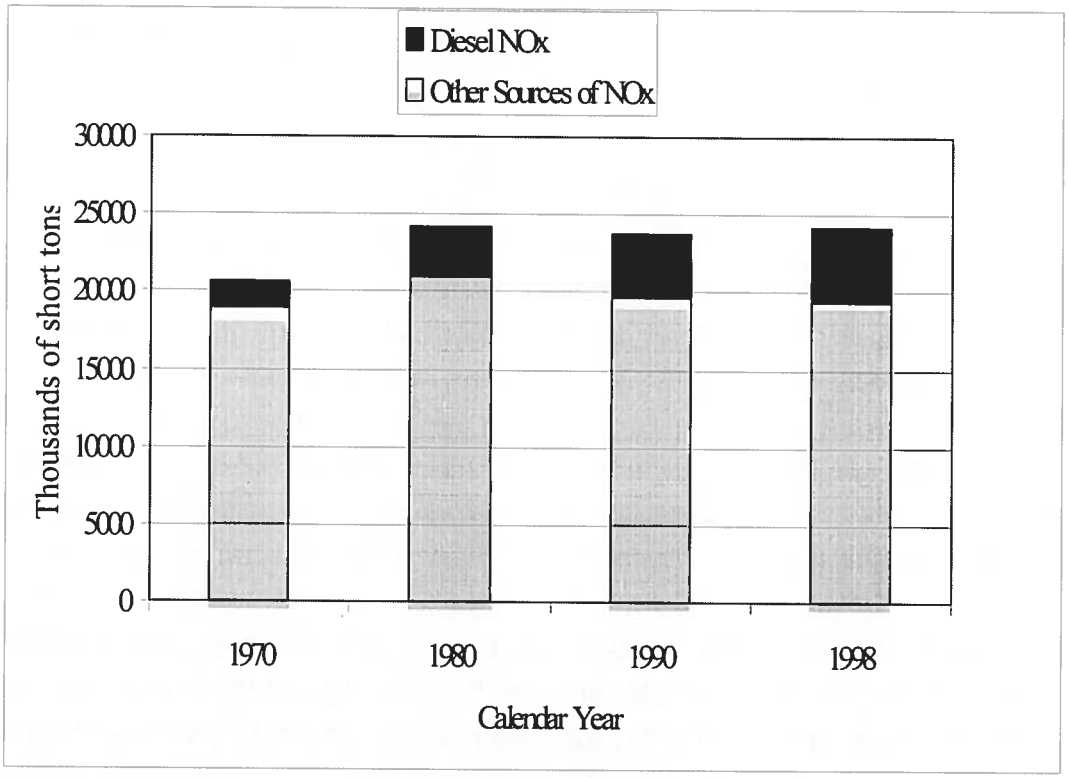


Figure 2-11. Trends in NO_x emissions from on-road and nonroad diesel engines combined and other anthropogenic sources of NO_x from 1970 to 1998 (excludes miscellaneous and natural sources).

Source: U.S. EPA, 2000a, National Air Pollutant Emission Trends, 1900-1998.

NO_x from LD gasoline vehicles decreased from 1980 to 1998, resulting in an overall decrease in on-road NO_x emissions of 9%, NO_x from diesel trucks and buses increased 7% (from 2,463,390 tons in 1980 to 2,630,120 tons in 1998), owing to the illegal use of electronic control devices that bypassed the trucks' emission control systems, as discussed in Section 2.2.5. NO_x emissions from nonroad diesel engines (including commercial marine and locomotives) have increased 46% (from 3,251,600 tons in 1980 to 4,752,800 tons in 1998) (Figure 2-12).

About 7% of SO_2 came from mobile sources in 1998, with diesels responsible for 74% of that total. EPA regulations for on-road diesel fuel sulfur content (which started in 1993) have significantly reduced SO_2 emissions from highway diesels. SO_2 emissions from highway diesel

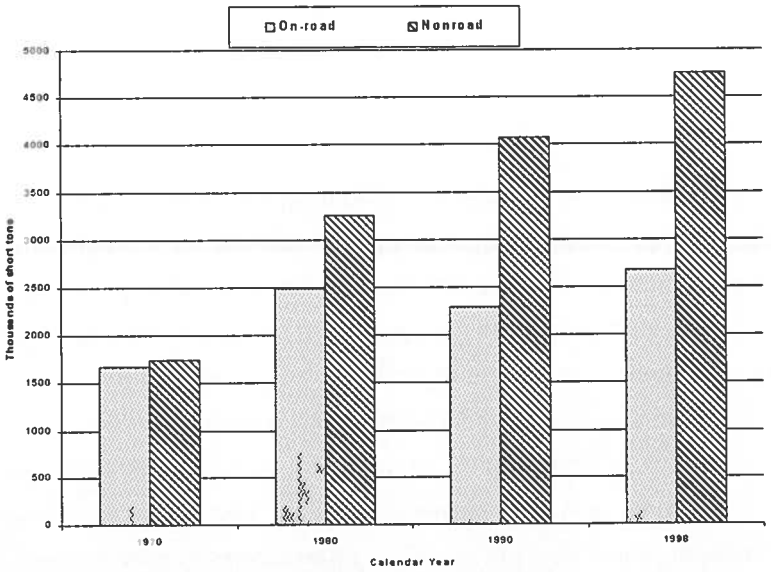


Figure 2-12. Trends in NO_x emissions from on-road and nonroad diesel engines from 1970 to 1998.

Source: U.S. EPA, 2000a, National Air Pollutant Emission Trends, 1900-1998.

engines have decreased 72% (from 303,000 tons in 1980 to 85,000 tons in 1998) (Figure 2-13). Similar trends are not apparent for nonroad diesels, although in 1998 nonroad diesel engines, excluding commercial marine vessels, emitted 785,000 tons of SO_2, accounting for 56% of mobile-source SO_2 emissions in 1998.

Diesel engines are not a large source of VOC emissions compared with gasoline engines. VOC emissions from diesel engines in 1998 were estimated at 2% of the total emissions from all sources. VOC emissions from diesel mobile sources decreased 9% (from 779,000 tons in 1980 to 721,000 tons in 1998) (Figure 2-14).

Diesel engines are also not a large source of CO emissions compared with gasoline engines. In 1998, mobile sources emitted 79% of all CO, and diesel engines accounted for 4% of the mobile-source CO. CO emissions from on-road diesel vehicles increased 34% between 1980 and 1998, during which time nonroad diesel emissions of CO increased 45% (Figure 2-15).

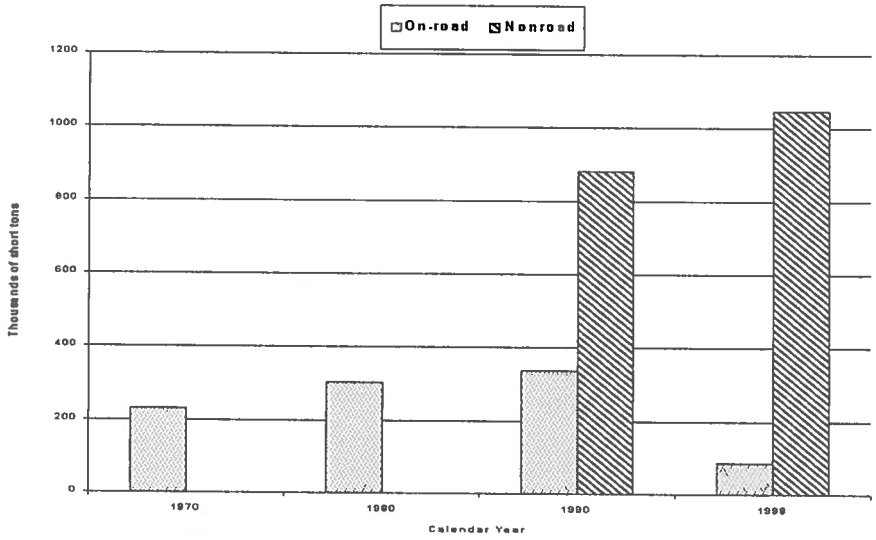


Figure 2-13. Trends in SO_2 emissions from on-road diesel engines from 1970 to 1998 and nonroad diesel engines from 1990 to 1998.

Source: U.S. EPA, 2000a, National air pollutant emission trends, 1900-1998.

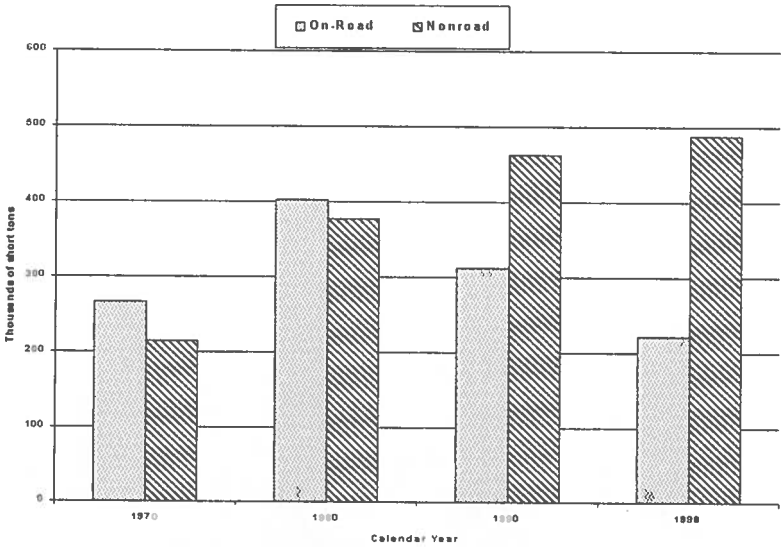


Figure 2-14. Trends in VOC emissions from on-road and nonroad diesel engines from 1970 to 1998.

Source: U.S. EPA, 2000a, National air pollutant emission trends, 1900-1998.

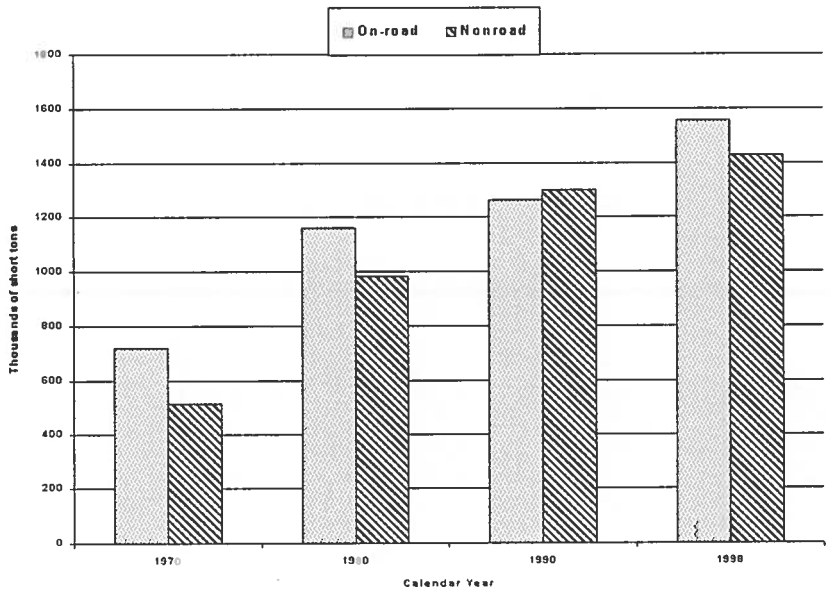


Figure 2-15. Trends in CO emissions from on-road and nonroad diesel engines from 1970 to 1998.

Source: U.S. EPA, 2000a, National Air Pollutant Emission Trends, 1900-1998.

2.2.4. Historical Trends in Diesel Fuel Use and Impact of Fuel Properties on Emissions

Use of diesel fuel increased steadily in the second half of the 20th century. According to statistics from the Federal Highway Administration (1995, 1997), in 1949 diesel fuel was approximately 1% of the total motor fuel used, and in 1995 it was about 18%. Over the same time, diesel fuel consumption in the United States increased from about 400 million gallons to 26 billion gallons per year, an increase by a factor of more than 60 (Figures 2-16 and 2-17).

The chemistry and properties of diesel fuel have a direct effect on emissions of regulated pollutants from diesel engines. Researchers have studied the NOx and DPM effect of sulfur content, total aromatic content, polyaromatic content, fuel density, oxygenate content, cetane number, and T90 on emissions of regulated pollutants. T90 is the 90% distillation point temperature. An increase in T90 has been observed to cause an increase in DPM emissions (Cunningham et al., 1990; Sienicki et al., 1990). Cetane number is a measure of the ignition quality, or ignition delay time, of a diesel fuel. The percent of cetane (less commonly referred to as hexadecane, $C_{16}H_{34}$) by volume in a blend with alpha-methylnaphthalene ($C_{10}H_7CH_3$) defines the cetane number that provides the same ignition delay time as the fuel in use.

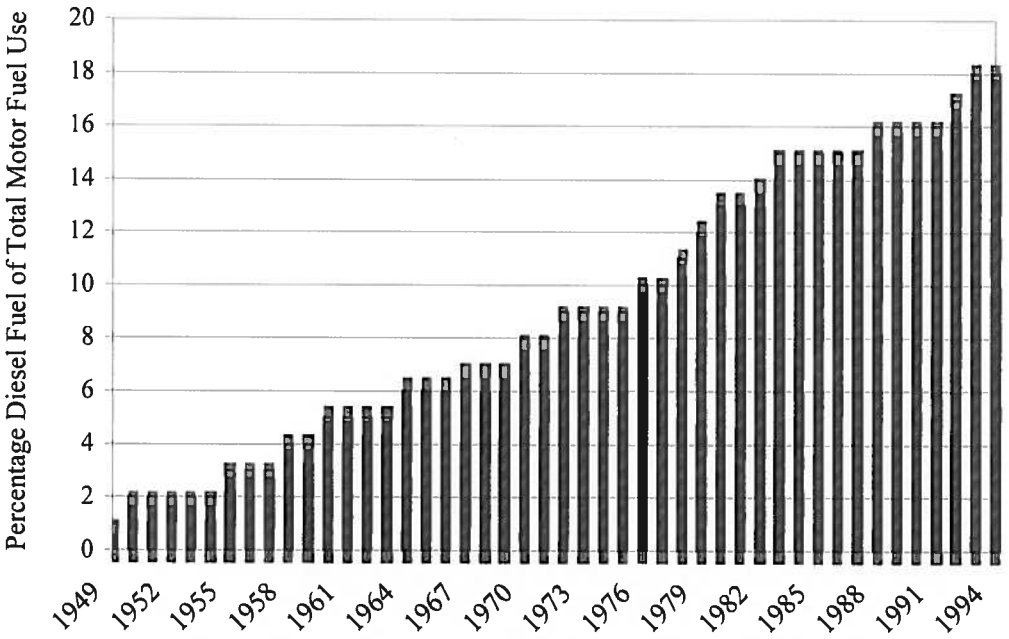


Figure 2-16. Percentage of total motor fuel use that is on-road diesel fuel since 1949.

Source: Federal Highway Administration, 1995.

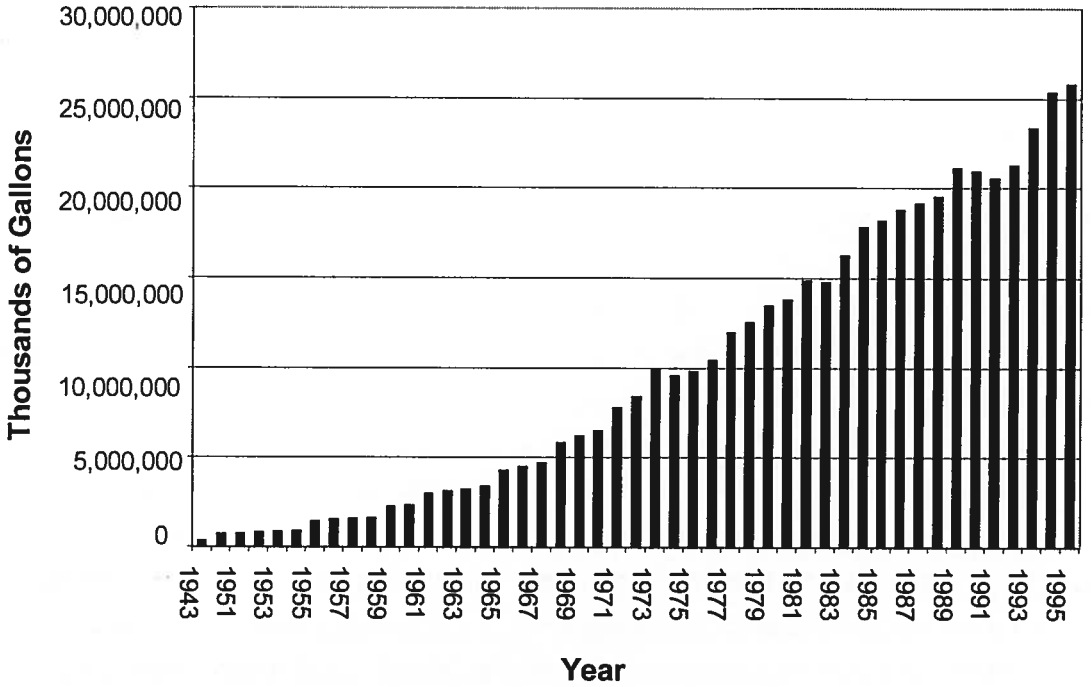


Figure 2-17. On-highway diesel fuel consumption since 1943, values in thousands of gallons.

Source: Federal Highway Administration, 1995.

Before 1993, diesel fuel sulfur levels were not federally regulated in the United States, although the State of California had such regulations. Industry practices that were in place (e.g., the ASTMD 975 specification for No. 2 oils) limited sulfur to 0.5%. During the years 1960 to 1986, fuel sulfur content showed no chronological increasing or decreasing trends and ranged from 0.23 to 0.28 wt% (NIPER, 1986). A maximum allowable on-road diesel fuel sulfur content in the United States was established at 0.05 mass % in 1993, in advance of the 1994 0.10 g/bhp-hr PM standard for HD on-highway trucks. Nationally, on-road fuels averaged 0.032% sulfur in 1994 while nonroad fuels averaged 10-fold the sulfur level of on-road fuel, or 0.32% (Dickson and Sturm, 1994). The reduction in diesel fuel sulfur reduced total DPM mass emissions through reduction of sulfate PM (primarily present as sulfuric acid).

Considerably higher sulfuric acid PM emissions are possible with DE aftertreatment systems containing precious metals (oxidation catalysts, lean NO_x catalysts, catalyzed DPM traps). At temperatures over 350 °C to 500 °C (depending on device), SO_2 in the exhaust can be oxidized to sulfuric acid (McClure et al., 1992; McDonald et al., 1995; Wall, 1998). Sulfur content remains at unregulated levels for off-highway diesel fuels and fuels used in railroad locomotives.

The chemical makeup of diesel fuel has changed over time, in part because of new regulations and in part because of technological developments in refinery processes. EPA currently regulates on-road diesel fuel and requires the cetane index (a surrogate for actual measurements of cetane number) to be greater than or equal to 40, or the maximum aromatic content to be 35% or less (CFR 40:80.29). EPA recently finalized a regulation that will limit the sulfur content of on-road diesel fuel to 15 ppm starting in 2006 (U.S. EPA, 2000b). California has placed additional restrictions on the aromatic content of diesel fuel (California Code of Regulations, Title 13, Sections 2281-2282) and requires a minimum cetane number of 50 and an aromatics cap of 10% by volume, with some exceptions for small refiners and alternative formulations as long as equivalent emissions are demonstrated. Diesel fuel from larger refiners is limited to 10% aromatic content, and for three small refiners (a small fraction of diesel sales) to 20% aromatic content. The refiners can also certify a fuel with higher aromatic content as being emissions-equivalent to the 10% (or 20%) aromatic content fuels by performing a 7-day engine dynamometer emissions test. This method is chosen by most, if not all, California refiners, and so a typical California diesel fuel has an aromatic content above 20%. Emissions equivalence has been obtained through use of cetane enhancers, oxygenates, and other proprietary additives. Nonroad diesel fuel is not regulated, and consequently, cetane index, aromatic content, and sulfur content vary widely with nominal values for cetane number around 43, 31% aromatics, and sulfur approximately 3,000 ppm.

The average cetane number of U.S. diesel fuel declined steadily from 50.0 to 45.1, or about 0.2% per year, from 1960 to 1986 (NIPER, 1986). The decline in cetane number was likely accompanied by an increase in aromatic content and density (Lee et al., 1998). A number of EPA-sponsored studies refer to fuels with nominally 22% aromatics content as "national average fuel" during the 1970s (Hare, 1977; Springer, 1979), whereas by the 1980s a so-called national average fuel contained 30% aromatics (Martin, 1981a,b). Shelton (1979, 1977) has reported a trend of increasing T90 from 1960 through the late 1970s, which is consistent with increasing density, aromatic content, and polyaromatic content. Unfortunately, aromatic content was not commonly measured before the 1980s.

Studies measuring the emissions impact of changes in cetane number and aromatic content for roughly 1990 model year engine technology find that increasing the aromatic content from 20% to 30%, with an accompanying decrease in the cetane number from 50 to 44, results in a 2% to 5% increase in NO_x and a 5% to 10% increase in total DPM (McCarthy et al., 1992; Ullman et al., 1990; Sienicki et al., 1990; Graboski and McCormick, 1996). These ranges may be reasonable upper bounds for the effect of changes in fuel quality on NO_x and DPM emissions during the years 1960–1990.

In the northern United States during wintertime, on-road No. 2 diesel may contain some percentage of No. 1 diesel to improve cold-flow properties. Discussions with refiners indicate that a typical wintertime No. 1 diesel blending level is 15 volume %; however, this number must be taken as a rough estimate. Blending of No. 1 may lower the aromatic content, resulting in improved emissions performance. Nationally, on-highway No. 1 fuels averaged 17% aromatic content in 1994 (Dickson and Sturm, 1994). Thus, there may also be some small but perceptible seasonal changes in emissions from diesel engines.

Railroad-grade diesel fuel is currently unregulated. Typically, railroad-grade diesel fuel is a blend of approximately 10% on-road fuel and 90% nonroad diesel fuel. There are no recent data on the composition of railroad-grade diesel fuel. Somewhat dated diesel fuel oil surveys (Shelton, 1979) reported that railroad-grade diesels had lower cetane number, higher density, and higher T90. Also, the cetane index for these fuels can be as much as 9 cetane units higher than the cetane number, an indication of a high aromatic content in railroad-grade diesels.

Fuel chemistry is also important for emission of particle-associated PAHs. In studies performed over more than a decade, Williams and Andrews of the University of Leeds have shown that the solvent-extractable PAHs from diesel particulate originate almost entirely in the fuel (Williams et al., 1987; Andrews et al., 1998; Hsiao-Hsuan et al., 2000). The PAH molecules are relatively refractory, so a significant fraction survive the combustion process and condense onto the DPM. These studies have been confirmed by other research groups (Crebelli et al., 1995; Tancell et al., 1995). There is a consensus among these researchers that

pyrosynthesis of PAHs occurs only at the highest temperature operating conditions in a diesel engine. Under these conditions, most of the DPM and other pyrolysis products are ultimately burned before exiting the cylinder. These results indicate that emissions of PAHs are more a function of the PAH content of the fuel than of engine technology. For a given refinery and crude oil, diesel fuel PAH correlates with total aromatic content and T90. Representative data on aromatic content for diesel fuels in the United States do not appear to be available before the mid-1980s. However, the decreasing trend in cetane number, increasing trend in T90, and the increasing use of light cycle oil from catalytic cracking beginning in the late 1950s suggest that diesel PAH content has increased over the past 40 years. Because PAHs have been implicated as one potential contributing component to the observed toxicity of DE, changes in PAH content of diesel fuel over time, as well as differences between diesel fuels used in different applications (on-road, nonroad, locomotive), may influence the hazard observed in exposed populations from different occupations. However, such a relationship would be difficult to differentiate in an epidemiologic study because there are several other properties of DE that may be contributing to the observed toxicity. Historical trends in PAH-measured emissions are discussed in Section 2.2.8.2.

2.2.5. Chronological Assessment of Emission Factors

2.2.5.1. *On-Road Vehicles*

Numerous studies have been conducted on emissions from in-use on-road HD diesel vehicles. HD vehicles are defined as having a rated gross vehicle weight (GVWR) of greater than 8,500 lb, and most over-the-road trucks have a GVWR of 80,000 lb. Emissions of regulated pollutants from these studies have been reviewed (Yanowitz et al., 2000); the review findings, which encompass vehicles from model years 1976 to 1998, are summarized below. In addition, a large amount of engine dynamometer data on HD diesel engines have been published since the mid-1970s. These data are used below to confirm and expand upon the findings from in-use vehicle testing.

Figure 2-18 shows chassis dynamometer data for more than 200 different vehicles (approximately one-half of which are transit buses), reported in 20 different published studies, as well as a large amount of additional data collected by West Virginia University (Yanowitz et al., 1999; Warner-Selph and Dietzmann, 1984; Dietzmann et al., 1980; Graboski et al., 1998a,b; McCormick et al., 1999; Clark et al., 1995, 1997; Bata et al., 1992; Brown and Rideout, 1996, Brown et al., 1997; Dunlap et al., 1993; Ferguson et al., 1992; Gautam et al., 1992; Katragadda

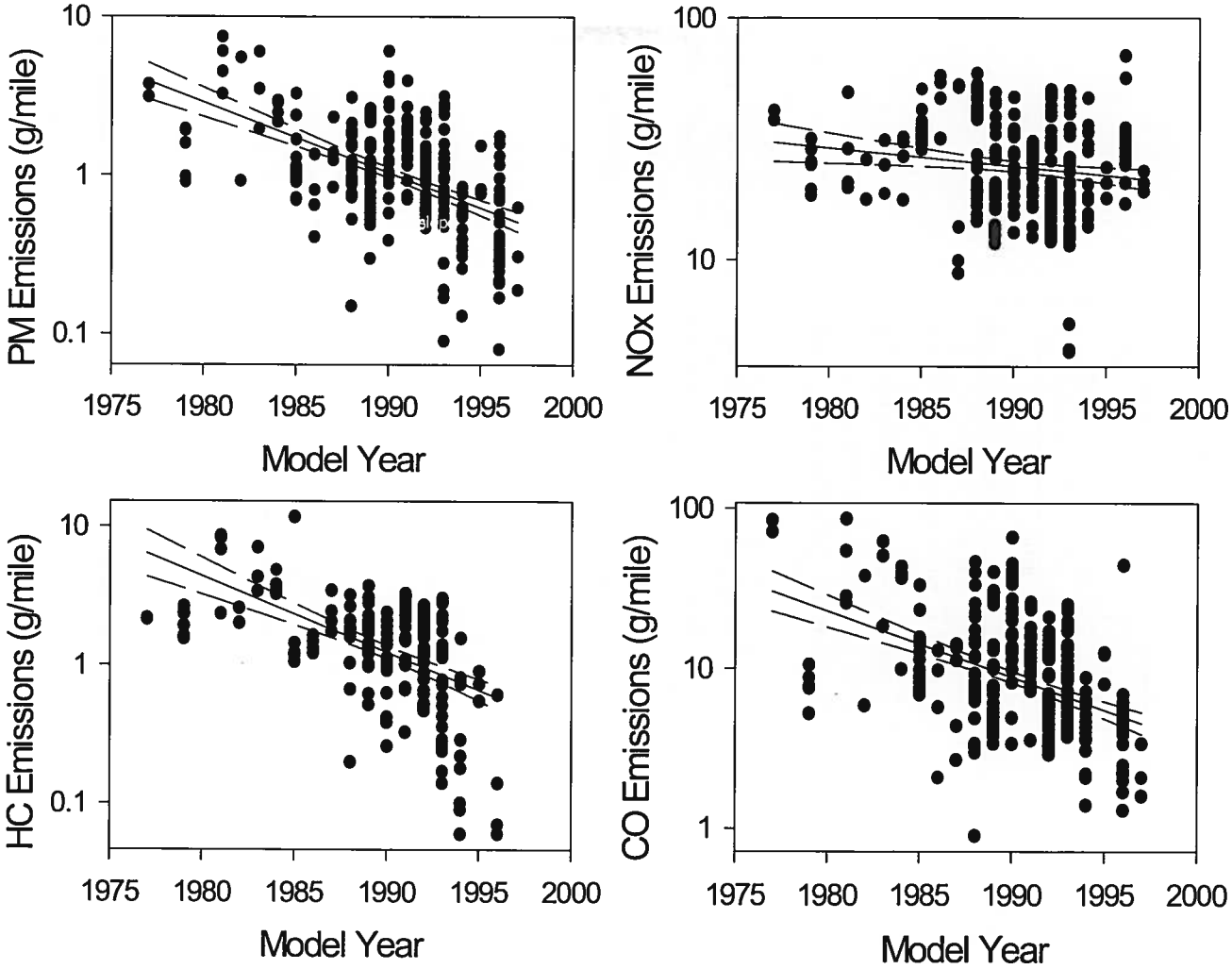


Figure 2-18. Model year trends in PM, NO_x, HC, and CO emissions from HD diesel vehicles (g/mile).

Source: Yanowitz et al., 2000.

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et al., 1993; Rideout et al., 1994; Wang et al., 1993, 1994; Williams et al., 1989; Whitfield and Harris, 1998; West Virginia University data available on the World Wide Web at www.afdc.nrel.gov). The results from vehicles tested more than once using the same test cycle, and without any additional mileage accumulated between tests, are averaged and reported as one data point. Buses were tested using the Central Business District (CBD) cycle, while most trucks were tested using the Urban Dynamometer Driving Schedule (UDDS), also known as the Schedule 1d cycle. Some of the trucks were tested using the West Virginia 5-peak cycle, which generates considerably lower g/mi emissions than the CBD or UDDS (Yanowitz et al., 1999). Emissions results from vehicles tested under different test cycles or at different points in the engine's life cycle have been reported as separate data points. Note that all NO_x mass emissions data are reported as equivalent NO_2. Table 2-7 compares the make-up of the fleet of trucks that was tested with the in-use truck fleet according to the 1997 Vehicle Inventory and Use Survey (U.S. Bureau of the Census, 1999a). The tested fleet is mostly vehicles in the 33,000-60,000 lb range. Analysis of the tested fleet also shows that the model year distribution is skewed toward newer vehicles. The 1997 Vehicle Inventory and Use Survey indicates a flat distribution with roughly the same number of in-use vehicles for each of the model years in the decade preceding 1997. The 1992 Truck Inventory and Use Survey (U.S. Bureau of the Census, 1995) shows the same trend, as shown in Figure 2-1. Analysis of odometer mileage for the tested fleet shows that 45% of the vehicles had less than 50,000 miles at the time of testing. Only 10% of the vehicles had more than 250,000 miles. Although the mileage distribution of the in-use fleet is unknown, it seems unlikely to be as heavily weighted to low-mileage vehicles. Because of the relatively low mileage of most of the vehicles tested, deterioration of emissions may not be reflected in the

Table 2-7. Comparison of in-use truck fleet with truck fleet tested on chassis dynamometer, percent of total vehicles

Class	In-use trucks, 1995 census	Tested trucks
3	17.7	1
4 & 5	13.3	0
6 & 7	25.0	17
8A	20.9	52
8B	23.1	30

results. Yanowitz and co-workers (2000) report that average emissions of regulated pollutants for vehicles of the different classes listed in Table 2-7 are approximately the same. This is clearly a reflection of the small number of vehicles in the lighter weight classes for this dataset, but it also indicates no real difference in emissions for vehicles in Classes 6–8. The data are mainly for vehicles of 19,500 lb and greater GVWR (Classes 6 and 7 and heavier), and predominantly for vehicles of 33,000 lb and greater GVWR (Class 8 trucks and buses).

Figure 2-18 shows emissions trends in g/mi. Least-squares linear regressions and 95% confidence intervals are plotted on each graph and yield the following equations for predicting emissions trends (applicable to the years 1976–98):

$$\text{Log } NO_x \text{ (g/mile)} = (\text{Model year} * -0.008) + 16.519 \quad R^2 = 0.024 \tag{2-1}$$

$$\text{Log PM (g/mile)} = (\text{Model year} * -0.044) + 88.183 \quad R^2 = 0.28 \tag{2-2}$$

$$\text{Log HC (g/mile)} = (\text{Model year} * -0.055) + 109.39 \quad R^2 = 0.27 \tag{2-3}$$

$$\text{Log CO (g/mile)} = (\text{Model Year} * -0.041) + 82.876 \quad R^2 = 0.22 \tag{2-4}$$

As shown in Figure 2-18, changes in NO_x emissions have been relatively small, with an emission rate averaging about 26 g/mi. The data reported in Figure 2-18 are real-world, in-use emissions measurements and therefore more accurately reflect emission factors than engine test data during this period. There are two potential causes for the relative constancy of NO_x emissions as described by Figure 2-18. The first is emissions deterioration due to engine wear. Weaver and Klausmeier (1988) have shown that diesel engine deterioration results in lower NO_x emissions and higher DPM emissions, and this finding has recently been confirmed by McCormick and co-workers (2000). Wear of mechanical devices that limit smoke, fuel pumps, and fuel injectors alters the effective injection timing to decrease NO_x. Because deterioration is more a function of maintenance than vehicle age or mileage, deterioration introduces a wide range in NO_x emission factors measured in the chassis dynamometer studies. The lack of a decreasing trend in NO_x emissions can also be attributed to the use of illegal emissions control devices that bypassed the trucks' emission control systems under some driving conditions such as steady-state cruise. EPA has reached a settlement with the diesel engine manufacturers to discontinue use of these devices. The illegal devices produced low NO_x emissions on the transient test (HD FTP) but operated in a high-NO_x/high-fuel-economy mode in use under highway cruise conditions.

Figure 2-19 shows engine certification data for NO_x emissions reported in the many studies that have employed the transient test over the past 25 years. The engine testing data are also listed in Table 2-8. The data compiled in Figure 2-19 show a significant decline in NO_x

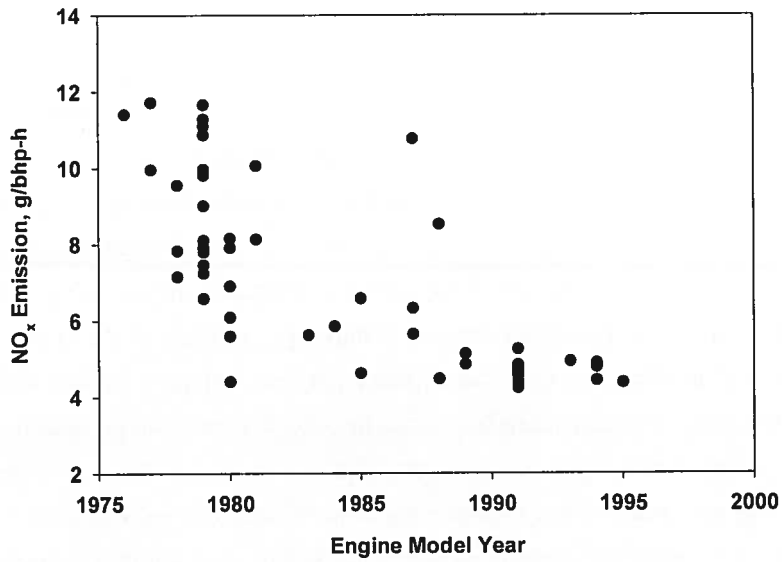

Figure 2-19. Diesel engine certification data for NO_x emissions as a function of model year.

Source: Data are from the transient test results provided in Table 2-8.

emissions, and all engines would appear to meet the regulatory standards for their year of manufacture because of the illegal emissions devices. From 1980 to 1997, the EPA emissions trends report (U.S. EPA, 1998a) predicted a decline in NO_x emissions from HD diesel vehicles because these data are based on engine test data. The emissions trend includes the growth in vehicle miles traveled over time as well as changes in emission factors. The more recent trends inventory (U.S. EPA, 2000a, discussed earlier) includes emission from the illegal emissions devices and accordingly demonstrates a slight increase in NO_x emissions from on-road HD diesel vehicles from 1990 to 1998.

DPM, CO, and THC emissions, although widely variable within any model year, have shown a pronounced declining trend (Figure 2-18). DPM emissions from chassis dynamometer tests decreased from an average of 3-4 g/mi in 1977 to an average of about 0.5 g/mi in 1997, suggesting a decrease in DPM emissions of a factor of about 6. Note that these data are for vehicles or engines tested on in-use or industry-average fuel at the time they were tested. Indications are that the observed decline in DPM is caused primarily by changes in engine

Table 2-8. Diesel engine emissions data from engine dynamometer tests

Reference	Engine[a]	Year	Test[b]	NO_x g/bhp-hr	PM g/bhp-hr	CO g/bhp-hr	THC g/bhp-hr	SOF g/bhp-hr	SOF Meth[c]	Total aldehyde, mg/bhp-hr	B[*a*]P (PAH) ug/bhp-hr[d]	1-NP (NPAH) ug/bhp-hr[e]
Hare, 1977	Cat 3208 (NA)	1976	SS	7.98	0.871	4.04	1.11	0.103	c-hexane		0.76	
	DDC 6V71 (blower)	1976	SS	10.24	1.92	6.55	0.71	0.937	c-hexane		0.24	
Springer, 1979	Mack ETAY(B)673A (DI, TC,AC)	1977	SS	6.613	0.61	1.588	0.476	0.098	Benz/cyc	65	2.23	
	Cat 3208 (EGR, NA)	1977	SS	3.747	2.21	6.200	1.163		Benz/cyc	161	1.72	
	Cat 3406 (DI, TC, AC)	1977	SS	9.79	0.35	2.34	0.35	0.063	Benz/cyc	73	0.15	
	Cat 3406 (DI, TC, AC, EGR)	1977	SS	5.49	0.93	4.81	0.17	0.181		80	0.08	
	Cat 3406 (IDI, TC, AC)	1977	SS	5.14	0.28	1.26	0.12	0.031	Benz/cyc	80	0.11	
	DB OM-352A (DI, TC, AC)	1977	SS	8.93	0.56			0.190	Benz/cyc	280	0.87	
	DB OM-352A (DI, NA)	1977	SS	7.46	0.99			0.287	Benz/cyc	280	1.07	
Perez, 1980	Cat (DI, NA)	1978	SS	8.12	0.77	5.92	0.77	0.19	DCM		1.08	
	Cat (DI, EGR)	1978	SS	5.16	1.21	5.37	0.57	0.079	DCM		4.34	
	Cat (DI, TC, AC)	1978	SS	7.66	0.33	2.20	0.27	0.037	DCM		0.34	
Martin, 1981a	Cat 3208	1978	T	7.83	1.06							
	Cummins NTC350	1976	T	11.41	0.81							
	DDC 6V92T (2S)	1978	T	9.55	0.72							
	Cummins NTCC350	1979	T	6.58	0.52							
	DDC 8V71N (2S)	1978	T	7.15	0.92							
	DDC 6V92TA (2S)	1979	T	7.80	0.65							
	IH DTI466B	1979	T	7.46	0.48							
	Mack ETAY(B)673A	1979	T	9.01	0.77							
	Mack ETSX676-01	1980	T	6.90	0.85							
	Cummins VTB-903	1979	T	8.10	0.53							
	Cat 3406	1979	T	11.28	0.69							
	Cat 3406PCTA	1979	T	7.24	0.49							
	Cummins BigCam NTC350	1979	T	9.97	0.54							
	IH DT466	1979	T	7.91	0.71							
	DDC 6V92TA (2S)	1979	T	11.66	0.73							
	DDC 8V71TA (2S)	1979	T	9.81	0.51							
	Cummins NTC290	1979	T	11.10	0.78							
	Cummins NH-250	1979	T	10.87	0.97							
Martin, 1981b	Cummins VTB-903	1980	T	5.59	0.67	2.0	2.23	0.228	DCM			
	DDC 8V71TA (2S)	1980	T	7.91	0.44	2.28	0.73	0.176	DCM			
	IH DTI466B	1980	T	4.41	0.62	2.35	0.87	0.186	DCM			
Ullman et al., 1984	DDAD 6V-71 (2S)	1980	T	6.09	0.56	3.86	1.42	0.298	DCM	23	--	
Martin, 1984	Cummins NTC300	1981	T	8.13	0.45	2.70	1.36	--				
Barry et al., 1985	Cat 3406B	1985	T	6.58	0.48	2.1	0.5	0.061	DCM	70	1	
	DDC 8V-92 TA (2S)	1980	T	8.15	0.45	2.61	0.53	--				

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Table 2-8. Diesel engine emissions data from engine dynamometer tests (continued)

Reference	Engine[a]	Year	Test[b]	NO_x g/bhp-hr	PM g/bhp-hr	CO g/bhp-hr	THC g/bhp-hr	SOF g/bhp-hr	SOF Meth[c]	Total aldehyde, mg/bhp-hr	B[*a*]P (PAH) ug/bhp-hr[d]	1-NP (NPAH) ug/bhp-hr[e]
			SS	6.64	0.36	1.83	0.38	0.0255				
Enga et al., 1985	DDC 8V-71 TAC (2S)	1984	T	5.85	1.26	2.99	1.48	--		--	--	
Baines, 1986	Cummins NTCC-400	1985	T	4.62	0.55	3.21	0.53					
Wachter, 1990	Iveco 8460	1991	T		0.22			0.0957	?			
McCarthy et al., 1992	Navistar DTA466 ES210	1993	T	4.93	0.082	1.3	0.28	0.0237	SFE			
Perez and Williams, 1989	Engine 1	1982	T		0.93			0.179	DCM		26	0.83
	Engine 2	1982	T		0.86			0.145	DCM		5.8	--
	Engine 3	1982	T		0.59			0.185	DCM		4.9	0.89
	Engine 4	1982	T		0.96			0.325	DCM		26	1.2
	Engine 5	1982	T		1.06			0.076	DCM		5.3	--
	Engine 6	1982	T		0.88			0.344	DCM			
Needham et al., 1989	Average of 16 engines	1988	T		0.37			0.12	DCM			
	Average of 3 engines	1991	T		0.24			0.10	DCM			
Kreso et al., 1998	Cummins L10-300	1988	SS	5.15	0.103		0.26	0.030	DCM			
	Cummins L10-310	1991	SS	4.70	0.035		0.067	0.022	DCM			
	Cummins M11-330E	1995	SS	3.82	0.037		0.16	0.016	DCM			
Bagley et al., 1998	Cat 3304 (IDI, NA) non-road	1983	SS		0.56			0.319	Benz/cyc		1.5(133)	2.2
Graboski, 1998b (and references therein)	DDC 6V-71N-77 (MUI, 2S)	1977	T	9.96	0.83	3.59	2.01	0.729	DCM			
	DDC 6V-92TA-91 (DDECII)	1991	T	4.23	0.197	1.51	0.72	0.0788	?			
	DDC-6V-92TA-87 (2S)	1987	T	10.77	0.59	0.71	--	--				
	DDC-6V92TA-83 (MUI, 2S)	1983	T	5.62	0.265	1.19	0.435	0.133	DCM			
	DDC 6V-92TA -88 (DDECII, 2S)	1988	T	8.52	0.2	1.6	0.6	0.116	Tol/EtOH			
	DDC 6V-92TA-91 (DDECII, 2S)	1991	T	4.4	0.276	1.65	0.42	0.07	Tol/EtOH			
	DDC 6V-71N-77 (MUI, 2S)	1977	T	11.72	0.282	3.18	0.86	0.212	DCM			
	DDC 6V-92TA-81/89 (MUI, 2S)	1981	T	10.06	0.268	2.16	0.42	0.144	DCM	--	--	
	DDC 6V-92TA-91 (DDECII, 2S)	1991	T	4.84	0.227	1.51	0.44	--		--	--	
	DDC 6V-92TA-89 (DDECII, 2S)	1989	T	4.855	0.338	2.499	0.526	--		--	--	
	DDC Series 60-91 DDECII	1991	T	4.635	0.300	4.458	0.164	--				
	Cummins L-10-87 (MUI)	1987	T	5.64	0.309	2.33	0.89	--				
	DDC Series 60-91 (DDECII)	1991	T	4.68	0.220	2.26	0.08	0.066	DCM			
	Cummins N-14-87 (MUI)	1987	T	6.32	0.369	2.20	0.58	0.100	?			
	DDC Series 60-89 (DDECII)	1989	T	5.128	0.252	4.008	0.154	--				--
	DDC Series 60-91 (DDECII)	1991	T	4.303	0.182	2.004	0.392	0.061	Tol/EtOH	--	--	
	Cummins B5.9	1995	T	4.37	0.106	1.47	0.30	0.05	DCM		0.24((18.5)	
Spreen et al., 1995	Navistar DTA466	1994	T	4.779	0.090	0.989	0.181	0.035	DCM	26		
Norbeck et al., 1998b	Cummins L10	1991	T	4.77	0.224	2.26	0.53	--		80	20(1725)	1.95(4.92)
	DDC Series 60	1994	T	4.89	0.112	1.402	0.065	0.043	DCM	17		
Sienicki et al., 1990	Navistar DTA466	1991	T	5.25	0.22	--	0.23	0.05	DCM			

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Table 2-8. Diesel engine emissions data from engine dynamometer tests (continued)

Reference	Engine[a]	Year	Test[b]	NO_x g/bhp-hr	PM g/bhp-hr	CO g/bhp-hr	THC g/bhp-hr	SOF g/bhp-hr	SOF Meth[c]	Total aldehyde, mg/bhp-hr	B[*a*]P (PAH) ug/bhp-hr[d]	1-NP (NPAH) ug/bhp-hr[e]
Ullman et al., 1990	DDC Series 60	1991	T	4.552	0.188	2.102	0.508	--				
Kado et al., 1998	Cat 3406E	1997	T						DCM		0.07(30)	0.34
Ullman, 1988	Cummins NTCC400	1988	T	4.47	0.42	2.22	0.53					
Mitchell et al., 1994	DDC Series 60	1994	T	4.43	0.111	2.17	0.22	0.021	DCM	34	(141)	0.04(0.12)
	Navistar DTA466	1994	T	4.86	0.099	1.10	0.34	0.046	DCM	56	0.11(242)	0.3(0.6)
Tanaka et al., 1998	Unknown	1994	SS	4.934	0.143	0.807	0.352	0.036	DCM		.076	
Rantanen et al., 1993	Scania	1990	SS	9.30	0.157			0.031	DCM			
	Valmet	1990	SS	8.67	0.157							
	Volvo	1990	SS	9.87	0.262							
	Volvo	1995	SS	4.56	0.135							

[a]NA=naturally aspirated. TC=turbocharged (engines not designated as NA or TC are turbocharged). AC=aftercooled. DI=direct injection. IDI=indirect injection. EGR=exhaust gas recirculation. 2S=two-stroke (engines not designated as 2S are four-stroke). MUI=mechanical unit injector (not electronically controlled). DDEC=Detroit Diesel Corporation's engine control module (electronic control).
[b]SS=various single or multimode steady-state tests. T=heavy-duty FTP (transient test).
[c]SOF extraction method. SFE=Supercritical fluid extraction. All others by Soxhlet extraction using the indicated solvents (? for unreported). DCM=dichloromethane. Tol/EtOH=toluene/ethanol mixture. Benz/cyc=benzene/cyclohexane mixture. C-hexane=cyclohexane.
[d]Number in parentheses is the total PAH emission obtained by summing emissions of all PAHs reported.
[e]Number in parentheses is the total NPAH emission obtained by summing emissions of all NPAHs reported.

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technology that often result from emission standards, as well as by the lowering of on-road diesel fuel sulfur content in 1993.

As the discussion above indicates, there is a reasonable amount of data upon which to base emission factor estimates for late 1970s and later HD vehicles. However, very little transient test data are available on engines earlier than the mid-1970s. The limited data available from six pre-1976 vehicles tested using the transient cycle suggests that PM emission rates ranged from 1.6 g/mi to 9.0 g/mi, which is a substantially greater range than in post-1976 engines (Fritz et al., 2001).

Although a substantial decreasing trend in DPM emissions from in-use chassis dynomometer testing and engine testing (Figure 2-20) is evident, these data reflect a wide range in emission factors within any given model year. For example, emission factors for model year 1996 range from less than 0.1 g/mi to more than 1 g/mi (Yanowitz et al., 2000; Graboski et al., 1998b). The high variability in DPM emissions measured in the chassis dynamometer tests is observed because of several factors, including differences in measurement methods and test conditions at the various testing facilities, deterioration, and engine-to-engine variation. Although there can be excellent agreement between chassis dynamometer testing facilities (Graboski et al., 1998a), there is no standard HD chassis dynamometer Federal test procedure, and no detailed procedures for such testing are described in any authoritative source such as the Code of Federal Regulations, which does contain such procedures for engine dynamometer

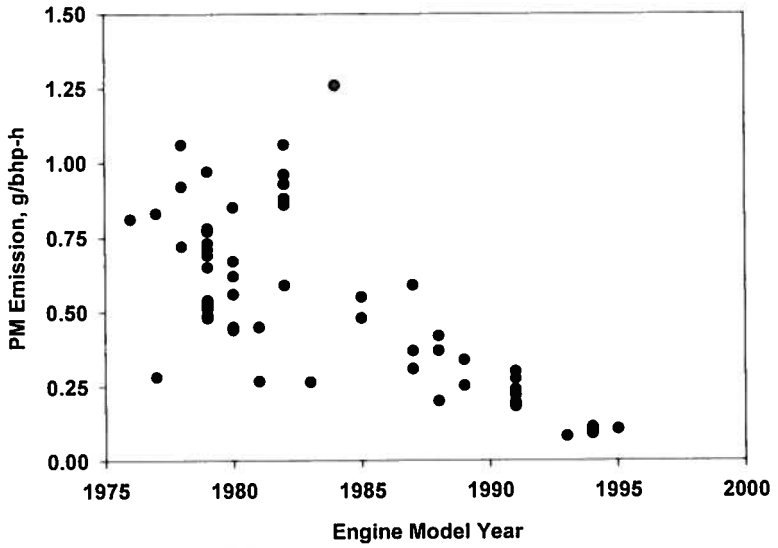


Figure 2-20. Diesel engine certification data for PM emissions as a function of model year.

Source: Data are from the transient test results provided in Table 2-8.

testing used for EPA emission regulations. Therefore, each facility has developed its own approach to HD testing. Clark et al. (1999) report that the test cycle can have a substantial effect on DPM emissions, with higher DPM emissions reported from test cycles that incorporate full-power accelerations. Test cycles incorporating full-power accelerations reflect urban HD vehicle driving for several types of vehicles (garbage trucks, buses) operating in urban areas. Clark et al. (1999) also report that aggressive acceleration produces higher DPM emission rates than does conservative acceleration, and Clark and co-workers suggest that real in-use driving is more likely to mimic aggressive acceleration. Although figures are currently unquantified, it is generally believed that the majority of DPM is generated under transient conditions such as heavy acceleration.

Weaver and Klausmeier (1988) have examined potential causes and frequency of DPM emissions deterioration for in-use HD diesel vehicles. Potential causes include manufacturing defects and malfunctions such as retarded timing, fuel injector malfunction, smoke-limiting mechanism problems, clogged air filter, wrong or worn turbocharger, clogged intercooler, engine mechanical failure, excess oil consumption, and electronics that have been tampered with or have failed. The recent report by McCormick and co-workers (2000) indicates that many of these malfunctions can have very large effects on DPM emissions, resulting in DPM increases of typically 50% to 100%. Although Yanowitz and co-workers (1999) found that DPM emissions were positively correlated with odometer mileage for a fleet of 21 vehicles, it is more likely that the vehicle state of maintenance will be more important than mileage for determining the degree of emissions deterioration. In fact, in a similar analysis performed on the chassis dynamometer results included in the review of Yanowitz et al. (2000), DPM emissions could not be correlated with odometer mileage. Differences in testing methods between various facilities as well as varying states of maintenance for vehicles of the same mileage and model year probably account for this lack of correlation.

It is difficult, given current information, to quantitatively assess the contribution of high-emitting or smoking diesel vehicles to ambient DPM. Emission models used to prepare diesel particulate emission inventories do not account for deterioration. The relative contribution of high-emitting diesel vehicles to the total mass and overall chemical composition of diesel particulates is being quantified. Some studies report numerous smoking diesel trucks. A study of the smoke opacity-based inspection and maintenance program in California found failure rates of 20% and higher, suggesting that high-emitting vehicles are not uncommon (CARB/EEAI, 1997). In the Northeast, smoke opacity testing conducted on 781 HD trucks found that 15% of the vehicles failed the smoke standard (40% opacity for 1991 and newer HD diesel vehicles and 50% opacity for pre-1991 HD diesel vehicles) (Cooper, 1999). Although the correlation between smoke and particulate emissions tends to be qualitative or semiquantitative (discussed

below), there is a good correlation between opacity and EC concentrations, and it is expected that high-emitting diesel vehicles may be an important part of the DPM emission inventory.

Others have attempted to determine if the effects of deterioration could be detected for in-use vehicles. In a study of 21 vehicles (Yanowitz et al., 1999), a linear multivariate regression analysis found that DPM emissions were positively correlated with odometer mileage (several other correlation factors were also identified, including model year). A similar analysis performed on the chassis dynamometer results included in the review of Yanowitz et al. (2000) found that DPM emissions could not be correlated with odometer mileage, probably because of differences in testing methods between the various facilities.

Other approaches for measuring emissions from in-use on-road diesel vehicles include tunnel tests and remote sensing, the latter of which measures gaseous, but not DPM, emissions. The literature reports of those studies are summarized in Tables 2-9 and 2-10. Several tunnel test studies have reported DPM emission factors (Pierson and Brachaczek, 1976; Japar et al., 1984; Pierson et al., 1983; Kirchstetter et al., 1999; Gertler et al., 1996, 1999).

The method for determining emission rates for vehicles traveling through a tunnel is explained in detail by Pierson et al. (1996). Briefly, the emissions of a species are determined by measuring the concentration of a pollutant entering and leaving a tunnel along with knowledge of the cross-section of the tunnel and measurements of the wind flux at the inlet and outlet of the tunnel. The emission rate is calculated by dividing the mass of the pollutant by the number of vehicles that passed through the tunnel and the length of the tunnel. The diesel and gasoline vehicle contributions to the total emission of the pollutant are separated by a simple regression analysis where the intercepts (100% HD and 100% LD) are the diesel and gasoline emission rates, respectively.

Emission factors from tunnel studies provide a snapshot of real-world emissions under driving conditions experienced in the tunnel and reflect emission factors representative of the mix of in-use vehicles and the atmospheric dilution and short-term transformation processes of DE. Emission factors derived from tunnel studies are often used as one source of information to study the impact of improved technology and fleet turnover on emissions because they allow random sampling of large numbers of vehicles, including a range of ages and maintenance conditions. However, tunnel studies are limited in that they represent driving conditions on a single roadway passing through a tunnel and represent mostly steady-state driving conditions, whereas most DPM is generated during transient modes of operation; also, tunnel studies do not include cold-start operations. Both of these factors need to be assessed to understand emission rates for DPM to which people are exposed (U.S. EPA, 1992, 1995). DPM emission factors from in-use fleets derived from tunnel studies in the 1970s and 1980s compared with the 1990s

Table 2-9. HD diesel emissions results from tunnel tests (adapted from Yanowitz et al., 1999)

Test	Tunnel location, year of study	Fuel efficiency (mi/gal)	NO_x[a] (g/mi)	NMHC (g/mi)	CO (g/mi)	DPM (g/mi)	CO_2 (g/mi)	NO_x[a] (g/gal)	NMHC (g/gal)	CO (g/gal)	DPM (g/gal)
Pierson and	Allegheny, 1974	5.42[b]				.90-1.80					4.9-9.8
Brachaczeck, 1983	Allegheny, 1975					1.75 ± 0.19					9.49±1.03
	Allegheny, 1976					1.5 ± 0.10					8.1 ± 0.54
	Allegheny, 1976					1.4 ± 0.07					7.6 ± 0.4
	Tuscarora, 1976					1.3 ± 0.19					7.0 ± 1.0
	Tuscarora, 1976					1.39 ± 26					7.5 ± 1.40
	Allegheny, 1977					1.3 ± 0.08					7.0 ± 0.43
	Allegheny, 1979					1.2 ± 0.03					6.5 ± 0.16
	Allegheny, 1979					1.4 ± 0.04					7.6 ± 0.19
Rogak et al., 1998	Cassiar Tunnel, 1995, Vancouver	8.03[b]	19.50 ± 4.22	-0.16 ± 0.88	6.79 ± 11.78		1,280 ± 40	157 ± 34	-1 ± 7	55 ± 95	
Miguel et al., 1998	Caldecott Tunnel, 1996, San Francisco	5.42[c]	23.82 ± 4.17			1.67 ± 0.24[d]		129 ± 23			9.0 ± 1.3[d]
Weingartner et al., 1997b	Gubrist Tunnel, 1993, Zurich	5.60[e]				0.62 ± 0.02[f]					3.5 ± 0.1[f]
Pierson et al., 1996	Fort McHenry Tunnel, downhill, 1992, Baltimore	11.46[b]	9.66 ± 0.32	0.92 ± 0.21	6.8 ± 1.5		897 ± 48	111 ± 4	11 ± 2	78 ± 17	
Pierson et al., 1996	Fort McHenry Tunnel, uphill, 1992, Baltimore	5.42[b]	22.50 ± 1.00	2.55 ± 1.05	14.3 ± 5.5		1,897 ± 168	122 ± 5	14 ± 6	78 ± 30	
Pierson et al., 1996	Tuscarora Tunnel 1992, Pennsylvania	6.44[b]	19.46 ± 0.85	0.68 ± 0.20	6.03 ± 1.61		1,596 ± 78	125 ± 5	4 ± 1	39 ± 10	
Kirchstetter et al., 1999	Caldecott Tunnel, 1997, San Francisco	5.42[c]	23.82 ± 2.98			1.43 ± 0.12[g]		129 ± 16			7.7 ± 0.6[g]
Gertler, 1999	Tuscarora Tunnel, 1999, Pennsylvania					0.29					

[a]NO_x reported as NO_2.
[b]Calculated from observed CO_2 emissions assuming fuel density 7.1 lb/gal and C is 87% of diesel fuel by weight.
[c]Since CO_2 emissions not available, fuel efficiency assumed to be the same as in slightly uphill tunnel (Fort McHenry).
[d]Reported as black carbon, assumed that 50% of total PM emissions are BC.
[e]Slope of tunnel unknown, so used average fuel efficiency for the United States.
[f]PM_3.
[g]$PM_{2.5}$.
[h]Uncertainty reported as ±1.0 standard deviation, except where literature report did not specify standard deviation; in those cases uncertainty listed as reported.

Table 2-10. Remote sensing results for HD vehicles

	Reference	Year study conducted	Emissions (g/gal)
NO_x	Jimenez et al., 1998	1997	150 [a,b,c]
	Cohen et al., 1997	1997	108 [a,b,c]
	Countess et al., 1999	1998	187 [a,b,c]
CO	Bishop et al., 1996	1992	59 [b]
	Cohen et al., 1997	1997	54 [b]
	Countess et al., 1999	1998	85 [b]
THC	Bishop et al., 1996	1992	0.002 HC/CO_2 mole ratio [d]
	Cohen et al., 1997	1997	0.00073 HC/CO_2 mole ratio [d]

[a]Remote sensing measures NO. The reported value was corrected to a NO_x (as NO_2) value by assuming 90% (mole fraction) of NO_x is NO.
[b]Emissions in g/gal calculated by assuming that fuel density is 7.1 lb/gal and C is 87% by weight of fuel.
[c]No humidity correction factor is included.
[d]In order to calculate emissions in g/gal, an average molecular weight is needed.

Source: Yanowitz et al., 1999.

suggest approximately a fivefold decrease in DPM mass emission factors over that time, with the most recent data from 1999 reporting an emission factor of 0.29 g/mi for the on-highway HD diesel fleet (Figure 2-21).

Emission factors vary substantially for the various tunnels, with NO_x emissions ranging from 9.7 to 23.8 g/mi in the 1990s, CO emissions ranging from 6 to 14 g/mi, and THC emissions ranging from 0.16 to 2.55 g/mi.

Remote sensing reports emission factors in terms of pollutant emissions per unit of fuel, not on a per-mile basis. Agreement between remote sensing and tunnel studies for NO_x emissions is reasonably good for the fleet as a whole, suggesting an average level for the fleet of about 130 g/gal, comparable to the average emissions factor measured in chassis dynamometer studies (remote sensing can measure emissions from an individual vehicle, whereas tunnel studies measure emissions from the fleet as a whole). Generally, chassis dynamometer tests and engine dynamometer test results are corrected for ambient humidity, in accordance with the Federal Test Procedure (CFR 40, Subpart N). Tunnel tests and remote sensing tests have typically not included corrections for humidity. Appropriate humidity corrections for NO_x and DPM can be greater than 20% and 10%, respectively (or a total difference of more than 45% and 20%, respectively, between low- and high-humidity areas), under normally occurring climatic conditions. Additionally, the remote sensing literature has not addressed how to determine the

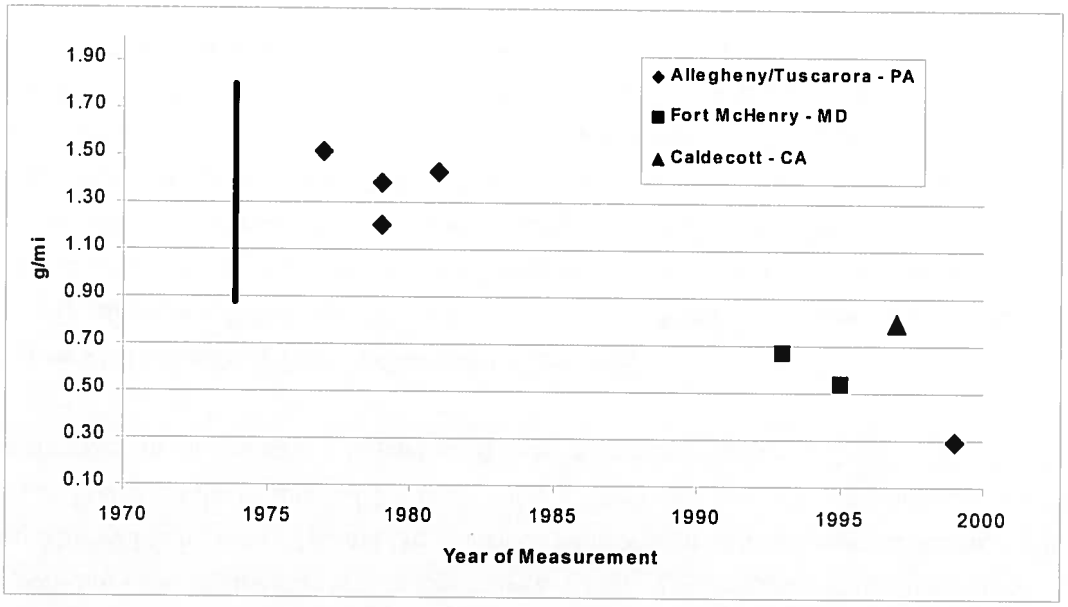


Figure 2-21. Emission factors from HD diesel vehicles from tunnel studies.

Source: Data from Pierson and Brachaczek, 1976; Japar et al., 1984; Pierson et al., 1996; Kirchstetter et al., 1999; Gertler et al., 1995, 1996; Gertler, 1999.

correct value for the NO/NO_x ratio, and there is reason to believe that this value may differ systematically from site to site, although almost all of the NO_x is NO as it leaves the vehicle.

In addition to the humidity correction discussed above, several factors must be taken into account when comparing DPM measurements from tunnel tests to chassis dynamometer measurements (Yanowitz et al., 2000): (1) Chassis testing measures only tailpipe emissions; tunnel tests can include emissions from other sources (tire wear, etc.), and (2) tunnel tests typically measure emissions under steady-speed freeway conditions, whereas most chassis dynamometer tests are measured on cycles that are more representative of stop-and-go urban driving conditions. This latter limitation also applies to remote sensing readings, which measure instantaneous emissions versus emissions over a representative driving cycle.

Because THC emissions for diesel vehicles are very low in total mass in comparison with gasoline vehicles, tunnel test results for THC have a high degree of uncertainty. A regression analysis to determine the contribution of the limited number of HD vehicles to THC emissions is unstable; small errors in the total measurements can change estimates substantially. Similarly,

CO emissions are comparable to automobile emissions on a per-vehicle-mile basis, but because there are generally many more automobiles than HD diesels in tunnel tests, CO measurements from diesels may also have a high degree of uncertainty.

2.2.5.2. *Locomotives*

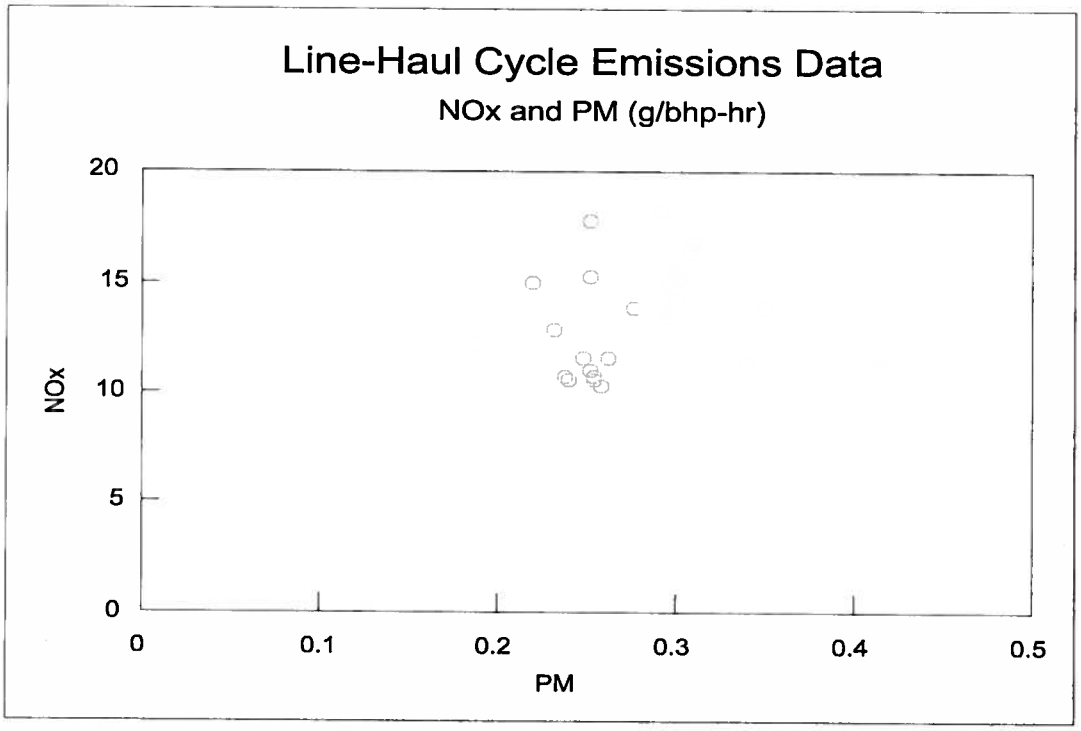
Locomotive engines generally range from 1,000 horsepower up to 6,000 horsepower. Similar to the much smaller truck diesel engines, the primary pollutants of concern are NO_x, DPM, CO, and HC. Unlike truck engines, most locomotive engines are not mechanically coupled to the drive wheels. Because of this decoupling, locomotive engines operate in specific steady-state modes rather than the continuous transient operation normal for trucks. Because the locomotive engines operate only at certain speeds and torques, the measurement of emissions is considerably more straightforward for locomotive engines than for truck engines. Emissions measurements made during the relatively brief transition periods from one throttle position to another indicate that transient effects are very short and thus could be neglected for the purposes of overall emissions estimates.

Emissions measurements are made at the various possible operating modes with the engine in the locomotive, and then weighting factors for typical time of operation at each throttle position are applied to estimate total emissions under one or more reasonable operating scenarios. In the studies included in this analysis, two scenarios were considered: line-haul (movement between cities or other widely separated points) and switching (the process of assembling and disassembling trains in a switchyard).

The Southwest Research Institute made emissions measurements for three different engines in locomotives in 1972 (Hare and Springer, 1972) and five more engines in locomotives using both low- and high-sulfur fuel in 1995 (Fritz, 1995). Two engine manufacturers (the Electro-Motive Division of GM, and GE Transportation Systems) tested eight different engine models and reported the results to EPA (U.S. EPA, 1998b). All available data on locomotives are summarized in the regulatory impact assessment and shown in Figure 2-22.

2.2.6. Engine Technology Description and Chronology

NO_x emissions, DPM emissions, and brake-specific fuel consumption (BSFC) are among the parameters that are typically considered during the development of a diesel engine. Many engine variables that decrease NO_x can also increase DPM and BSFC. One manifestation of the interplay among NO_x, DPM, and BSFC is that an increase in combustion temperatures will tend to increase NO formation. Higher temperatures will also often improve thermal efficiency, can improve BSFC, and can increase the rate of DPM oxidation, thus lowering DPM emissions. One example of this is the tradeoff of DPM emissions and BSFC versus NO_x emissions with fuel



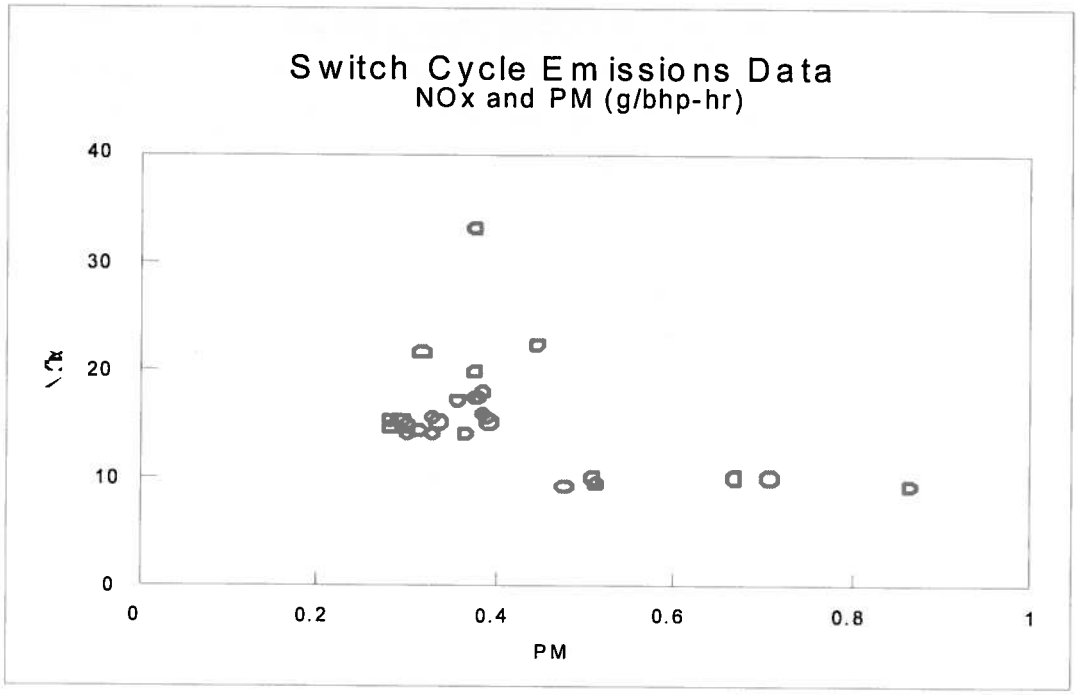


Figure 2-22. Line-haul and switch emissions data.

Source: U.S. EPA, 1998a.

injection timing. Many recent advances in reducing the emissions of diesel engines without aftertreatment are combinations of technologies that provide incremental improvements in the tradeoffs among these emissions and fuel consumption. The sum total, however, can be considerable reductions in regulated emissions within acceptable levels of fuel consumption.

The majority of current HD diesel truck engines certified for use in the United States utilize:

- A four-stroke cycle
- Direct-injection, high-pressure (1,200 bar to >2,000 bar) fuel injection systems with electronic control of injection timing and, in some cases, injection rate
- Centrally located multihole injection nozzles
- Three or four valves per cylinder
- Turbochargers
- In many cases, air-to-air aftercooling
- In some cases, the use of an oxidation catalyst.

These features have phased into use with HD truck engines because they offer a relatively good combination of fuel consumption, torque-rise, emissions, durability, and the ability to better "tune" the engines for specific types of applications. Fuel consumption, torque-rise, and drivability have been maintained or improved while emissions regulations have become more stringent. Many Class 8a and 8b diesel truck engines are now capable of 700,000 to 1,000,000 miles of driving before their first rebuild and can be rebuilt several times because of their heavy construction and the use of removable cylinder liners. These engines are expected to last longer and therefore have a useful life longer than the regulatory estimate of full useful life for HD engines (~1,000,000 miles) previously used by EPA (for 1980 engines that were driven less than 300,000 miles between rebuilds and were rebuilt up to three times). Current four-stroke locomotive engines use engine technology similar to on-highway diesel engines, except that electronic controls have only recently been introduced.

It is difficult to separate the components of current high-speed diesel engines for discussion of their individual effects on emissions. Most of the components interact in numerous ways that affect emissions, performance, and fuel consumption.

2.2.6.1. *Indirect and Direct Injection High-Speed Diesel Engines*

Prior to the 1930s, diesel engine design was limited to relatively low-speed applications because sufficiently high-pressure fuel injection equipment was not available. With the advent of high-speed and higher pressure pump-line-nozzle systems, introduced by Robert Bosch in the

1930s, it became possible to inject the fuel directly into the cylinder for the first time, although indirect injection (IDI) diesel engines continued in use for many years. As diesels were introduced into the heavy truck fleet in the 1930s through the 1950s, both IDI and direct injection (DI) naturally aspirated variants were evident. A very low-cost rotary injection pump technology was introduced by Roosa-Master in the 1950s, reducing the cost of DI systems and allowing their introduction on smaller displacement, higher speed truck engines. After this time, only a small fraction of truck engines used an IDI system.

DI diesel engines have now all but replaced IDI diesel engines for HD on-highway applications.[2] IDI engines typically required much more complicated cylinder head designs but generally were capable of using less sophisticated, lower pressure injection systems with less expensive single-hole injection nozzles. IDI combustion systems are also more tolerant of lower grades of diesel fuel. Fuel injection systems are likely the single most expensive component of many diesel engines. Caterpillar continued producing both turbocharged and naturally aspirated IDI diesel engines for some on-highway applications into the 1980s. Caterpillar and Deutz still produce engines of this type, primarily for use in underground mining applications. IDI combustion systems are still used in many small-displacement (<0.5 L/cylinder), very high-speed (>3,000 rpm rated speed) diesel engines for small nonroad equipment (small imported tractors, skid-steer loaders), auxiliary engines, and small generator sets, and they were prevalent in diesel automotive engines in the 1980s; IDI designs continue to be used in automotive diesel engines.

IDI engines have practically no premixed burn combustion and thus are often quieter and have somewhat lower NO_x emissions than DI engines. Electronic controls, high-pressure injection (e.g., GM 6.5), and four-valve/cylinder designs (e.g., the six-cylinder Daimler LD engine) can be equally applied to IDI diesel engines as in DI, but they negate advantages in cost over DI engines. DI diesel engines of the same power output consume 15% to 20% less fuel than IDI engines (Heywood, 1988). Considering the sensitivity of the HD truck market to fuel costs, this factor alone accounts for the demise of IDI diesel engines in these types of applications. Throttling and convective heat transfer through the chamber-connecting orifice, and heat rejection from the increased surface area of IDI combustion systems, decrease their efficiency and can cause cold-start difficulties when compared to DI designs. Most IDI diesel engine designs require considerably higher than optimum compression ratios (from an efficiency standpoint) to aid in cold-starting (19:1 to 21:1 for IDI engines vs. ~15:1 to 17:1 for DI engines).

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[2]The GM Powertrain/AM General 6.5L electronically controlled, turbocharged IDI-swirl chamber engine, certified as a light HD diesel truck engine, is the last remaining HD on-highway IDI engine sold in the United States.

Because of the early introduction of DI technology into truck fleets, it is likely that by the end of the 1960s, only a small fraction of the HD diesel engines sold for on-highway use were IDI engines. It is unlikely that the shift from IDI to DI engine designs through the 1950s and 1960s occurred rapidly and likely that this shift had little significant impact on emissions. Springer (1979) reports a comparison of nearly identical Caterpillar 3406 engines (turbocharged and aftercooled) in DI and IDI configurations tested on an engine dynamometer under steady-state conditions, which limits the usefulness of these data. There was no significant difference in emissions of DPM, SOF, aldehydes, or DPM-associated B[*a*]P (Table 2-8). Note that IDI designs continue to be used in automotive diesel engines.

2.2.6.2. *Injection Rate*

Decreasing the duration of diffusion combustion and promoting EC oxidation during the expansion stroke can reduce formation of EC agglomerates (Stone, 1995) and reduce the particulate carbon fraction at high load (Needham et al., 1989). Both of these effects are enhanced by increasing the fuel injection rate. The primary means of accomplishing this is by increasing fuel injection pressure. In 1977 Robert Bosch introduced a new type of high-pressure pump capable of producing injection pressures of 1,700 bar at the nozzle (Voss and Vanderpoel, 1977). This increased fuel injection pressure by roughly a factor of 10. Unit injection, which combines each fuel injection nozzle with individual cam-driven fuel pumps, can achieve very high injection pressures (>2,000 bar). The first combination of unit injectors with electronically controlled solenoids for timing control was offered in the United States by Detroit Diesel Corporation in the 1988 model year (Hames et al., 1985). Replacement of the injection cam with hydraulic pressure, allowing a degree of injection rate control, was made possible with the hydraulic-electronic unit injection jointly developed by Caterpillar and Navistar, introduced on the Navistar T444E engine (and variants) in 1993.

It is widely known that high fuel injection pressures have been used to obtain compliance with the PM standards that went into effect in 1988 (Zelenka et al., 1990). Thus, it is likely that a transition to this technology began in the 1980s, with the vast majority of new engine sales employing this technology by 1991, when the 0.25 g/bhp-hr Federal PM standard went into effect.

The use of electronic control of injection rate is rapidly increasing on medium HD diesel engines. Engines are currently under development, perhaps for 2002–2004 introduction, that use common-rail fuel injection systems with even more flexible control over injection pressure and timing than previous systems.

Increased injection rate and pressure can significantly reduce EC emissions, but it can also increase combustion temperatures and cause an increase in NO_x emissions (Springer, 1979;

Watson and Janota, 1982; Stone, 1995). Low NO_x, low DPM, and relatively good BSFC and brake mean engine pressure (BMEP) are possible when combined with turbocharging, aftercooling, and injection timing retard.

2.2.6.3. *Turbocharging, Charge-Air Cooling, and Electronic Controls*

Use of exhaust-driven turbochargers to increase intake manifold pressure has been applied to both IDI and DI diesel engines for more than 40 years. Turbocharging can decrease fuel consumption compared with a naturally aspirated engine of the same power output. Turbocharging utilizes otherwise wasted exhaust heat and pressure to generate intake boost. The boosted intake pressure effectively increases air displacement and increases the amount of fuel that can be injected to achieve a given fuel-air ratio. Turbocharging increases the power density of an engine. Boosting intake pressure via turbocharging and reducing fuel-to-air ratio at a constant power can significantly increase both intake temperatures and NO_x emissions. Increased boost pressure can significantly reduce ignition delay, which reduces VOC and DPM SOF emissions (Stone, 1995) and increases the flexibility in selection of injection timing. Injection timing on turbocharged engines can be retarded further for NO_x emission control with less of an effect on DPM emissions and fuel consumption. This allows a rough parity in NO_x emissions between turbocharged (non-aftercooled) and naturally aspirated diesel engines (Watson and Janota, 1982).

Turbocharging permits the use of higher initial injection rates (higher injection pressure),

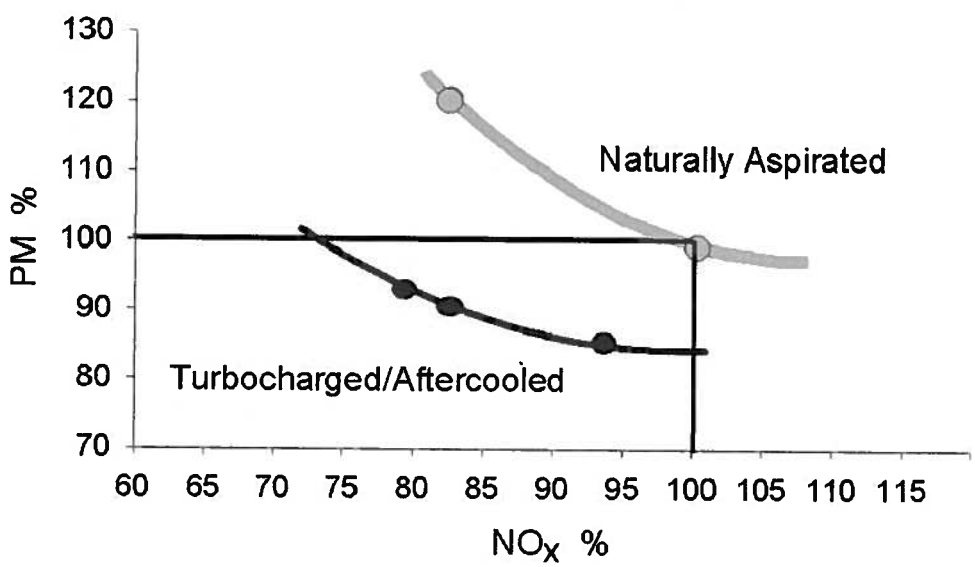

Figure 2-23. Effect of turbocharging and aftercooling on NO_x and PM.

Source: Mori, 1997.

which can reduce particulate emissions. Although this may offer advantages for steady-state operation, hard accelerations can temporarily cause overly fuel-rich conditions because the turbocharger speed lags behind a rapid change in engine speed (turbo-lag). This can cause significant increases in DPM emissions during accelerations. Before the advent of electronic controls, the effect of acceleration on DPM emissions could be limited by mechanically delaying demand for maximum fuel rate with a "smoke-puff eliminator." Because this device also limited engine response, there was considerable incentive for the end-users to remove or otherwise render the device inactive. Charge-air cooling, for example, using an air-to-air aftercooler (air-cooled heat exchanger) between the turbocharger compressor and the intake manifold, can greatly reduce intake air and peak combustion temperatures. When combined with injection timing retard, charge-air cooling allows a significant reduction in NO_x emissions with acceptable BSFC and DPM emissions when compared to either non-aftercooled or naturally aspirated diesel engines (Hardenberg and Fraenkle, 1978; Pischinger and Cartellieri, 1972; Stone, 1995). The use of charge-air cooling effectively shifts the NO_x-DPM tradeoff curve, as shown in Figure 2-23.

Electronic control of fuel injection timing allowed engine manufacturers to carefully tailor the start and length of the fuel injection events much more precisely than through mechanical means. Because of this, newer on-highway turbocharged truck engines have virtually no visible smoke on acceleration (although emissions of DPM are substantial during this driving mode). Electronic controls also allowed fuel injection retard under desirable conditions for NO_x reduction, while still allowing timing optimization for reduced VOC emissions on start-up, acceptable cold-weather performance, and acceptable performance and durability at high altitudes. Previous mechanical unit injected engines (e.g., the 1980s Cummins L10, the Non-Electronic Control Detroit Diesel 6V92) were capable of reasonably high injection pressures, but they had fixed injection timing that only varied based on the hydraulic parameters of the fuel system. Many other engines with mechanical in-line or rotary injection pumps had only coarse injection timing control or fixed injection timing.

Precise electronic control of injection timing over differing operating conditions also allowed HD engine manufacturers to retard injection timing to obtain low NO_x emissions during highly transient urban operation, similar to that found during emissions certification. HD engine manufacturers also advanced injection timing during less transient operation (such as freeway driving) for fuel consumption improvements (~3% to 5%) at the expense of greatly increased NO_x emissions (approximately three to four times regulated levels). This particular situation resulted in the recent consent decree settlements between the Federal Government and most HD engine manufacturers to ensure effective NO_x control in all driving conditions, including on-

highway high-speed steady-state driving.

Turbocharged engines entered the market very slowly beginning in the 1960s. Data for DPM emissions from naturally aspirated engines of model years 1976 to 1983 are compared with DPM emissions from turbocharged engines in Figure 2-24. There is no consistent difference in DPM emissions between turbocharged and naturally aspirated engines. Although not plotted, the data also show no difference in emissions of NO_x, DPM SOF, or DPM-associated B[*a*]P and 1-nitropyrene (1-NP).

Charge-air cooling was introduced during the 1960s and was initially performed in a heat exchanger using engine coolant. Cooling of the charge air using ambient air as the coolant was introduced into heavy trucks by Mack in 1977 with production of the ETAY(B)673A engine (Heywood, 1988). Use of ambient air allowed cooling of the charge air to much lower temperatures. Most HD diesel engines sold today employ some form of charge air cooling, with air-to-air aftercooling being the most common. Johnson and co-workers (1994) have presented a comparison of similar engines that differ in that the charge air is cooled by engine coolant (1988 engine) and by ambient air, with a higher boost pressure for the second (1991 engine). The 1991 engine also used higher pressure fuel injectors. The 1991 engine exhibited both lower DPM emissions (50% lower than the 1988 engine) and lower NO_x emissions. Higher injection pressure is likely to have enabled the reduced DPM emissions, whereas the lower charge-air

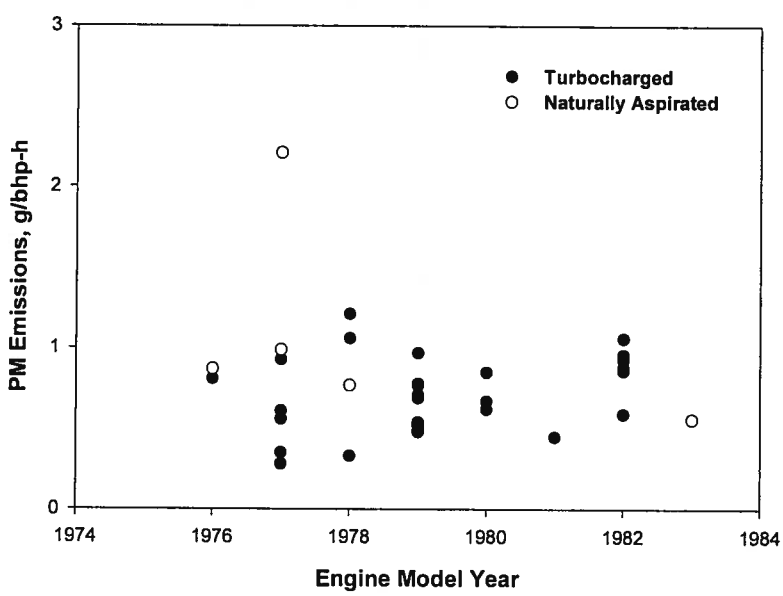

Figure 2-24. Comparison of diesel engine dynamometer PM emissions for four-stroke, naturally aspirated, and turbocharged engines.

Source: Data are from Table 2-8.

temperature and the ability to electronically retard the injection timing under some conditions likely enabled the lower NO_x emissions.

It is apparent on the basis of both the literature and certification data that turbochargers with aftercoolers can be used in HD engines in conjunction with other changes to produce a decrease in emissions. On the advent of a NO_x standard in 1985, NO_x was probably reduced on the order of 10% to 30% in turbocharged aftercooled engines with retarded injection timing. This decrease is not evident in the in-use chassis testing data because of deterioration and the use of illegal emissions devices as described above. Overall, it is expected that engines in the 1950s to mid-1970s timeframe would have similar DPM emission rates, whereas post-1970 engines would have somewhat lower DPM emission rates.

2.2.6.4. *Two-Stroke and Four-Stroke High-Speed Diesel Engines*

A detailed discussion of the two- and four-stroke engine cycles can be found in the literature (Heywood, 1988; Taylor, 1990; Stone, 1995). Nearly all high-speed two-stroke diesel engines utilize uniflow scavenging assisted by a positive-displacement blower (Figure 2-25). Uniflow-scavenged two-stroke diesels use poppet exhaust valves similar to those found in four-stroke engines. The intake air enters the cylinder through a pressurized port in the cylinder wall. A crankshaft-driven, positive-displacement blower (usually a roots-type) pressurizes the intake port to ensure proper scavenging. A turbocharger may be added to the system to provide additional boost upstream of the blower at higher speeds and to reduce the size and parasitic losses associated with the positive-displacement blower.

Two-stroke diesel engines can achieve efficiency comparable to four-stroke counterparts and have higher BMEP (torque per unit displacement) (Heywood, 1988). It is useful to note that two-stroke cycle fires each cylinder once every revolution, whereas the four-stroke cycle fires every other revolution. Thus, for a given engine size and weight, two-strokes can produce more power. However, two-stroke diesel engines are less durable than their four-stroke counterparts. Lubricating oil is transferred from the piston rings to the intake port, which causes relatively high oil consumption relative to four-stroke designs. Durability and low oil consumption are desirable for on-highway truck applications. This may be why four-stroke engines have been favored for these applications since the beginning of dieselization in the trucking industry, with the notable exception of urban bus applications. Although it is no longer in production, the Detroit Diesel 6V92 series of two-stroke diesel engines is still the most popular for urban bus applications, where the high power density allows the engine to be more easily packaged within limited spaces. The primary reason that two-stroke engines like the 6V92 are no longer offered for urban bus applications is excessive DPM emissions. The lubricating oil control with two-strokes tends to be lower than for four-stroke engines, and therefore, emissions have higher VOC

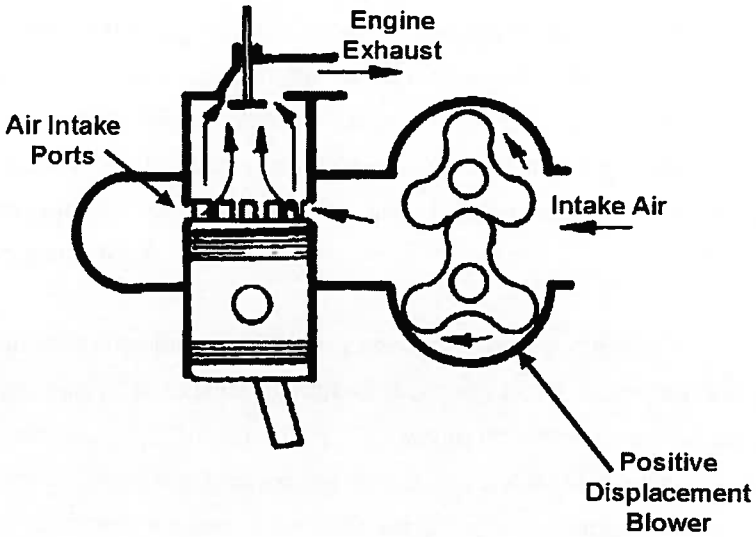

Figure 2-25. An example of uniflow scavenging of a two-stroke diesel engine with a positive displacement blower. Scavenging is the process of simultaneously emptying the cylinder of exhaust and refilling with fresh air.

Source: Adapted from Taylor, 1990.

and organic DPM emissions relative to four-stroke designs. This was particularly problematic for urban bus applications because urban bus engines must meet tighter Federal and California PM emissions standards. The current urban bus PM standard (0.05 g/bhp-hr) is one-half of the current on-highway HD diesel engine PM standard, although EPA is in the process of proposing more strict standards for HD diesel truck engines along with further reductions in diesel fuel sulfur levels. No two-stroke diesel engine designs have been certified to meet the most recent urban bus PM emissions standards, and Detroit Diesel Corporation has not certified a two-stroke diesel engine for on-highway truck use since 1995.

A comprehensive review of emissions from hundreds of vehicles (1976–98 model years) that had been tested on chassis dynamometers found that DPM emissions vary substantially within a given model year and that within that variation there are no discernible differences in DPM emissions between two- and four-stroke vehicles (Figure 2-26) (Yanowitz et al., 2000). DPM emission factors reported for engine tests also indicate that two- and four-stroke engines have comparable emission factors, as these engines all had to meet the same regulatory standard (Figure 2-27). In contrast to DPM emissions, evidence suggests that mid-1970s two-stroke engines exhibited very high SOF levels compared with four-stroke engines, with later model years showing similar SOF emissions for two- and four-stroke engines (Figure 2-28). For aldehydes, benzo[a]pyrene, and 1-nitropyrene, data are available for only one two-stroke engine,

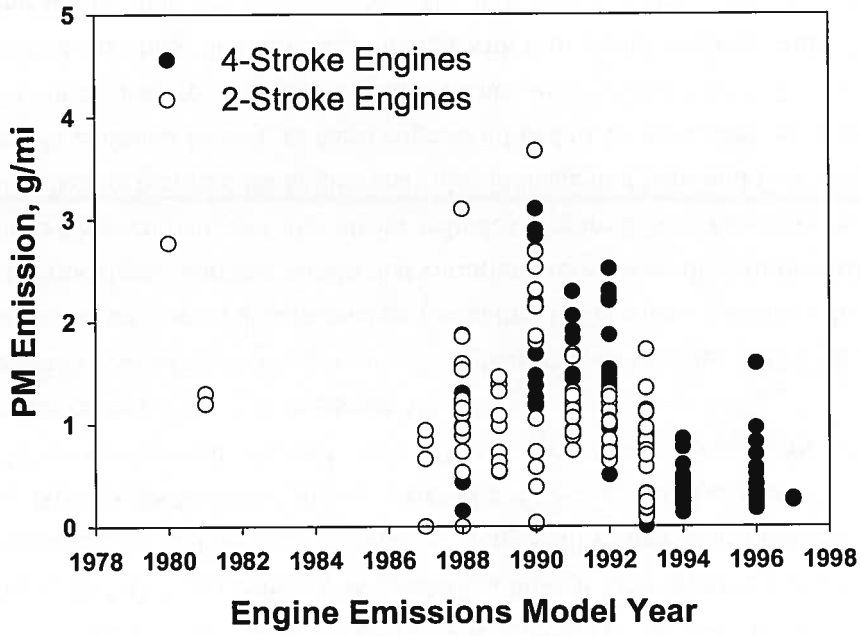

Figure 2-26. Comparison of two- and four-stroke vehicle diesel PM emissions from chassis dynamometer studies.

Source: Yanowitz et al., 2000.

but they indicate no significant difference in emissions from comparable model year four-stroke engines. Overall, regulated emissions changes attributable to changing proportions of two- and four-stroke engines in the in-use fleet do not appear to have influenced DPM emission levels, but the transition to four-stroke engines in the 1970s would have decreased the fraction of SOF associated with the DPM. It appears that the proportion of two-stroke engines in the in-use fleet was relatively constant until the late 1980s, when it began to decline.

2.2.7. Air Toxic Emissions

HD diesel vehicle exhaust contains several substances that are known, likely, or possible human or animal carcinogens, or that have serious noncancer health effects. These substances include, but are not limited to, benzene, formaldehyde, acetaldehyde, 1,3-butadiene, acrolein, dioxin, PAH, and nitro-PAH (the complete list of chemically characterized compounds present in DE is provided in Section 2.3.1). Very few historical data are available to examine changes in emission rates over time. In this section, trends in aldehyde emissions over time and a summary

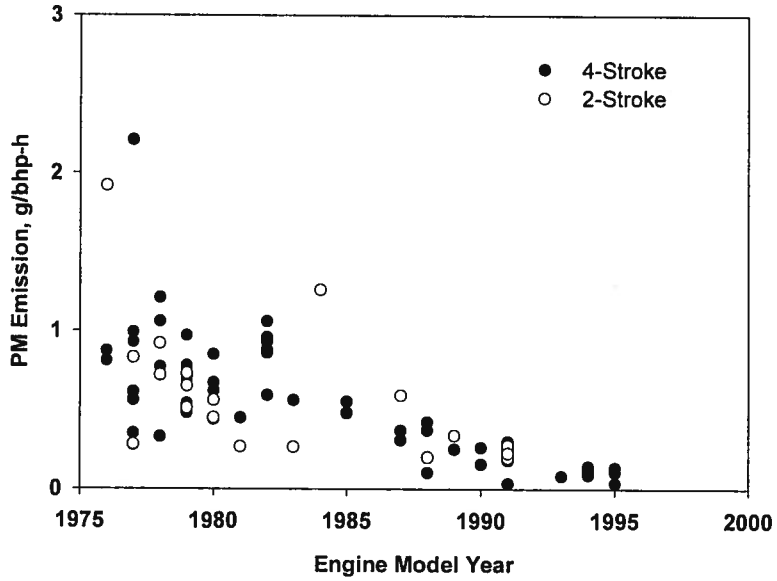

Figure 2-27. Comparison of two- and four-stroke engine diesel PM emissions from engine dynamometer studies.

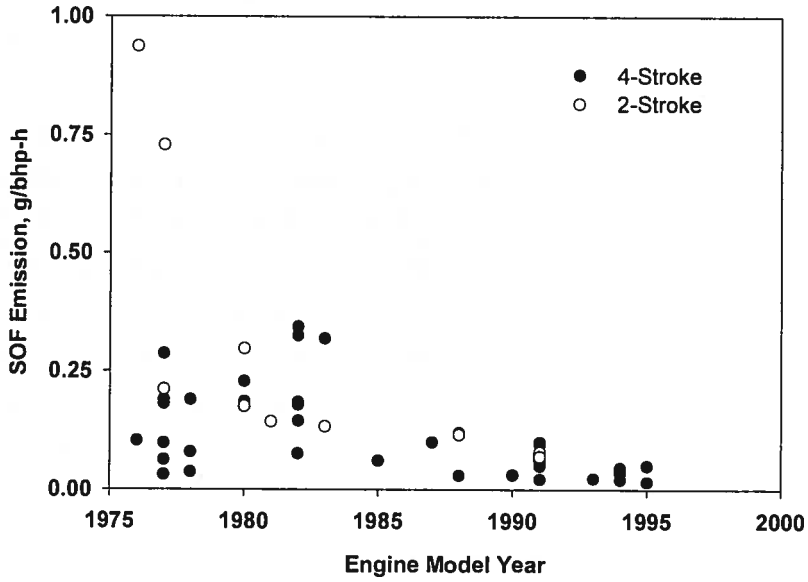

Figure 2-28. Diesel engine dynamometer SOF emissions from two- and four-stroke engines. SOF obtained by dichloromethane extraction in most studies.

Source: Data are from Table 2-8.

of dioxin emission factors are presented. PAH and nitro-PAH emission factors are discussed in Section 2.2.8.2.

2.2.7.1. *Aldehyde Emissions*

Among the gaseous components emitted by diesel engines, the aldehydes are particularly important because they constitute an important fraction of the gaseous emissions and they are probable carcinogens that also produce noncancer health effects. Formaldehyde makes up the majority of the aldehyde emissions (65% to 80%), with acetaldehyde being the second most abundant aldehyde in HD diesel emissions. Total aldehyde emissions reported from chassis dynamometer testing suggest that aldehyde emissions have declined since 1980; however, only two tests reported aldehydes from engines made after 1985 (Figure 2-29). Engine dynamometer studies also suggest a downward trend in the emissions of aldehydes in the time period from 1976 to 1994 (Figure 2-30). Engine dynamometer studies report aldehyde emission levels of 150–300 mg/bhp-hr for late 1970s engines with no significant effect of turbocharging, or IDI versus DI. High-pressure fuel injection may have resulted in a marginal increase in aldehyde emissions (Springer, 1979). By comparison, 1991 model year engines (DI, turbocharged) exhibited aldehyde emissions in the 30–50 mg/bhp-hr range (Mitchell et al., 1994).

2.2.7.2. *Dioxin and Furans*

Ballschmiter et al. (1986) reported detecting polychlorinated dibenzo-p-dioxins (CDDs) and polychlorinated dibenzofurans (CDFs) in used motor oil and thus provided some of the first evidence that CDDs and CDFs might be emitted by the combustion process in diesel-fueled engines. Incomplete combustion and the presence of a chlorine source in the form of additives in the oil or the fuel were speculated to lead to the formation of CDDs and CDFs. Since 1986, several studies have been conducted to measure or estimate CDD/CDF concentrations in emissions from diesel-fueled vehicles. These studies can be characterized as direct measurements from the engine exhaust and indirect measurements from the sampling of air within transportation tunnels.

Table 2-11 is a summary of various CDD/CDF emission characterization studies reported in the United States and Europe for diesel-fueled cars and trucks. Hagenmaier et al. (1990) reported an emission factor for LD diesel vehicles of 24 pg TEQ per liter of diesel fuel consumed. TEQ, or the toxic equivalency factor, rates each dioxin and furan relative to that of 2,3,7,8-TCDD, which is arbitrarily assigned a TEQ of 1.0 based on animal assays. Schwind et al. (1991) and Hutzinger et al. (1992) studied emissions of CDDs/CDFs from German internal combustion engines running on commercial diesel fuels and reported a range of CDD/CDF emission rates across the test conditions (in units of pg TEQ per liter of diesel fuel consumed) of 10–130 pg TEQ/L for diesel car exhaust and 70–81 pg TEQ/L for diesel truck exhaust.

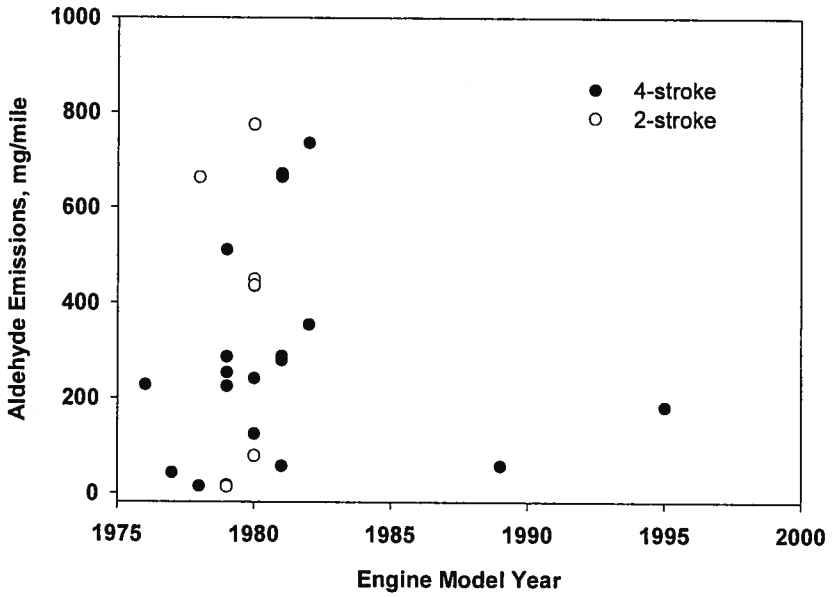

Figure 2-29. Diesel engine aldehyde emissions measured in chassis dynamometer studies.

Source: Data are from Warner-Selph and Dietzmann, 1984; Schauer et al., 1999; Unnasch et al., 1993.

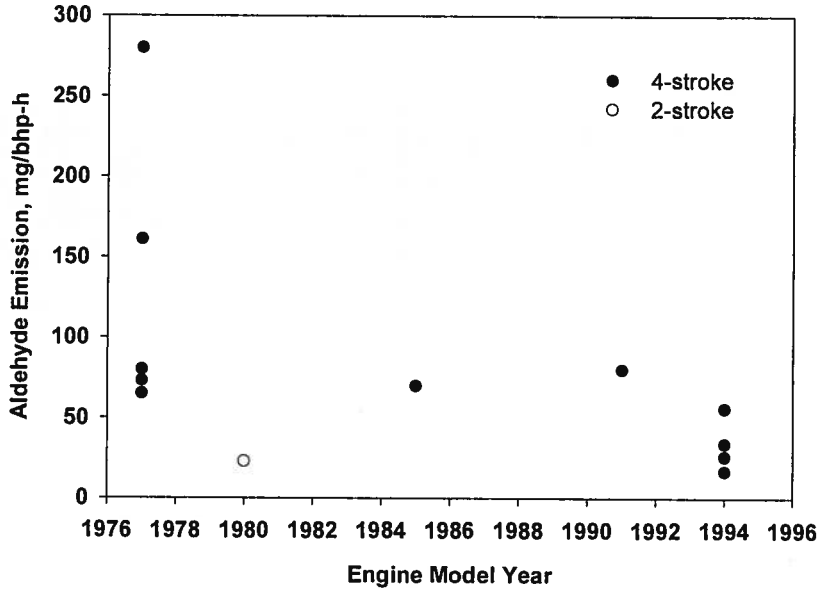

Figure 2-30. Diesel engine aldehyde emissions from engine dynamometer studies.

Source: Data from Table 2-8.

Table 2-11. Summary of CDD/CDF emissions from diesel-fueled vehicles

Study	Country	Vehicle tested	Number of test vehicles	Emission factor (pg TEQ/km driven)	Driving cycle; sampling location
CARB, 1987; Lew, 1996	United States	Diesel truck	1	663–1,300	6-hr dynamometer test at 50 km/hr
Marklund et al., 1990	Sweden	Diesel truck	1	not detected (<18)[a]	U.S. Federal mode 13 cycle; before muffler
Hagenmaier et al., 1990	Germany	Diesel car	1	2.4[a]	Comparable to FTP-73 test cycle; in tailpipe
Hagenmaier, 1994	Germany	Diesel bus	1	not detected (< 1 pg/L)	On-the-road testing
Oehme et al., 1991 (tunnel study)	Norway	—	(b)	520[c] 38[c] avg = 280 9,500[c] 720[c] avg = 5,100	Cars moving uphill (3.5% incline) at 60 km/hr Cars moving downhill (3.5% decline) at 70 km/hr Trucks moving uphill (3.5% incline) at 60 km/hr Trucks moving downhill (3.5% decline) at 70 km/hr
Schwind et al., 1991 Hutzinger et al., 1992	Germany	Diesel car Diesel truck	1 1	5.0–13[a] 13–15[a]	Various test conditions (i.e., loads and speeds) Various test conditions (i.e., loads and speeds)
Gertler et al., 1996 (tunnel study)	United States	Diesel trucks	(d)	mean = 172	Mean of seven 12-hour samples
Gullett and Ryan, 1997	United States	Diesel truck	1	mean - 29.0	Mean of five sample routes

[a]Results reported were in units of pg TEQ/liter of fuel. For purposes of this table, the fuel economy factor used by Marklund et al. (1990), 10 km/L or 24 miles/gal, was used to convert the emission rates into units of pg TEQ/km driven for the cars. For the diesel-fueled truck, the fuel economy factor reported in CARB (1987a) for a 1984 heavy-duty diesel truck, 5.5 km/L (or 13.2 miles/gal), was used.

[b]Tests were conducted over portions of 4 days, with traffic rates of 8,000-14,000 vehicles/day. Heavy-duty vehicles (defined as vehicles over 7 meters in length) ranged from 4% to 15% of total.

[c]Emission factors are reported in units of pg Nordic TEQ/km driven; the values in units of I-TEQ/km are expected to be about 3% to 6% higher.

[d]Tests were conducted over 5 days with heavy-duty vehicle rates of 1,800-8,700 vehicles per 12-hour sampling event. Heavy-duty vehicles accounted for 21% to 28% of all vehicles.

In 1994, Hagenmaier reported CDD/CDF emissions from a diesel-fueled bus and found no detectable levels in the exhaust (at a detection limit of 1 pg/L of fuel consumed) for individual congeners. In 1987, the California Air Resources Board (CARB) produced a draft report of a HD engine tested under steady-state conditions indicating a TEQ emission factor of 7,290 pg/L of fuel burned (or 1,300 pg/km driven) if nondetected values are treated as one-half the detection limit. Treating nondetected values as zeros yields a TEQ concentration equivalent to 3,720 pg/L of fuel burned (or 663 pg/km driven) (Lew, 1996). Norbeck et al. (1998c) reported emission factors for dioxin and furans from a Cummins L10 HD diesel engine running on pre-1993 fuel of 0.61 pg/L and 0.41 pg/L for the same engine running on reformulated fuel. The low emission factors reported by Norbeck et al. (1998c) were attributed to losses of dioxin and furan compounds to the dilution tunnel walls.

EPA has directly sampled the exhaust from a HD diesel truck for the presence and occurrence of CDDs/CDFs (Gullett and Ryan, 1997). The average of five tests (on highway and city street driving conditions) was 29.0 pg TEQ/km with a standard deviation of 38.3 pg TEQ/km; this standard deviation reflects the 30-fold variation in the two city driving route tests.

Tunnel studies are an indirect means of measuring contaminants that may be associated with emissions from cars and trucks. In these studies, scrapings of carbonaceous matter from the interior walls of the transportation tunnel or the tunnel air are sampled and analyzed for the target contaminants. Several European studies and one recent U.S. study evaluated CDD/CDF emissions from vehicles by measuring the presence of CDDs/CDFs in tunnel air. This approach has the advantage of allowing random sampling of large numbers of vehicles passing through the tunnel, including a range of ages and maintenance levels. The disadvantage of this approach is that it relies on indirect measurements (rather than tailpipe measurements), which may introduce unknown uncertainties into the interpretation of results.

Oehme et al. (1991) reported the emission rates associated with HD diesel trucks as follows: uphill = 9,500 pg TEQ/km; downhill = 720 pg TEQ/km; mean = 5,100 pg TEQ/km. The mean values are the averages of the emission rates corresponding to the two operating modes: vehicles moving uphill on a 3.5% incline at an average speed of 37 mi/hr and vehicles moving downhill on a 3.5% decline at an average speed of 42 mi/hr.

Wevers et al. (1992) measured the CDD/CDF content of air samples taken during the winter of 1991 inside a tunnel in Antwerp, Belgium. The results obtained indicated that the tunnel air had a dioxin TEQ concentration about twice as high as the outside air (80.3 fg TEQ/m^3 for tunnel air vs. 35 fg TEQ/m^3 for outside air for one set of measurements and 100 fg TEQ/m^3 for tunnel air vs. 58 fg TEQ/m^3 for outside air for a second set of measurements).

During October/November 1995, Gertler et al. (1996, 1998) measured CDDs/CDFs in the Fort McHenry Tunnel in Baltimore, Maryland. The emission factors calculated, assuming that all CDDs/CDFs emitted in the tunnel were from HD vehicles, are presented in Table 2-12. The average TEQ emission factor was reported to be 172 pg TEQ/km. The major uncertainties in the study were tunnel air volume measurement, sampler flow volume control, and analytical measurement of CDDs/CDFs (Gertler et al., 1996, 1998).

The relative strengths of the Gertler et al. (1996; 1998) study include: (1) The study is a recent study conducted in the United States and thus reflects current U.S. fuels and technology; (2) virtually no vehicle using the tunnel used leaded gasoline, which is associated with past emissions of CDDs and CDFs from gasoline-powered vehicles; (3) the tunnel walls and streets were cleaned 1 week before the start of sampling, and in addition, the study analyzed road dust and determined that resuspended road dust contributed only about 4% of the estimated emission factors; and (4) HD vehicles made up, on average 25.7% of vehicles using the tunnel.

Using the emissions factor from the Gertler et al. studies, the EPA Office of Research and Development's dioxin source emission inventory estimates that 33.5 g of dioxin TEQ (total 2,3,7,8-TCDD equivalents) were emitted from HD U.S. trucks in 1995. This is a very small contribution (1.2%) compared with the national annual emission of 2,800 g CDDs/CDFs.

2.2.8. Physical and Chemical Composition of Diesel Exhaust Particles

DPM is defined by the measurement procedures summarized in Title 40 CFR, Part 86, subpart N. This definition and the basic characteristics of DPM have been summarized in Section 2.2.2. As described there, DE particles are aggregates of primary spherical particles that consist of solid carbonaceous material and ash and contain adsorbed organic and sulfur compounds (sulfate) combined with other condensed material. The organic material includes unburned fuel, engine lubrication oil, and low levels of partial combustion and pyrolysis products.

The organic material is absorbed to the EC core and is also found in heterogeneously nucleated aerosol. This fraction of the DPM is frequently quantified as the SOF (i.e., the fraction that can be extracted by an organic solvent). Because of the toxicological significance of the organic components associated with DPM, it is important to understand, to the extent possible, the historical changes in the composition of SOF and potential changes in the fraction of SOF associated with DPM.

Various researchers have attempted to apportion the SOF to unburned oil and fuel sources by thermogravimetric analysis and have found that the results vary with test cycle and engine (Abbass et al., 1991; Wachter, 1990). Kittelson (1998) estimates that a typical composition of

Table 2-12. Baltimore Harbor Tunnel Study: estimated CDD/CDF emission factors for HD vehicles

Congener/congener group	Run-specific emission factors							Mean emission factors (pg/km)
	Run no. 2 (pg/km)	Run no. 3 (pg/km)	Run no. 5 (pg/km)	Run no. 6 (pg/km)	Run no. 8 (pg/km)	Run no. 9 (pg/km)	Run no. 10 (pg/km)	
2,3,7,8-TCDD	24.5	61.6	0.0	21.2	37.8	40.1	54.9	34.3
1,2,3,7,8-PeCDD	40.2	20.6	15.4	5.6	38.4	0.0	83.0	29.0
1,2,3,4,7,8-HxCDD	18.2	25.2	46.5	8.3	64.5	0.0	123	40.8
1,2,3,6,7,8-HxCDD	37.5	28.2	64.3	19.6	153	71.1	186	80.0
1,2,3,7,8,9-HxCDD	53.6	56.5	91.6	48.4	280	126	370	147
1,2,3,4,6,7,8-HpCDD	0	401	729	111	2,438	963	2,080	960
OCDD	0	3,361	3,382	1,120	9,730	5,829	7,620	4,435
2,3,7,8-TCDF	0	94.3	67.6	152.8	155.8	73.4	61.7	86.5
1,2,3,7,8-PeCDF	0	48.9	72.6	23.6	53.3	0.0	43.3	34.5
2,3,4,7,8-PeCDF	24.5	75.7	131	46.6	85.0	63.9	108	76.4
1,2,3,4,7,8-HxCDF	15.4	139	204	93.8	124	164	166	129
1,2,3,6,7,8-HxCDF	0.3	75.1	73.7	51.0	61.3	54.4	95.5	58.8
1,2,3,7,8,9-HxCDF	27.7	14.8	75.6	0	20.6	37.2	63.5	34.2
2,3,4,6,7,8-HxCDF	15.2	82.5	152	55.7	93.0	86.8	111	85.2
1,2,3,4,6,7,8-HpCDF	12.6	280	445	154	313	354	308	267
1,2,3,4,7,8,9-HpCDF	0	58.5	60.8	31.1	25.0	2.3	34.9	30.4
OCDF	0	239	401	175	416	534	370	305
Total 2,3,7,8-CDD	174	3,954	4,328	1,335	12,743	7,028	10,515	5,725
Total 2,3,7,8-CDF	95.7	1,108	1,684	784	1,347	1,371	1,362	1,107
Total TEQ	73.8	175	170	96	235	153	303	172
Total TCDD	245	0	140	165	311	109	97.3	152
Total PeCDD	110	21.9	83.3	35.6	174	0.0	165	84.2
Total HxCDD	677	0	753	54.5	2,009	1,666	2,971	1,162
Total HpCDD	0	802	1,498	142	5,696	1,933	4,377	2,064
Total OCDD	0	3361	3,382	1,120	9,730	5,829	7,620	4,435
Total TCDF	0	901	1,314	656	2,416	1,007	687	997
Total PeCDF	124	119	1,152	78.4	1,055	282	626	491
Total HxCDF	136	319	852	67.6	444	719	619	451
Total HpCDF	0	223	814	144	513	354	637	384
Total OCDF	0	239	401	175	416	534	370	305
Total CDD/CDF	1,291	5,987	10,390	2,638	22,766	12,434	18,168	10,525
HD vehicles as % of total vehicles	21.2	22.0	22.6	34.0	28.8	24.2	27.4	25.7

Notes:
(1) Listed values are based on the difference between the calculated chemical mass entering the tunnel and the mass exiting the tunnel.
(2) All calculated negative emission factors were set equal to zero.
(3) All CDD/CDF emissions were assumed to result from heavy-duty diesel-fueled vehicles. The table presents in the last row the percent of total traffic that was heavy-duty vehicles.

Source: Gertler et al., 1996.

SOF is about one-fourth unburned fuel and three-fourths unburned engine lubrication oil. Partial combustion and pyrolysis products represented a very small fraction of the SOF on a mass basis (Kittelson, 1998), which is confirmed in numerous other studies.

A number of investigators have tried to separate the organic fraction into various classes of compounds. Schuetzle (1983) analyzed the dichloromethane extract of DPM from a LD diesel engine and found that approximately 57% of the extracted organic mass is contained in the nonpolar fraction. About 90% of this fraction consists of aliphatic HCs from approximately C_{14} to about C_{40} (Black and High, 1979; Pierson and Brachaczek, 1983). PAHs and alkyl-substituted PAHs account for the remainder of the nonpolar mass. The moderately polar fraction (~9% w/w of extract) consists mainly of oxygenated PAH species, substituted benzaldehydes, and nitrated PAH. The polar fraction (~32% w/w of extract) is composed mainly of n-alkanoic acids, carboxylic and dicarboxylic acids of PAH, hydroxy-PAH, hydroxynitro-PAH, and nitrated N-containing heterocyclic compounds (Schuetzle, 1983; Schuetzle et al., 1985).

Rogge et al. (1993) reported the composition of the extractable portion of fine DPM emitted from two HD diesel trucks (1987 model year). The DPM filters were extracted twice with hexane, then three times with a benzene/2-propanol mixture. The extract was analyzed by capillary gas chromatography/mass spectrometry (GC/MS) before and after derivatization to convert organic acids and other compounds having an active H atom to their methoxylated analogues. Unidentified organic compounds made up 90% of the eluted organic mass and were shown to be mainly branched and cyclic HCs. From the mass fraction that was resolved as discrete peaks by GC/MS, ~42% were identified as specific organic compounds. Most of the identified resolved organic mass (~60%) consisted of n-alkanes, followed by n-alkanoic acids (~20%). PAH accounted for ~3.5% and oxy-PAH (ketones and quinones) for another ~3.3%.

The distribution of the emissions between the gaseous and particulate phases is determined by the vapor pressure of the individual species, by the amount and type of the DPM present (adsorption surface available), and by the temperature (Ligocki and Pankow, 1989). Two-ring and smaller compounds (e.g., naphthalene) exist primarily in the gas phase, whereas five-ring and larger compounds (e.g., benzo[a]pyrene) are almost completely adsorbed on the particles. Three- and four-ring compounds are distributed between the two phases. The vapor pressures of these intermediate PAHs can be significantly reduced by their adsorption on various surfaces. Because of this phenomenon, the amount and type of DPM present play an important role, together with temperature, in the vapor-particle partitioning of semivolatile organic compounds (SOCs).

The measurements of gas/particulate phase distribution are often accomplished by using a high-volume filter followed by an adsorbent such as polyurethane foam (PUF), Tenax, or XAD-2 (Cautreels and Van Cauwenberghe, 1978; Thrane and Mikalsen, 1981; Yamasaki et al., 1982).

The pressure drop behind a high-volume filter or cascade impactor can contribute to volatilization of the three- to five-ring PAHs from the PM proportional to their vapor pressures. The magnitude of this blow-off artifact depends on a number of factors, including sampling temperature and the volume of air sampled (Van Vaeck et al., 1984; Coutant et al., 1988). Despite these problems from volatilization, measurements with the high-volume filters followed by a solid adsorbent have provided most estimates of vapor-particle partitioning of SOCs in ambient air, as well as insights into the factors influencing SOC adsorption onto aerosols. Significant fractions of phenanthrene, anthracene, and their alkylated derivatives, along with fluoranthene and pyrene, exist in the gas phase. PAHs with molecular weight greater than that of pyrene are typically not observed on PUF samples. During the collection of particulate organic compounds, adsorption of semivolatile PAHs can also occur, as well as chemical transformation of the semivolatile compounds (Schauer et al., 1999; Cantrell et al., 1988; Feilberg et al., 1999; Cautreels and Van Cauwenberghe, 1978).

Most of the sulfur in the fuel is oxidized to SO_2, but a small amount (1% to 4%) is oxidized to sulfuric acid in the exhaust. Sulfate emissions are roughly proportional to sulfur in the fuel. Since the reduction of the allowable sulfur content in diesel fuel in 1993, sulfate emissions have declined from roughly 10% of the DPM mass to around 1%. Particulate emissions from numerous vehicles tested using low-sulfur fuel were found to have a sulfate content of only about 1% (Yanowitz et al., 1999). Water content is on the order of 1.3 times the amount of sulfate (Wall et al., 1987).

Metal compounds and other elements in the fuel and engine lubrication oil are exhausted as ash. Hare (1977) examined 1976 Caterpillar 3208 and Detroit Diesel Corporation 6V-71 engines and found the most abundant elements emitted from the 6V-71 engine were silicon, copper, calcium, zinc, and phosphorus. From the Caterpillar engine the most abundant elements were lead, chlorine, manganese, chromium, zinc, and calcium. Calcium, phosphorus, and zinc were present in the engine lubrication oil. The two-stroke 6V-71 engine had higher engine lubrication oil emissions and therefore emitted higher levels of zinc, calcium, and phosphorus than the Caterpillar 3208 engine. Other elements may have been products of engine wear or contaminants from the exhaust system. Springer (1979), in his study of 1977 Mack ETAY(B)673A and Caterpillar 3208 (EGR) engines, found that calcium was the most abundant metallic element in DPM samples, with levels ranging from 0.01 to 0.29 wt% of the DPM. Phosphorus and silica were the next most abundant elements reported, and sodium, iron, nickel, barium, chromium, and copper were either present at very low levels or were below detection limits. Roughly 1 wt% of the total DPM was represented by the analyzed metals. There was no consistent difference in metal emissions between the engines tested by Springer or between modes. Springer tested both engines on a 13-mode steady-state test. Dietzmann and co-workers

(1980) examined metal emission rates from four HD vehicles tested using the UDDS chassis cycle. For the single two-stroke engine tested (1977 Detroit Diesel Corporation 8V-71), calcium, phosphorus, and zinc emission rates were more than 10 times higher than metal levels observed for three 1979 model year four-stroke engines because of higher engine lubrication oil emissions. Metals accounted for 0.5% to 5% of total DPM, depending on engine model. In addition to these studies, other source profiles for HD diesel engine emissions report levels of chromium, manganese, mercury compounds, and nickel at levels above the detection limit (Cooper et al., 1987).

In more recent studies, Hildemann and co-workers (1991) examined metals in DPM from the same two 1987 trucks (four-stroke engines) studied by Rogge and co-workers (1993). Aluminum, silicon, potassium, and titanium were the only metals observed at statistically significant levels. Taken together these made up less than 0.75 wt% of total DPM mass. Lowenthal and co-workers (1994) also report metals emission rates for a composite sample of several diesel vehicles. The most abundant metals were zinc, iron, calcium, phosphorus, barium, and lanthanum. Together these represented less than 0.3% of total DPM mass, with an emissions rate of 3.3 mg/mi. Norbeck and co-workers (1998b) report engine transient test emissions of metals for a 1991 Cummins L10 engine. Silicon, iron, zinc, calcium, and phosphorus were observed and together made up about 0.5% of total DPM, with an emissions rate of 1.2 mg/bhp-hr.

2.2.8.1. *Organic and EC Content of Particles*

2.2.8.1.1. ***Measurement of the organic and EC fraction.*** Various methods have been used to quantify the organic fraction of DPM. The most common method has been Soxhlet extraction with an organic solvent. Following extraction, the solvent can be evaporated and the mass of extracted material (the SOF) determined, or alternatively the PM filter is weighed before and after extraction and the extracted material can be further analyzed to determine concentrations of individual organic compounds. Vacuum oven sublimation is used to measure a comparable quantity, the volatile organic fraction (VOF), which can be further speciated by GC with a flame ionization detector. Other methods have also been employed, including thermal methods, microwave extraction, sonication with an organic solvent, supercritical fluid extraction, thermogravimetric analysis, and thermal desorption GC. Abbass et al. (1991) compared various methods, including vacuum oven sublimation and 8 hours of Soxhlet extraction, with 4:1 benzene/methanol solvent for determination of SOF and found reasonably good agreement between the two methods. The VOF value was typically 10% higher; however, this variation was less than the coefficient of variation between measurements using the same method.

Levson (1988) reviewed literature regarding the extraction efficiency of various solvents and found contradictory results in many cases. He concluded that there is strong evidence that the most commonly used solvent, dichloromethane, leads to poor recoveries of higher molecular weight PAH. More recently, Lucas et al. (1999) reported the effect of varying dichloromethane/benzene ratios in the solvent (from 25% to 100% dichloromethane) and changing extraction times and found that the most effective extraction (i.e., the largest extracted mass) utilized a 70% dichloromethane/30% benzene mixture and extraction times several times longer than the commonly used 8-hour extraction period. Extractions of 70 hours using pure dichloromethane were found to result in about twice as much SOF as extractions of only 12 hours. Between 6 and 24 hours of extraction time (the typical range of extraction times used), the SOF recovered increased by about one-third. Using the most effective extraction conditions (Soxhlet, 70 hours, 70:30 dichloromethane:benzene ratio), Lucas et al. (1999) were able to extract more than 90% of the total particulate mass.

Other researchers have investigated the relative quantities of mass removed by sequential extraction by polar, moderately polar, and nonpolar solvents. The extracted nonpolar fraction (cyclohexane) ranged from 56% to 90% of the SOF, the moderately polar (dichloromethane) from 6% to 22%, and the polar fraction (acetonitrile) from 4% to 29% (Dietzmann et al., 1980). Water and sulfate are not soluble in cyclohexane or dichloromethane but are soluble in acetonitrile.

Although the reports on the extraction efficiencies for PAHs are in part contradictory, it appears that Soxhlet extraction and the binary solvent system composed of aromatic solvent and alcohol yield the best recovery of PAHs, as determined by C-B[*a*]P^{14} (benzo[a]pyrene) spiking experiments (Schuetzle and Perez, 1983). Limited recovery studies have shown that there is little degradation or loss of diesel POM on the HPLC column. More than 90% of the mass and 70% to 100% of the Ames *S. typhimurium*-active material injected onto the column has been recovered (Schuetzle et al., 1985).

Two thermal methods of organic and EC analysis include thermal optical reflectance (TOR) and thermal optical transmittance (TOT). The extractable portion of total carbon, although commonly used as a measure of organic compound content, is not equivalent to the OC fraction as measured by TOR or TOT. In addition, methodological differences between TOR and TOT also give rise to significant differences in the fraction of total carbon reported as organic and EC (Birch, 1998; Norris et al., 2000; Chow et al., 2000). Although total carbon reported using TOR or TOT provides results that are comparable (within 10%) (Norris et al., 2000) the EC content of samples analyzed by TOR is higher than that measured by TOT. This difference is primarily attributed to the temperature used to evolve carbon from the quartz filter onto which it is collected. In an analysis of urban $PM_{2.5}$ samples, Norris et al. (2000) found that

the EC content of samples analyzed by TOR was a factor of two higher than the EC content of the same samples analyzed by TOT. Experiments are ongoing to test specific source materials (including DPM) because some of the difference between methods appears to depend on the type of OC present on the sample.

The analytical technique used to measure OC and EC can have a significant effect on the quantity of reported. In the discussion that follows, every effort has been made to compare only studies using comparable methods and to state the analysis method employed.

2.2.8.1.2. ***Trends in SOF emissions.*** SOF emission values are highly dependent on the test cycle used. Various studies have shown that SOF generally increases at light engine loads and high engine speeds because these conditions lead to low exhaust temperatures, where fuel and oil are not as effectively oxidized (Scholl et al., 1982; Kittelson, 1998; Springer, 1979; Schuetzle and Perez, 1983; Martin, 1981b; Shi et al., 2000). These conditions are more typically observed in LD diesel vehicle applications, and thus DPM from these vehicles typically has a higher SOF component than HD diesel vehicles (Norbeck et al., 1998c). Acceleration modes normally cause increased emission of EC and an increase in total DPM emissions, whereas organic components are more dominant when motoring (Wachter, 1990). Additionally, cold-start test emissions of SOF have been shown to be approximately 25% higher than hot-start emissions (Wachter, 1990).

The quantity of sulfur in diesel fuel has been suggested to have a role in the quantity of SOF emitted (Sienicki et al., 1990; Tanaka et al., 1998). Sienicki et al. (1990) reported an approximate 25% increase in SOF when sulfur concentrations are increased from 0.08% to 0.33%. The cause is unclear but several explanations have been put forth, including increased absorption of organic compounds from the vapor phase onto the DPM by sulfates or sorbed sulfuric acid. Alternatively, it has been proposed that the measured SOF may include some sulfate, so that the apparent increase in organic material is due instead to sulfate. Other fuel effects include an increase in SOF emissions with a higher T90 (or T95) and with an increase in aromatic content (Barry et al., 1985; Sienicki et al., 1990; Tanaka et al., 1998; Rantanen et al., 1993).

Figures 2-31 and 2-32 show SOF emissions as a function of year for transient emissions tests on chassis and engines, respectively. Both figures suggest a significant decline in SOF emissions of approximately a factor of 5 since about 1980. The highest SOF emissions are for two-stroke engines built in the 1970s (up to approximately 1.2 g/mi). These data indicate that SOF emission factors for newer model year vehicles are lower than SOF emission factors for pre-1990 model year vehicles and that this decrease is similar to that observed for emissions of total DPM by model year. In a recent test of six pre-1976 HDDVs, Fritz et al. (2001) reported the

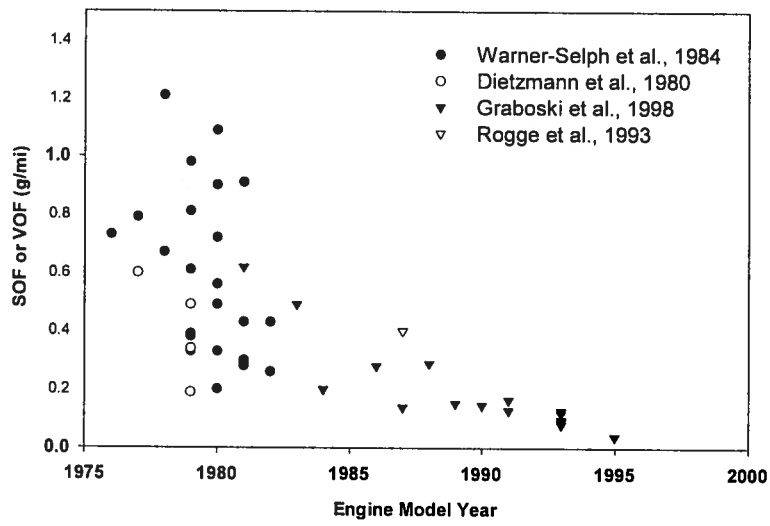

Figure 2-31. Trend in SOF emissions based on chassis dynamometer testing of HD diesel vehicles. Warner-Selph and co-workers: dichloromethane for 8 hours. Dietzman and co-workers: hexane followed by dichloromethane, extraction times not reported. Graboski and co-workers: VOF by vacuum sublimation at 225° C for 2.5 to 3 hours. Rogge and co-workers: cyclohexane followed by a benzene/2-propanol mixture that may extract significantly more organic matter.

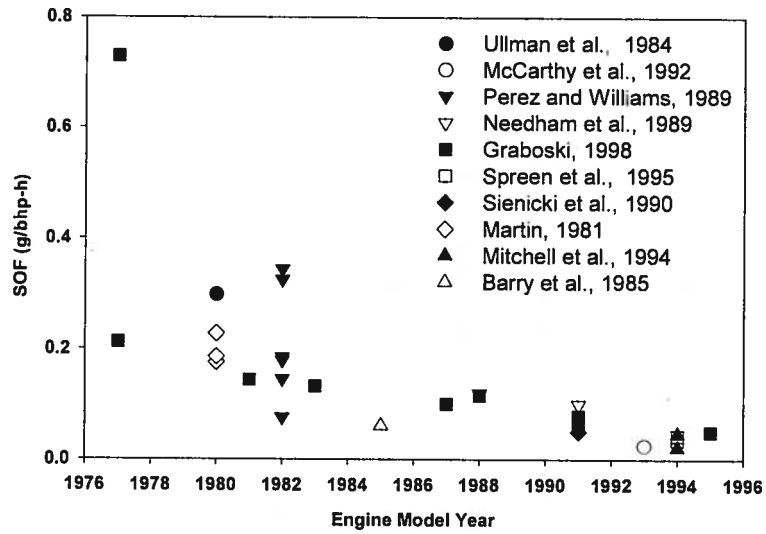

Figure 2-32. Trend in SOF emissions for transient engine dynamometer testing of HD diesel engines. Various extraction methods used; see Table 2-8.

volatile organic fraction (VOF) ranged from 0.4 g/mi to 4.5 g/mi. These data highlight the wide range in emission rates for of OC, as have been observed for total PM.

Steady-state testing conducted on late-1970s engines reported SOF at levels between 0.1 and 0.9 g/bhp-hr, whereas engines from the late 1980s and 1990s all emitted 0.03 g/bhp-hr or less (Table 2-8). Hori and Narusawa (1998) measured emissions from engines produced two decades apart, using identical analytical procedures, and found that SOF emission factors and the percentage contribution of SOF to DPM were lower in the new engine compared with the old engine, under all tested engine load and speed conditions and with different fuels. The authors reported that the decrease in SOF was due to lower emissions of both lubricating oil and unburned fuel. To meet the 1991 and 1994 U.S. emission standards, SOF emission rates would need to be reduced from the levels of the previous decade, although one may expect differences in SOF fractions of DPM with transient cycles used to determine compliance with emission standards verus steady-state conditions used in earlier test programs (Kawatani et al., 1993; Wachter, 1990). Finally, in the past three decades, for economic reasons engine manufacturers have made efforts to reduce oil consumption and increase the fuel efficiency of diesel engines, both of which would be expected to reduce SOF emissions. Problems in achieving SOF reductions from two-stroke engines were one factor leading to the phaseout of these engines for on-road use during the 1990s. No data are available prior to 1976 on SOF emissions from HD diesel vehicles. The engine technology changes that occurred between the mid-1950s and mid-1970s (high-pressure direct injection and turbocharging, primarily) might be expected to increase the efficiency of combustion and thereby reduce fuel-related SOF. SOF emissions levels in the mid- to late 1970s may be used as a conservative (low) estimate of SOF emissions during the preceding two decades.

The fraction of DPM attributed to SOF from chassis dynamometer studies also shows a decreasing trend over time, from SOFs that ranged up to approximately 50% in the 1980s to 20% SOF or less in the 1990s (Figure 2-33). The recent study by Fritz et al. (2001) reported the fraction of DPM attributed to VOF from 10% to 60% for HDDVs of model years 1951-1974. The wide range in SOF as a percent of DPM displayed in Figure 2-33 is suspected to result from factors such as engine deterioration and test cycle. The vehicle emissions data reported in Figure 2-33 do not overrepresent buses that are likely to emit DPM with a greater fraction of SOF than other vehicles. Figure 2-34 presents SOF as a fraction of DPM from the same engine dynamometer studies reported in Figure 2-32. These data do not reflect a downward trend in SOF as a fraction of DPM. Because similar extraction methods were used in reports of the SOF in both the chassis and engine dynamometer studies, this does not appear to be a source of the wide variability observed in the fraction of SOF reported. In some of the engine studies, improved air:fuel ratio control was tested in an attempt to lower carbonaceous DPM formation.

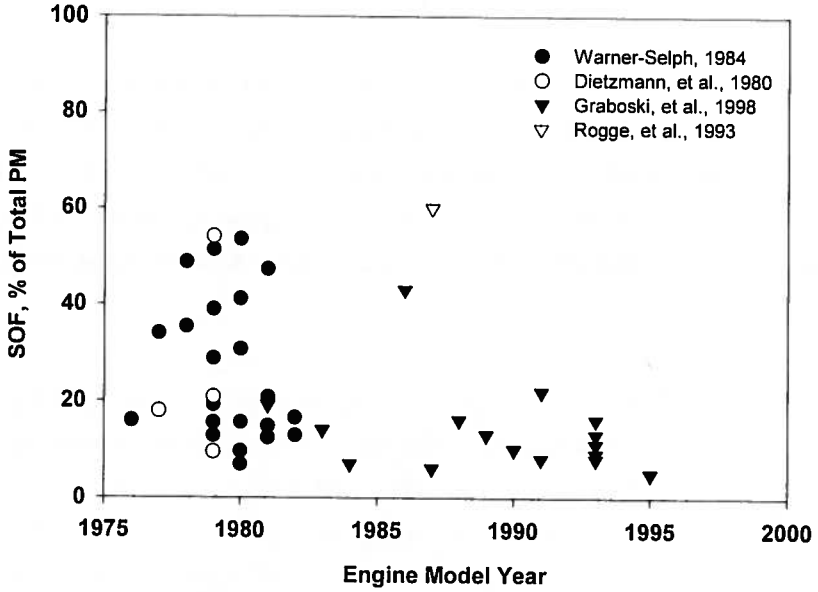

Figure 2-33. Trend in SOF emissions as a percent of total PM based on chassis dynamometer testing of HD diesel vehicles. Warner-Selph and co-workers: dichloromethane for 8 hours. Dietzman and co-workers: hexane followed by dichloromethane, extraction times not reported. Graboski and co-workers: VOF by vacuum sublimation at 225° C for 2.5 to 3 hours. Rogge and co-workers: cyclohexane followed by a benzene/2-propanol mixture that may extract significantly more organic matter.

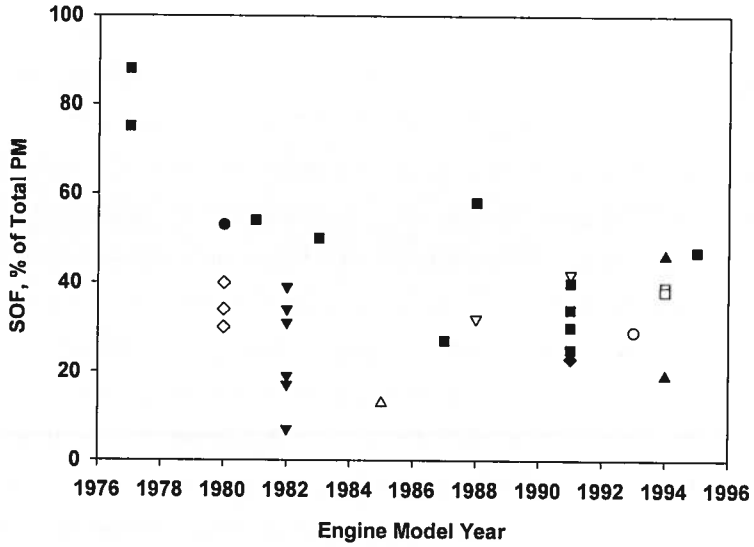

Figure 2-34. Trend in SOF emissions as a percentage of total PM from engine dynamometer testing. Data are from Table 2-8. (See Figure 2-32 for figure key.)

Therefore, substantial differences in SOF as a percent of total DPM could be the result of different engine technology or test conditions. The engine dynamometer results presented in Figures 2-32 and 2-34 are from new, or relatively new, engines, that is, engines with no deterioration, whereas the older engines tested on a chassis dynamometer may have experienced significant deterioration that would increase SOF emissions as a percent of DPM. One of the main differences suspected for the lack of a decreasing trend in the percent of SOF in the engine dynamometer studies is the test cycle used. The engine dynamometer tests typically include test modes, such as high speed and low load, or low-speed lugging modes, that produce much higher SOF relative to DPM than the driving cycles used on the chassis tests.

It appears that as a fraction of total DPM, SOF from new model year HD diesel vehicles is lower than that from older (pre-1990) HD diesel vehicles. However, as with total DPM emissions, a wide range in the fraction of SOF can be observed under different driving conditions and from vehicles with extensive engine wear. In general, DPM emissions have a lower fraction of organic matter compared to gasoline PM (Table 2-13). Recent testing of HD engines at the Desert Research Institute suggests that the OC fraction of DPM is approximately 19%, whereas earlier studies reported in the U.S. EPA SPECIATE database suggest a slightly higher organic fraction of DPM from HD diesel vehicles, ranging from 21% to 36%. The SPECIATE database represents older vehicles that, as discussed above, tend to have higher SOF emissions. The OC emissions from LD diesel vehicles recently reported by Norbeck et al. (1998c) and those reported by the U.S. EPA SPECIATE suggest that LD diesel vehicles emit DPM with a slightly higher organic content than that from HD diesel vehicles, ranging from 22% to 43%. Gasoline engine PM emissions have recently been analyzed at the Desert Research Institute by Fujita et al. (1998) and Watson et al. (1998) for hot stabilized, visibly smoking vehicles, and cold-starts. These data all indicate that LD gas vehicles emit PM with a higher fraction of organic matter than diesel vehicles, with the highest organic content measured from smoking and high-emitting gasoline vehicles (averaging 76% OC). One new finding from the data reported by Fujita et al. (1998) is the roughly equivalent emission of organic and EC from cold-start emissions of gasoline vehicles. Additional information is needed to characterize a range of OC for DPM from smoking and high-emitting diesel vehicles as well as cold-start HD diesel vehicles.

2.2.8.1.3. ***Trends in EC content.*** Because EC is a major component of the chemical source profile of DE, it is commonly used to determine the contribution of diesel vehicles to ambient PM samples (i.e., in source apportionment via chemical mass balance modeling). EC is not, strictly speaking, a regulated pollutant, and so EC emissions are not routinely measured in tests of diesel vehicles and engines. The scant data available on measured EC emissions from HD

Table 2-13. Organic and elemental carbon fractions of diesel and gasoline engine PM exhaust

Engine type	% OC	% Elemental carbon
HD diesel engines[a]	19 ± 8	75 ± 10
HD diesel engines (SPECIATE)[b]	21-36	52-54
LD diesel engines[c]	30 ± 9	61 ± 16
LD diesel engines (SPECIATE)[b]	22-43	51-64
Gasoline engines (hot stabilized)[a]	56 ± 11	25 ± 15
Gasoline engines (smoker and high emitter)[a,c]	76 ± 10	7 ± 6
Gasoline engines (cold start)[a]	46 ± 14	42 ± 14

[a] Fujita et al., 1998, and Watson et al., 1998.
[b] U.S. EPA SPECIATE database.
[c] Norbeck et al., 1998c.

diesel vehicles are plotted in Figure 2-35. Different analytical methods were employed for these studies, making the comparison of emission rates difficult. Results from the three studies, all performed on HD trucks, suggest a decline in EC emission rates by model year since the early 1980s. In a study conducted in 1992, four HD vehicles of unknown vintage were tested and a combined EC emission rate of 0.81 g/mi was reported, which is consistent with the 1990 timeframe in Figure 2-35 (Lowenthal et al., 1994). EC as a percentage of total DPM in these studies ranged from 30% to 90%, most likely as a result of different testing cycles and different engines and different analytical methods.

Figure 2-36 presents these data as EC fraction of total fine PM. The EC content of DPM varied widely in the 1980s from approximately 20% to 90%, whereas in more recent years, the data suggest a smaller range in the EC fraction, from approximately 50% to 90% (with one data point at 30%). Recent emission profiles for HD diesel vehicles suggest that 75% ± 10% of the DPM is attributable to EC, whereas approximately 25% of gasoline PM is composed of EC, except for PM emissions during gasoline vehicle cold-starts, which were found to have an EC content of approximately 42% (Table 2-13). These data also provide evidence that newer model year HD engines generally emit DPM that is more rich in EC than older HD engines.

2.2.8.2. *PAHs and Nitro-PAH Emissions*

PAHs, nitro-PAHs, and oxidized derivatives of these compounds have attracted considerable attention because of their known mutagenic and, in some cases, carcinogenic

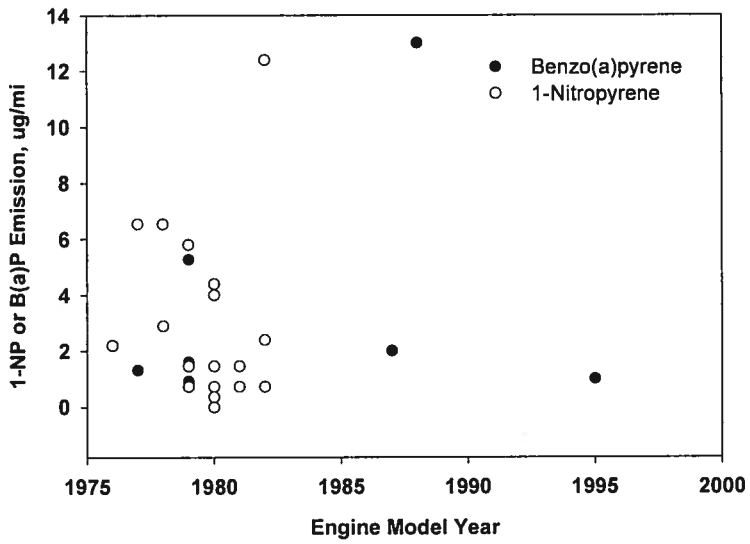

Figure 2-35. EC emission rates for diesel vehicles.

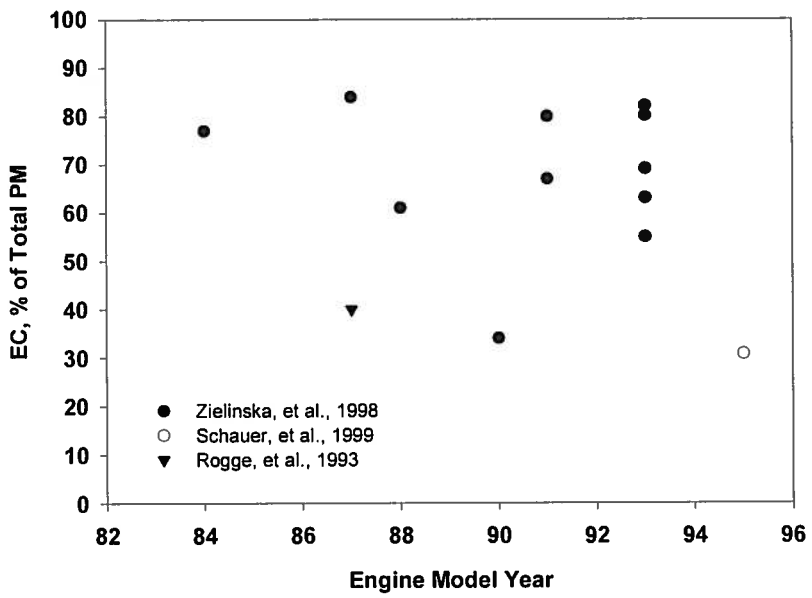

Figure 2-36. EC content as percent of fine PM for DPM samples obtained in chassis dynamometer studies.

character (National Research Council, 1982). In this section, PAH and nitro-PAH concentrations and emission rates and trends in emissions over time are presented.

2.2.8.2.1. ***PAHs identified in DE.*** At least 32 PAHs have been identified in the exhaust of LD diesel vehicles and HD diesel vehicles (Table 2-14) (Watson et al., 1998; Zielinska et al., 1998). Table 2-15 lists the PAHs and thioarenes identified in three LD diesel vehicles' DPM extracts, reported as ng/g of DPM (Tong et al., 1984). SOF fractions accounted for 11% to 15% of the total DPM mass for the LD diesel vehicles reported by Tong et al. (1984), which is lower than the LD diesel vehicles organic fraction reported by Norbeck et al. (1998c) in Table 2-13. Among the PAHs reported by Watson et al. (1998) and Zielinska et al. (1998), the higher molecular weight compounds (pyrene through coronene) that are expected to partition to the particle phase have emission rates from HD diesel vehicles ranging from below detection limits up to 0.071 mg/mi. HD diesel vehicle emission rates for the lower molecular weight PAHs ranged up to 2.96 mg/mi for dimethylnaphthalenes. In general, among the vehicles tested, PAH emission rates were higher for LD diesel vehicles compared with HD diesel vehicles. Table 2-16 presents emission rates of four representative particle-phase PAHs from HD diesel vehicles, LD diesel vehicles, and gasoline (with and without catalytic converter) engines. Emission rates for benzo[a]pyrene were higher in diesel emissions compared with gasoline emissions, except for the report by Rogge et al. (1993), who used extraction methods different from those in other studies (discussed above).

2.2.8.2.2. ***Nitro-PAHs identified in DE.*** Positive isomer identification for 16 nitro-PAHs has been made utilizing the GC retention times of authentic standards and low- and high-resolution mass spectra as identification criteria. These include 1-nitropyrene; 2-methyl-1-nitronaphthalene; 4-nitrobiphenyl; 2-nitrofluorene; 9-nitroanthracene; 9-methyl-10- nitroanthracene; 2-nitroanthracene; 2-nitrophenanthrene; 1-methyl-9-nitroanthracene; 1-methyl-3-nitropyrene; 1-methyl-6-nitropyrene; 1-methyl-8-nitropyrene; 1,3-, 1,6-, and 1,8-dinitropyrene; and 6-nitrobenzo[a]pyrene. In addition, two nitrated heterocyclic compounds were identified, 5- and 8-nitroquinoline. Forty-five additional nitro-PAHs were tentatively identified in this diesel particulate extract (Paputa-Peck et al., 1983). The concentration of nitro-PAHs adsorbed on diesel particles varies substantially from sample to sample. Usually 1-nitropyrene is the predominant component, and concentrations ranging from 7 to 165 μg/g of particles are reported (Levson, 1988).

Table 2-17 gives the approximate concentrations of several of the abundant nitro-PAHs quantified in the early 1980s LD diesel particulate extracts (with the exception of

Table 2-14. Emission rates of PAH (mg/mi) from LD and HD diesel vehicles

PAH	Light-duty diesel	Heavy-duty diesel
Naphthalene	5.554 ± 0.282	2.451 ± 0.154
2-Menaphthalene	3.068 ± 0.185	2.234 ± 0.152
1-Menaphthalene	2.313 ± 0.134	1.582 ± 0.103
Dimethylnaphthalenes	5.065 ± 0.333	2.962 ± 0.488
Biphenyl	0.743 ± 0.041	0.505 ± 0.037
2-Methylbiphenyl	0.203 ± 0.015	0.049 ± 0.024
3-Methylbiphenyl	1.048 ± 0.063	0.401 ± 0.036
4-Methylbiphenyl	0.447 ± 0.028	0.144 ± 0.021
Trimethylnaphthalenes	6.622 ± 0.563	1.940 ± 0.221
Acenaphthylene	0.422 ± 0.024	0.059 ± 0.087
Acenaphthene	0.096 ± 0.008	0.030 ± 0.040
Phenanthrene	1.411 ± 0.072	0.084 ± 0.011
Fluorene	0.442 ± 0.038	0.066 ± 0.022
Methylfluorenes	1.021 ± 0.091	0.071 ± 0.055
Methylphenanthrenes	1.115 ± 0.064	0.124 ± 0.069
Dimethylphenanthrenes	0.637 ± 0.047	0.090 ± 0.096
Anthracene	0.246 ± 0.025	0.052 ± 0.016
9-Methylanthracene	0.013 ± 0.002	0.434 ± 0.082
Fluoranthene	0.213 ± 0.014	0.044 ± 0.026
Pyrene	0.245 ± 0.020	0.071 ± 0.017
Methyl(pyrenes/fluoranthenes)	0.548 ± 0.045	0.022 ± 0.082
Benzonaphthothiophene	0.002 ± 0.002	0.001 ± 0.027
Benz[a]anthracene	0.020 ± 0.005	0.066 ± 0.046
Chrysene	0.029 ± 0.005	0.009 ± 0.021
Benz[b+j+k]fluoranthene	0.056 ± 0.005	0.009 ± 0.022
Benzo[e]pyrene	0.019 ± 0.003	0.010 ± 0.014
Benzo[a]pyrene	0.013 ± 0.004	0.013 ± 0.044
Indeno[1,2,3-cd]pyrene	0.010 ± 0.003	0.001 ± 0.037
Dibenzo[a]anthracene	0.002 ± 0.003	0.000 ± 0.053
Benzo[b]chrysene	0.001 ± 0.002	0.001 ± 0.027
Benzo[ghi]perlyne	0.018 ± 0.004	0.013 ± 0.048
Coronene	0.006 ± 0.006	0.001 ± 0.095

Table 2-15. Polycyclic aromatic hydrocarbons identified in extracts of diesel particles from LD diesel engine exhaust

Compound	Molec. wt.	Concentration ng/mg extract
Acenaphthylene	152	30
Trimethylnaphthalene	170	140–200
Fluorene	166	100–168
Dimethylbiphenyl	182	30–91
C_4 -Naphthalene	184	285–351
Trimethylbiphenyl	196	50
Dibenzothiophene	184	129–246
Phenanthrene	178	2,186–4,883
Anthracene	178	155–356
Methyldibenzothiophene	198	520–772
Methylphenanthrene	192	2,028–2,768
Methylanthracene	192	517–1,522
Ethylphenanthrene	206	388–464
4H-Cyclopenta[*def*]phenanthrene	190	517–1,033
Ethyldibenzothiophene	212	151–179
2-Phenylnaphthalene	204	650–1,336
Dimethyl(phenanthrene/anthracene)	206	1,298–2,354
Fluoranthene	202	3,399–7,321
Benzo[*def*]dibenzothiophene	208	254–333
Benzacenaphthylene	202	791–1,643
Pyrene	202	3,532–8,002
Ethylmethyl (phenanthrene/anthracene)	220	590–717
Methyl(fluoranthene/pyrene)	216	1,548–2,412
Benzo[*a*]fluorene/benzo[*b*]fluorene	216	541–990
Benzo[*b*]naphtho[2,1-*d*]thiophene	234	30–53
Cyclopentapyrene	226	869–1,671
Benzo[*ghi*]fluoranthene	226	217–418
Benzonaphthothiophene	234	30–126
Benz[*a*]anthracene	228	463–1,076
Chrysene or triphenylene	228	657–1,529
1,2-Binapthyl	254	30–50
Methylbenz[*a*]anthracene	242	30–50
3-Methylchrysene	242	50–192
Phenyl(phenanthrene/anthracene)	254	210–559
Benzo[*j*]fluoranthene	252	492–1,367
Benzo[*b*]fluoranthene	252	421–1,090
Benzo[*k*]fluoranthene	252	91–289
Benzo[*e*]pyrene	252	487–946
Benzo[*a*]pyrene	252	208–558
Benzo[*ah*]anthracene	278	50–96
Indeno[1,2,3-[*cd*]pyrene	276	30–93
Benzo[*ghi*]perylene	276	443–1,050
Dibenzopyrene	302	136–254

Source: Tong et al., 1984.

Table 2-16. Emission rates of particle-bound PAH (μg/mi) from diesel and gasoline engines

PAH	Diesel engines					Gasoline engines			
	HDD			LDD		Noncatalyst		Catalyst	
	(a)	(b)	(c)	(a)	(d)	(c)	(e)	(a)	(c)
Pyrene	71	17.6	36.2	245	66	49.6	45	248	4.0
Fluoranthene	44	27.2	20.8	213	50	77.3	32	196	3.6
Benzo[a]pyrene	13	<0.1	2.1	13	NA	69.6	3.2	1.0	3.0
Benzo[e]pyrene	10	0.24	4.2	19	NA	73.3	4.8	1.0	3.6

(a) Watson et al., 1998 included gas-phase PAH .
(b) Westerholm et al., 1991.
(c) Rogge et al., 1993.
(d) Smith, 1989; 1986 Mercedes Benz.
(e) Alsberg et al., 1985.

3-nitrobenzanthrone, reported recently) in μg/g of particles. Concentrations for some of the nitro-PAHs identified range from 0.3 μg/g for 1,3-dinitropyrene to 8.6 μg/g for 2,7-dinitro-9-fluorenone and 75 μg/g for 1-nitropyrene. More recent nitro-PAH and PAH data for HD diesel engines are reported in units of g/bhp-hr or mass/volume of exhaust, making it impossible to directly compare them to the older data (Norbeck et al., 1998b; Bagley et al., 1996, 1998; Baumgard and Johnson, 1992; Opris et al., 1993; Hansen et al., 1994; Harvey et al., 1994; Kantola et al., 1992; Kreso et al., 1998; McClure et al., 1992; Pataky et al., 1994).

2.2.8.2.3. ***PAH and nitro-PAH emission changes over time.*** It is difficult to compare PAH emissions from different studies because not all investigators analyze for total PAH or the same suite of PAH compounds. Most studies have reported emissions of B[*a*]P or 1-nitropyrene (1-NP) because of their toxicological activity. The results of chassis dynamometer studies in which B[*a*]P or 1-NP were measured are displayed in Figure 2-37. Dietzmann and co-workers (1980) examined four vehicles equipped with late 1970s turbocharged DI engines. Emissions of B[*a*]P from particle extracts ranged from 1.5 to 9 μg/mi. No relationship between engine technology (one of the engines was two-stroke) and B[*a*]P emissions was observed. Rogge and co-workers (1993) reported total particle-associated PAH and B[*a*]P emissions from two 1987 model year trucks (averaged together, four-stroke and turbocharged engines). The total particle-phase PAH emission rate was 0.43 mg/mi and the B[*a*]P emission rate was 2.7 μg/mi. Particle-phase PAH in the Rogge et al. (1993) study accounted for approximately 0.5% of total DPM mass. Schauer and co-workers (1999) recently reported a particle-phase PAH emission rate of 1.9 mg/mi (accounting for about 0.7% of total DPM mass) for a 1995 MD turbocharged and aftercooled truck. B[*a*]P emissions were not reported, but emissions of individual species of similar

Table 2-17. Concentrations of nitro-PAHs identified in LD diesel particulate extracts

Nitro-PAH[a]	Concentration (µg/g of particles)
4-nitrobiphenyl	2.2
2-nitrofluorene	~1.8
2-nitroanthracene	4.4
9-nitroanthracene	1.2
9-nitrophenanthrene	1.0
3-nitrophenanthrene	4.1
2-methyl-l-nitroanthracene	8.3
1-nitrofluoranthene	1.8
7-nitrofluoranthene	0.7
3-nitrofluoranthene	4.4
8-nitrofluoranthene	0.8
1-nitropyrene	18.9; 75[b]
6-nitrobenzo[a]pyrene	2.5
1,3-dinitropyrene[b]	0.30
1,6-dinitropyrene[b]	0.40
1,8-dinitropyrene[b]	0.53
2,7-dinitrofluorene[c]	4.2; 6.0
2,7-dinitro-9-fluorenone[c]	8.6; 3.0
3-nitrobenzanthrone[d]	0.6 to 6.6

[a]From Campbell and Lee (1984) unless noted otherwise. Concentrations recalculated from µg/g of extract to µg/g of particles using a value of 44% for extractable material (w/w).
[b]From Paputa-Peck et al, 1983.
[c]From Schuetzle, 1983.
[d]From Enya et al., 1997 (Isuzu Model 6HEL 7127cc).

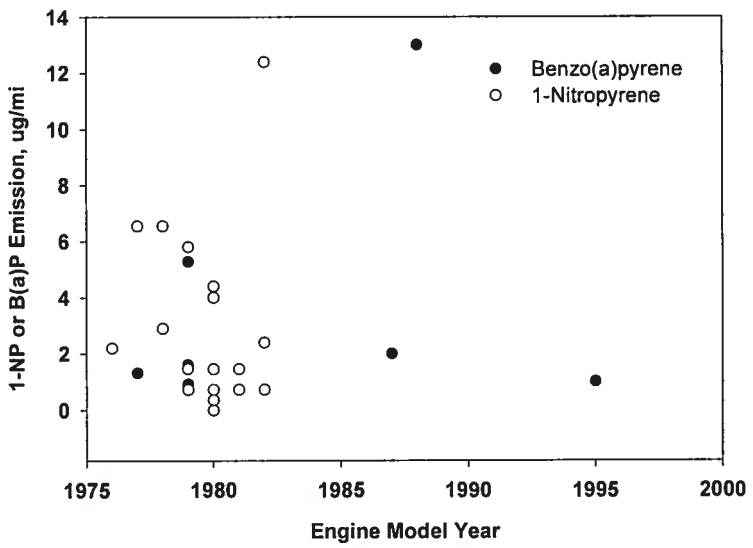

Figure 2-37. Diesel engine emissions of benzo[*a*]pyrene and 1-nitropyrene measured in chassis dynamometer studies.

Source: Schuetzle and Perez, 1983; Zielinska et al., 1988; Kado et al., 1996; Dietzmann et al., 1980; Warner-Selph and Dietzmann, 1984; Rogge et al., 1993; Schauer et al., 1999.

molecular weight were approximately 10 μg/mi. Schauer et al. (1999) also reported a gas-phase PAH emission rate of 6.9 mg/mi for the same truck. Measurements of particle- and gas-phase PAHs conducted for the Northern Front Range Air Quality Study in Colorado (Zielinska et al., 1998) showed an average B[*a*]P emission rate of 13 μg/mi for 15 vehicles ranging from 1983 to 1993 model years. The combined gas- and particle-phase PAH emission rate reported for the NFRAQS study was 13.5 mg/mi. B[*a*]P emissions from chassis studies are summarized in Figure 2-37. Zielinska (1999) reports a decreasing trend in particle-associated DE PAH from 11 measurements made on vehicles from model year 1984 to 1993 with a low correlation coefficient of 0.29.

B[*a*]P emissions reported from diesel engine dynamometer studies are summarized in Figure 2-38. Springer (1979) compared B[*a*]P emissions from naturally aspirated and turbocharged engines and found that naturally aspirated engines emitted about 1 μg B[*a*]P/bhp-hr, and DI and IDI engines emitted about 0.15 μg B[*a*]P/bhp-hr (Table 2-8). The difference between 1 and 0.15 μg/bhp-hr could not be attributed to specific technology changes. The majority of engine test data indicate that B[*a*]P emissions have generally ranged from approximately 1 to 4 μg/bhp-hr over the past 25 years.

Emissions reported for 1-NP from diesel engines tested by chassis dynamometer range from 0.1 to 12 μg/mi (Figure 2-37), and diesel engine dynamometer studies report 1-NP emission factors ranging from 1 to 4 μg/bhp-hr (Figure 2-38). Too few measurements are available to discern trends in the emission rates of these compounds.

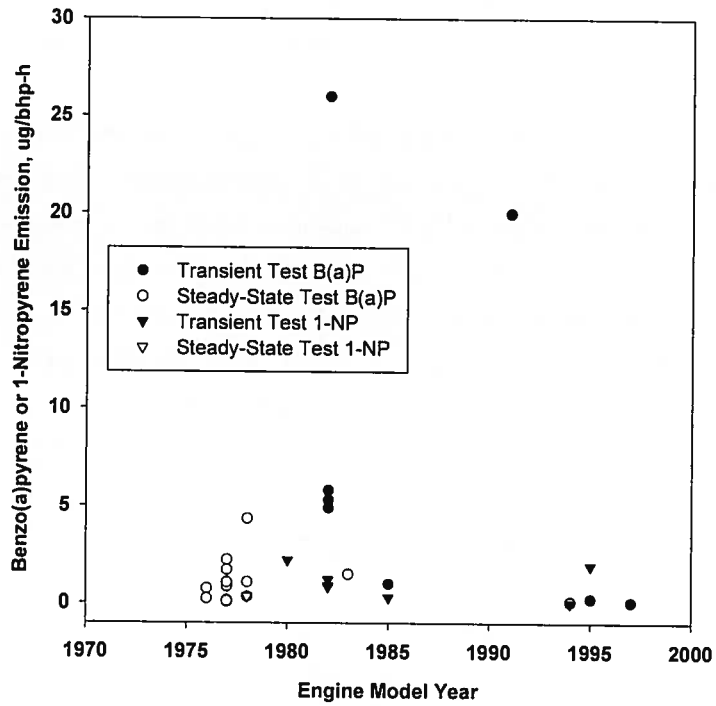

Figure 2-38. Diesel engine dynamometer measurements of benzo[*a*]pyrene and 1-nitropyrene emissions from HD diesel engines.

Source: Data are from Table 2-8.

As discussed in Section 2.2.4, Williams et al. (1987) and Andrews et al. (1998) of the University of Leeds have demonstrated that the solvent-extractable PAH from diesel particulate originates primarily in the fuel. PAH molecules are relatively refractory, so a significant fraction survives the combustion process and is exhausted as DPM. These studies have been confirmed by other research groups (Crebelli et al., 1995; Tancell et al., 1995) that included the use of isotopic labeling of fuel PAH. Additionally, engine oil was found to be a reservoir for PAH that originates in the fuel. Pyrosynthesis of PAH occurs during very high temperature conditions in a diesel engine, and under these conditions many of the DPM and other pyrolysis products are ultimately oxidized before exiting the cylinder. Thus, pyrogenic formation of PAH is thought to contribute a small fraction of the total PAH in diesel engine exhaust. As discussed above, fuel

PAH content is expected to have slowly increased over a 30-year period until 1993, after which PAH content of diesel fuel is expected to have remained constant. Increasing use of catalytic cracking over time may lead to increasing proportions of PAH in distillates; however, fuel standards limit the aromaticity of fuel to 35% (Section 2.2.4).

Recently, Norbeck et al. (1998a) reported on the effect of fuel aromatic content on PAH emissions. Three diesel fuels were used in a Cummins L10 engine: pre-1993 fuel containing 33% aromatic HC and 8% PAH; low aromatic fuel containing a maximum content of 10% aromatic HC and maximum of 1.4% PAH; and a reformulated fuel containing 20% to 25% aromatic HC and 2% to 5% PAH. The investigators found that emission rates for the low-molecular-weight PAHs (PAHs with three or fewer rings) were significantly lower when the engine was tested using the low aromatic fuel compared to when the engine was run on the pre-1993 or reformulated fuel (Table 2-18). Although emission rates reported for several higher molecular weight (particle-associated) PAHs were lower (ranging from 4% to 28% lower) for the low aromatic fuel compared with the other two fuels, the differences were not statistically significant except for coronene.

On the basis of these limited data it is difficult to draw a precise, quantitative conclusion regarding how PAH, B[*a*]P, or 1-NP emissions have changed over time and in response to fuel and engine changes. A decrease in the emissions of PAH from post-1990 model year vehicles and engines compared with pre-1990 vehicles and engines is suggested by the data; however, the data also suggest that differences in a vehicle's engine type and make, general engine condition, fuel composition, and test conditions can influence the emission levels of PAH.

2.2.8.3. *Particle Size*

Figure 2-39 shows a generic size distribution for diesel particulate based on mass and particle number. Approximately 50% to 90% of the number of particles in DE are in the ultrafine size range (nuclei-mode), with the majority of diesel particles ranging in size from 0.005-0.05 μm and the mode at about 0.02 μm. These aerosol particles are formed from exhaust constituents and consist of sulfuric acid droplets, ash particles, condensed organic material, and primary carbon spherules (Abdul-Khalek et al., 1998; Baumgard and Johnson, 1996). Although it accounts for the majority of particles, ultrafine DPM accounts for only 1% to 20% of the mass of DPM.

Approximately 80% to 95% of diesel particle mass is in the size range from 0.05 to 1.0 μm, with a mean particle diameter of about 0.2 μm. The EC core has a high specific surface area of approximately 30 to 50 m^2/g (Frey and Corn, 1967), and Pierson and Brachaczek (1976) report

that after the extraction of adsorbed organic material, the surface area of the diesel particle core

Table 2-18. Average emission rates for polycyclic aromatic hydrocarbons for different fuel types (units are µg/bhp-hr)

PAH	**Pre-1993 diesel fuel** Cetane No. >40 Aromatic 33% v. PAH 8% wt.	**Low aromatic diesel fuel** Cetane No. >48 Aromatic 10% v. PAH 1.4% wt.	**Reformulated diesel blend** Cetane No. 50-55 Aromatic 20%-25% v. PAH 2%-5% wt.
2,3,5-trimethyl naphthalene	283.68 ± 5.27	14.77 ± 2.42	56.21 ± 2.82
Phenanthrene	336.71 ± 9.08	160.92 ± 15.54	220.73 ± 52.68
Anthracene	38.89 ± 1.43	18.54 ± 2.13	26.16 ± 6.86
Methylphenanthrenes/anthracenes	331.32 ± 16.07	25.17 ± 1.41	111.98 ± 28.74
Fluoranthene	128.45 ± 7.60	132.36 ± 18.30	123.07 ± 26.21
Pyrene	193.03 ± 16.51	211.19 ± 37.35	206.82 ± 39.04
Benzo[c]phenanthrene	3.03 ± 0.24	1.74 ± 0.14	1.54 ± 0.26
Benzo[ghi]fluoranthene	24.84 ± 2.68	18.93 ± 2.14	16.94 ± 2.31
Cyclopenta[cd]pyrene	21.44 ± 4.11	26.15 ± 3.12	21.25 ± 3.46
Benz[a]anthracene	16.42 ± 1.67	10.57 ± 1.15	10.96 ± 2.42
Chrysene + triphenylene	17.36 ± 1.66	10.38 ± 0.54	12.20 ± 2.72
Benzo[b+j+k]fluoranthene	31.05 ± 4.17	23.17 ± 1.98	29.18 ± 7.93
Benzo[e]pyrene	16.71 ± 2.72	14.55 ± 1.34	18.99 ± 5.58
Benzo[a]pyrene	20.46 ± 3.27	16.48 ± 1.56	20.59 ± 5.75
Perylene	4.32 ± 0.88	3.71 ± 0.74	4.18 ± 1.16
Indeno[1,2,3-cd]fluoranthene	0.34 ± 0.07	0.21 ± 0.02	0.17 ± 0.00
Benzo[c]chrysene	0.29 ± 0.05	0.18 ± 0.05	0.14 ± 0.04
Dibenz[a,h]anthracene	0.93 ± 0.05	0.55 ± 0.10	0.67 ± 0.09
Indeno[1,2,3-cd]pyrene	19.45 ± 2.71	14.04 ± 1.99	22.16 ± 9.11
Dibenz[a,h+a,c]anthracene	1.54 ± 0.15	0.87 ± 0.12	1.48 ± 0.67
Benzo[b]chrysene	0.40 ± 0.01	0.15 ± 0.05	0.27 ± 0.05
Benzo[ghi]perylene	49.17 ± 9.63	39.81 ± 7.22	60.74 ± 26.60
Coronene	9.49 ± 3.13	4.93 ± 0.47	7.48 ± 1.59
Dibenzo[a,l]pyrene	2.84 ± 0.45	1.25 ± 0.15	2.31 ± 0.48
Dibenzo[a,e]pyrene	1.10 ± 0.29	0.61 ± 0.06	1.13 ± 0.15
Dibenzo[a,i]pyrene	0.91 ± 0.21	0.27 ± 0.09	0.71 ± 0.15
Dibenzo[a,h]pyrene	1.33 ± 0.25	0.75 ± 0.07	0.84 ± 0.20

Source: Norbeck et al., 1998a.

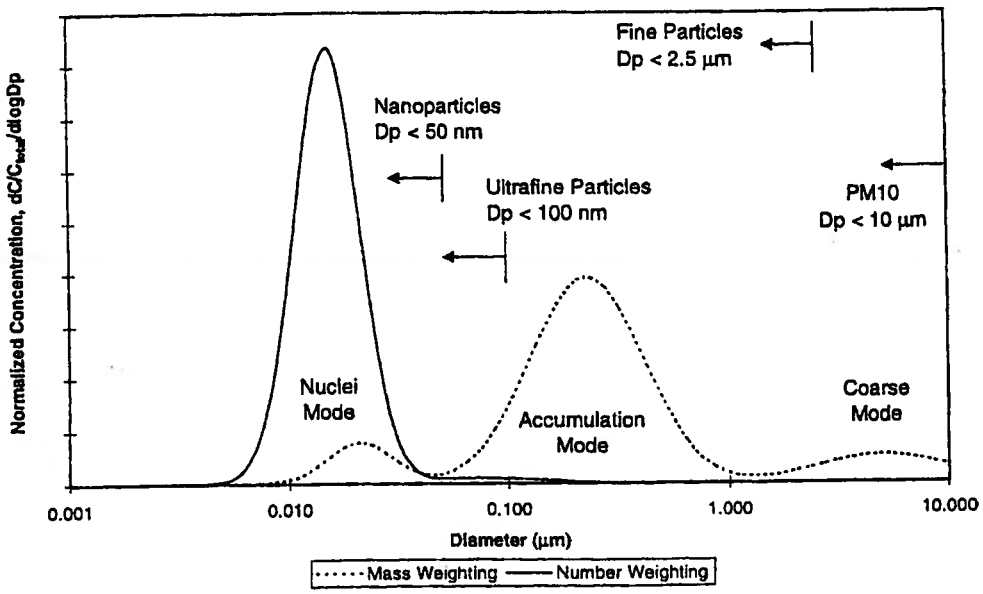

Figure 2-39. Particle size distribution in DE.

Source: Kittelson, 1998.

is approximately 90 m^2/g. Because these particles have a very large surface area per gram of mass, it makes them excellent carriers for adsorbed inorganic and organic compounds; potentially enhancing penetration of such compounds to lower portions of the respiratory tract upon inhalation. In addition, ultrafine aerosols can also reach the same areas of the lung.

Considerable caution is required when reporting particle size measurements from diesel engine exhaust because dilution conditions during the measurement process significantly affect size distributions (i.e., the size distribution is largely a function of how it was measured), and DPM size distributions obtained in dilution tunnel systems may not be relevant to size distributions resulting from the physical transformation of engine exhaust in the atmosphere. Measurements made on diluted DE typically show higher numbers of nuclei-mode particles than do measurements made on raw exhaust because of condensation to form nuclei-mode aerosol upon cooling of the exhaust. To understand particle size distributions emitted from diesel engines, investigators employ various dilution techniques, none of which have been standardized. Dilution ratio, sampling temperature, humidity, relative concentrations of carbon and volatile matter, and other sampling factors can therefore have a large impact on the number and makeup of nuclei-mode particles (Abdul-Khalek et al., 1999; Shi and Harrison, 1999; Lüders

et al., 1998; Brown et al., 2000). Dilution air temperature and humidity can have a large effect on particle number and size distribution, especially in the size range below 0.05 μm (also referred to as nanoparticles). Shi and Harrison (1999) report that a high dilution ratio and high relative humidity favor the production of ultrafine particles in diesel engine exhaust. Abdul-Khalek et al. (1998) report that an increase in the residence time of the exhaust during dilution resulted in an increase in the number of particles in exhaust. Khatri et al. (1978) report increased gas-phase HC condensation to DPM with a decrease in dilution air temperature. Some studies report no peak in diesel particles in the ultrafine size range (Kleeman et al., 2000). Kittelson (2000) reports that nanoparticle formation can be prevented by an oxidizing catalyst, which burns organic components of the exhaust, making them unavailable for nucleation or condensation to form an aerosol.

Experiments conducted in a dilution tunnel represent the atmospheric behavior of DE only under the conditions specific to the dilution tunnel and do not represent the full range of atmospheric conditions. Gertler (1999) demonstrated an increase in 0.02 μm particles as the fraction of diesel vehicles in the Tuscarora Mountain tunnel increased from 13% to 78%. These data suggest that the mode at 0.02 μm for ultrafine DPM from DE is evidenced under some real-world conditions.

Several groups have shown that decreasing sulfur content decreases the number of nuclei-mode particles measured in the exhaust, assuming temperature is low enough and residence time is long enough for nucleation and condensation of sulfate aerosol and water in the dilution tunnel (Baumgard and Johnson, 1992, 1996; Opris et al., 1993; Abdul-Khalek et al., 1999). The application of this finding to real-world conditions is difficult to predict, as the number of nuclei-mode particles formed from sulfate and water in the atmosphere will be determined by atmospheric conditions, not by dilution tunnel conditions. With all other factors held constant, it appears that reducing fuel sulfur content reduces the number of sulfate nuclei-mode particles. Thus, the reduction in on-road fuel sulfur content that occurred in 1993 reduced the amount of sulfur dioxide and sulfate available for particle formation. As discussed above, the contribution of sulfate to total DPM mass ranges from 1% to 5% and is therefore not a substantial portion of DPM mass.

More controversial is the suggestion that the DPM emission size distribution from newer technology engines (1991 and later) may be shifted to a much higher number concentration of nuclei-mode particles, independent of fuel sulfur content (Kreso et al., 1998; Abdul-Khalek et al., 1998; Baumgard and Johnson, 1996; Bagley et al., 1996). For example, Kreso and co-workers (1998) compared emissions from a 1995 model year engine with measurements made on 1991 and 1988 model year engines in earlier studies (Bagley et al., 1993, 1996). Nuclei-mode particles made up 40% to 60% of the number fraction of DPM emissions for the 1988 engine and

97%+ of the DPM from the 1991 and 1995 engines. Number concentrations were roughly two orders of magnitude higher for the newer engines. SOF made up 25% to 30% of DPM mass in the 1988 engine and 40% to 80% of DPM mass for the newer engines. Total DPM mass was significantly reduced for the newer engines. It was suggested that increased fuel injection pressure leads to improved fuel atomization and evaporation, in turn leading to smaller primary carbonaceous particles. Dilution conditions (relatively low temperature, low primary dilution ratio, long residence time of more than 3 seconds) strongly favor the formation of nucleation products. The 1991 and 1988 engines were tested with 100 ppm sulfur fuel whereas the 1995 engine was tested with 310 ppm sulfur fuel, which may confound the results to some extent.

The results of Kreso and co-workers (1998) and of Bagley and co-workers (1993, 1996) have been called into question because the high level of SOF emitted by the 1991 engine, particularly at high-load test modes, was inconsistent with SOF values measured for other engines using similar types of technology (Last et al., 1995; Ullman et al., 1995). Kittelson (1998) notes that there is far less carbonaceous DPM formed in newer engines compared with older engines. Accumulation-mode particles may have provided a high surface area for adsorption of sulfate and unburned organic compounds. In the absence of this surface area for adsorption, higher number concentrations of small particles are formed from nucleation of HCs and sulfuric acid.

A study performed at EPA by Pagan (1999) suggested that increased injection pressure can lead to the formation of more nuclei-mode particles in the exhaust. Particle size distributions were measured for diluted exhaust from an engine in which injection pressure could be varied from roughly 35 to 110 MPa (about 5,000–16,000 psi), comparable to pressures obtained with injection technology introduced in the 1980s. The dilution system and particle size measurement setup were identical in all experiments, removing some of the uncertainty in earlier studies that compared engine tests performed years apart. The results showed a clear increase in the number of nuclei-mode particles and a decrease in the number of accumulation-mode particles as injection pressure was increased. This shift did not occur, however, at high engine speeds and loads, but only at low to intermediate speeds and loads. The increase in number concentration of nuclei-mode particles was much lower than the two orders of magnitude increase reported by Kreso et al. (1998) or Bagley et al. (1996). One must use caution in applying the results of Pagan to modern high-injection pressure diesel engines with turbocharging/charge-air cooling because the engine used by Pagan was a naturally aspirated engine to which high-pressure common rail injection was applied. This would likely preclude this particular engine from meeting current on-highway PM or NO_x standards. Although some studies have suggested that increased injection pressure can lead to elevated ultrafine DPM number counts, Kittelson et al.

(1999) cite a German study that reported a decrease in ultrafine DPM number and mass with increasing injection pressure.

Although the majority of particles in DE from modern on-road diesel engines are in the ultrafine size range, evidence regarding a change in the size distribution over time is unclear. To understand the size distribution of DPM to which people are exposed will require measurements under conditions that more closely resemble ambient conditions.

2.3. ATMOSPHERIC TRANSFORMATION OF DIESEL EXHAUST

Primary diesel emissions are a complex mixture containing hundreds of organic and inorganic constituents in the gas and particle phases, the most abundant of which are listed in Table 2-19. The more reactive compounds with short atmospheric lifetimes will undergo rapid transformation in the presence of the appropriate reactants, whereas more stable pollutants can be transported over greater distances. A knowledge of the atmospheric transformations of gaseous and particulate components of diesel emissions and their fate is important in assessing environmental exposures and risks. This section describes some of the major atmospheric transformation processes for gas-phase and particle-phase DE, focusing on the primary and secondary organic compounds that are of significance for human health. For a more comprehensive summary of the atmospheric transport and transformation of diesel emissions, see Winer and Busby (1995).

2.3.1. Gas-Phase Diesel Exhaust

Gas-phase DE contains organic and inorganic compounds that undergo various chemical and physical transformations in the atmosphere, depending on the abundance of reactants and meteorological factors such as wind speed and direction, solar radiation, humidity, temperature, and precipitation. Gaseous DE will react primarily with the following species (Atkinson, 1988):

- Sunlight, during daylight hours
- Hydroxyl (OH) radical, during daylight hours
- Ozone (O_3), during daytime and nighttime
- Hydroperoxyl (HO_2) radical, typically during afternoon/evening hours
- Gaseous nitrate (NO_3) radicals or dinitrogen pentoxide (N_2O_5), during nighttime hours
- Gaseous nitric acid (HNO_3) and other species such as nitrous acid (HONO) and sulfuric acid (H_2SO_4).

Table 2-19. Classes of compounds in diesel exhaust

Particulate phase		Gas phase	
Heterocyclics, hydrocarbons (C_{14}-C_{35}), and PAHs and derivatives:		Heterocyclics, hydrocarbons (C_1-C_{10}), and derivatives:	
Acids	Cycloalkanes	Acids	Cycloalkanes, Cycloakenes
Alcohols	Esters	Aldehydes	Dicarbonyls
Alkanoic acids	Halogenated cmpds.	Alkanoic acids	Ethyne
n-Alkanes	Ketones	n-Alkanes	Halogenated cmpds.
Anhydrides	Nitrated cmpds.	n-Alkenes	Ketones
Aromatic acids	Sulfonates	Anhydrides	Nitrated cmpds.
	Quinones	Aromatic acids	Sulfonates
			Quinones
Elemental carbon		Acrolein	
Inorganic sulfates and nitrates		Ammonia	
Metals		Carbon dioxide, carbon monoxide	
Water		Benzene	
		1,3-Butadiene	
		Formaldehyde	
		Formic acid	
		Hydrogen cyanide, hydrogen sulfide	
		Methane, methanol	
		Nitric and nitrous acids	
		Nitrogen oxides, nitrous oxide	
		Sulfur dioxide	
		Toluene	
		Water	

Sources: Mauderly, 1992, which summarized the work of Lies et al., 1986; Schuetzle and Frazier, 1986; Carey, 1987; Zaebst et al., 1988, updated from recent work by Johnson, 1993; McDonald, 1997; Schauer et al., 1999.

The major loss process for most of the DE emission constituents is oxidation, which occurs primarily by daytime reaction with OH radical (Table 2-20). For some pollutants, photolysis, reaction with O_3, and reactions with NO_3 radicals during nighttime hours are also important removal processes. The atmospheric lifetimes do not take into consideration the potential chemical or biological importance of the products of these various reactions. For example, the reaction of gas-phase PAHs with NO_3 appears to be of minor significance as a PAH loss process, but it is more important as a route of formation of mutagenic nitro-PAHs. The reaction products for some of the major gaseous DE compounds are listed in Table 2-21 and are discussed briefly below.

2.3.1.1. *Organic Compounds*

The organic fraction of diesel is a complex mixture of compounds, very few of which have been characterized. The atmospheric chemistry of several organic constituents of DE (which are also produced by other combustion sources) has been studied. A few of these

Table 2-20. Calculated atmospheric lifetimes for gas-phase reactions of selected compounds present in automotive emissions with important reactive species

Compound	Atmospheric lifetime resulting from reaction with:				
	OH[a]	O_3[b]	NO_3[c]	HO_2[d]	hv[e]
NO_2	1.3 days	12 h	24 min	2 h	2 min
NO	2.5 days	1 min	1.2 min	20 min	—
HNO_3	110 days	—	—	—	—
SO_2	16 days	>200 years	>1.4×10[4] years	>600 years	—
NH_3	90 days	—	—	—	—
Propane	12 days	>7,000 years	—	—	—
n-Butane	5.6 days	>4,500 years	3.6 years	—	—
n-Octane	1.9 days	—	1.2 years	—	—
Ethylene	1.9 days	9 days	1.2 years	—	—
Propylene	7 h	1.5 days	6 days	—	—
Acetylene	19 days	6 years	>5.6 years	—	—
Formaldehyde	1.9 days	>2 - 104 years	84 days	23 days	4 h
Acetaldehyde	0.6 day	>7 years	20 days	—	60 h
Benzaldehyde	1.2 days	—	24 days	—	—
Acrolein	0.6 day	60 days	—	—	—
Formic acid	31 days	—	—	—	—
Benzene	11 days	600 years	>6.4 years	—	—
Toluene	2.5 days	300 years	3.6 years	—	—
m-Xylene	7 h	75 years	0.8 years	—	—
Phenol	6 h	—	8 min	—	—
Naphthalene[f]	6.8 h	>80 days	1.5 years	—	—
2-Methylnaphthalene[f]	2.8 h	>40 days	180 days		—
1-Nitronaphthalene[f]	2.3 days	>28 days	1 8 years		1.7 h
Acenaphthene[f]	1.5 h	>30 days	1.2 h	—	—
Acenaphthylene[f]	1.3 h	~43 min	6 min	—	—
Phenanthrene[f]	11.2 h	41 days	4.6 h	—	—
Anthracene[f]	8.6 h	—	—	—	—
Fluoranthene[f]	~2.9 h	—	~1 year	—	—
Pyrene[f]	~2.9 h	—	~ 120 days	—	—

[a] For 12-h average concentration of OH radical of 1.6×10^6 molecule/cm^3 (Prinn et al., 1992).
[b] For 24-h average O_3 concentration of 7×10^{11} molecule/cm^3.
[c] For 12-h average NO_3 concentration of 5×10^8 molecule/cm^3 (Atkinson, 1991).
[d] For 12-h average HO_2 concentration of 10^8 molecule/cm^3.
[e] For solar zenith angle of 0°.
[f] Lifetimes from Arey (1998), for 12-h concentration of OH radical of 1.9×10^6 molecule/cm^3.

Source: Winer and Busby, 1995, unless noted otherwise.

Table 2-21. Major components of gas-phase diesel engine emissions, their known atmospheric transformation products, and the biological impact of the reactants and products

Gas-phase emission component	Atmospheric reaction products	Biological impact
Carbon dioxide	—	Major contributor to global warming.
Carbon monoxide	—	Highly toxic to humans; blocks oxygen uptake.
Oxides of nitrogen	Nitric acid, ozone	Nitrogen dioxide is a respiratory tract irritant and major ozone precursor. Nitric acid contributes to acid rain.
Sulfur dioxide	Sulfuric acid	Respiratory tract irritation. Contributor to acid rain.
Hydrocarbons:		
Alkanes ($\leq C_{18}$)	Aldehydes, alkyl nitrates, ketones	Respiratory tract irritation. Reaction products are ozone precursors (in the presence of NO_x).
Alkenes ($\leq C_4$) (e.g., 1,3-butadiene)	Aldehydes, ketones	Respiratory tract irritation. Some alkenes are mutagenic and carcinogenic. Reaction products are ozone precursors (in the presence of NO_x).
Aldehydes:		
Formaldehyde	Carbon monoxide, hydroperoxyl radicals	Formaldehyde is a probable human carcinogen and an ozone precursor (in the presence of NO_x).
Higher aldehydes (e.g., acetaldehyde, acrolein)	Peroxyacyl nitrates	Respiratory tract and eye irritation; causes plant damage.
Monocyclic aromatic compounds (e.g., benzene, toluene)	Hydroxylated and hydroxylated-nitro derivatives[a]	Benzene is toxic and carcinogenic in humans. Some reaction products are mutagenic in bacteria (Ames assay).
PAHs ($\leq$4 rings) (e.g., phenanthrene, fluoranthene)[b]	Nitro-PAHs (4 rings)[c]	Some of these PAHs and nitro-PAHs are known mutagens and carcinogens.
Nitro-PAHs (2 and 3 rings) (e.g., nitronaphthalenes)	Quinones and hydroxylated-nitro derivatives	Some reaction products are mutagenic in bacteria (Ames assay).

[a]Some reaction products expected to partition into the particle phase.
[b]Nitro-PAHs with more than two rings will partition into the particle phase.
[c]PAHs containing four rings are usually present in both the vapor and particle phases.

Source: Health Effects Institute, 1995.

2.3.1.1. *Organic Compounds*

The organic fraction of diesel is a complex mixture of compounds, very few of which have been characterized. The atmospheric chemistry of several organic constituents of DE (which are also produced by other combustion sources) has been studied. A few of these reactions and their products are discussed below. For a complete summary of the atmospheric chemistry of organic combustion products, see Seinfeld and Pandis (1998).

Acetaldehyde forms peroxyacetyl nitrate (via formation of peroxyl radicals and reaction with NO_2), which has been shown to be a direct-acting mutagen toward *S. typhimurium* strain TA100 (Kleindienst et al., 1985) and is phytotoxic. Benzaldehyde, the simplest aromatic aldehyde, forms peroxybenzoyl nitrate or nitrophenols following reaction with oxides of nitrogen (Table 2-21).

For those PAHs present in the gas phase, reaction with the OH radical is the major removal route, leading to atmospheric lifetimes of a few hours in daylight. The gas-phase reaction of PAHs containing a cyclopenta-fused ring such as acenaphthene, acenaphthylene, and acephenanthrylene with the nitrate radical may be an important loss process during nighttime hours. Relatively few data are available concerning the products of these gas-phase reactions. It has been shown that in the presence of NO_x, the OH radical reactions with naphthalene, 1- and 2-methylnaphthalene, acenaphthylene, biphenyl, fluoranthene, pyrene, and acephenanthrylene lead to the formation of nitroarenes (Arey et al., 1986; Atkinson, 1986; Atkinson et al., 1990; Zielinska et al., 1988, 1989a; Arey, 1998). In addition, in a two-step process involving OH radical reaction and NO_2 addition, 2-nitrofluoranthene and 2-nitropyrene can be formed and eventually partition to the particle phase, as will other nitro-PAHs.

The addition of the NO_3 radical to the PAH aromatic ring leads to nitroarene formation (Sweetman et al., 1986; Atkinson et al., 1987, 1990; Zielinska et al., 1989a). The gas-phase reactions of NO_3 radical with naphthalene, 1- and 2-methylnaphthalene, acenaphthene, phenanthrene, anthracene, fluoranthene, and pyrene produce, in general, the same nitro-PAH isomers as the OH radical reaction, but with different yields (Arey et al., 1989; Sweetman et al., 1986; Atkinson et al., 1987, 1990; Zielinska et al., 1986, 1989a). For example, the same 2-nitrofluoranthene is produced from both OH radical and NO_3 gas-phase reactions, but the reaction with NO_3 produces a much higher yield. The production of several nitroarene compounds has been studied in environmental chambers (Arey et al., 1989; Zielinska et al., 1990; Atkinson and Arey, 1994; Arey, 1998; Feilberg et al., 1999), and generally the same nitro-PAH isomers formed from reaction with OH and NO_3 radicals are observed in ambient air samples. Secondary formation of nitroarenes through the gas-phase reactions of the 2-, 3-, and 4-ring PAHs is the major source for many of the nitroarenes observed in ambient air (Pitts et al., 1985a-c; Arey et al., 1986; Zielinska et al., 1988). Photolysis is the major removal pathway for

nitroarenes with lifetimes of approximately 2 hours (Feilberg et al., 1999; Nielsen and Ramdahl, 1986).

2.3.1.2. *Inorganic Compounds*

SO_2 and oxides of nitrogen (primarily NO) are emitted from diesel engines. SO_2 is readily oxidized by the OH radical in the atmosphere, followed by formation of the HO_2 radical and HSO_3, which rapidly reacts with water to form H_2SO_4 aerosols. Because SO_2 is soluble in water, it is scavenged by fog, cloud water, and raindrops. In aqueous systems, SO_2 is readily oxidized to sulfate by reaction with hydrogen peroxide (H_2O_2), O_3, or O_2 in the presence of a metal catalyst (Calvert and Stockwell, 1983). Sulfur emitted from diesel engines is predominantly (~98%) in the form of SO_2, a portion of which will form sulfate aerosols by the reaction described above. Nonroad equipment, which typically uses fuel containing 3,300 ppm sulfate, emits more SO_2 than on-road diesel engines, which use fuels currently containing an average of 340 ppm sulfur because of EPA regulations effective in 1993 decreasing diesel fuel sulfur levels. EPA estimates that mobile sources are responsible for about 7% of nationwide SO_2 emissions, with diesel engines contributing 74% of the mobile source total (the majority of the diesel SO_2 emissions originate from nonroad engines) (U.S. EPA, 1998b).

NO is also oxidized in the atmosphere to form NO_2 and particulate nitrate. The fraction of motor vehicle NO_x exhaust converted to particulate nitrate in a 24-hour period has been calculated using a box model to be approximately 3.5% nationwide, a portion of which can be attributed to DE (Gray and Kuklin, 1996). EPA estimates that in 1997, mobile sources were responsible for about 50% of nationwide NO_x emissions, with diesel engines being responsible for approximately one-half of the mobile source total (U.S. EPA, 1998b).

2.3.1.3. *Atmospheric Transport of Gas-Phase DE*

Gas-phase DE can be dry deposited, depending on the deposition surface, atmospheric stability, and the solubility and other chemical properties of the compound. Dry deposition of organic species is typically on the order of weeks to months, with dry deposition velocities of approximately 10^{-4} cm/sec (Winer and Busby, 1995). In contrast, inorganic species such as SO_2 and nitric acid have relatively fast deposition rates (0.1–2.5 cm/sec) and will remain in the atmosphere for shorter time periods compared with the organic exhaust components. Some gas-phase species will also be scavenged by aqueous aerosols and potentially deposited via precipitation. These processes can greatly reduce the atmospheric concentration of some vapor-phase species. Atmospheric lifetimes for several gas-phase components of DE are on the order of hours or days, during which time atmospheric turbulence and advection can disperse these pollutants widely.

2.3.2. Particle-Phase Diesel Exhaust

Particle-associated DE is composed of primarily carbonaceous material (organic and EC) with a very small fraction composed of inorganic compounds and metals. The OC fraction adsorbed on DPM is composed of high-molecular-weight compounds, such as PAHs, which are generally more resistant to atmospheric reactions than PAHs in the gas phase. The EC component of DE is inert to atmospheric degradation, whereas the PAH compounds are degraded by reaction with the following species:

- Sunlight, during daytime hours
- O_3, during daytime and nighttime
- NO_3 and N_2O_5, during nighttime hours
- OH and HO_2
- NO_2, during nighttime and daytime hours
- H_2O_2
- HNO_3 and other species such as HONO and H_2SO_4.

Because many of the PAH derivatives formed by reaction with some of the reactants listed above have been found to be highly mutagenic, a brief discussion of PAH photolysis, nitration, and oxidation follows. Some of the major degradation products from particulate DE and their biological impact are listed in Table 2-22.

2.3.2.1. *Particle-Associated PAH Photooxidation*

Laboratory studies of photolysis of PAHs adsorbed on 18 different fly ashes, carbon black, silica gel, and alumina (Behymer and Hites, 1985, 1988) and several coal stack ashes (Yokely et al., 1986; Dunstan et al., 1989) have shown that the extent of photodegradation of PAHs depends very much on the nature of the substrate to which they are adsorbed. The dominant factor in the stabilization of PAHs adsorbed on fly ash was the color of the fly ash, which is related to the amount of carbon black present. It appears that PAHs were stabilized if the carbon black content of the fly ash was greater than approximately 5%. On black substrates, half-lives of PAHs studied were on the order of several days (Behymer and Hites, 1988). The environmental chamber studies of Kamens et al. (1988) on the daytime decay of PAHs present on residential wood smoke particles and on gasoline internal combustion emission particles showed PAH half-lives of approximately 1 hour at moderate humidities and temperatures. At very low angle sunlight, very low water vapor concentration, or very low temperatures, PAH daytime half-lives increased to a period of days. The presence and

Table 2-22. Major components of particle-phase diesel engine emissions, their known atmospheric transformation products, and the biological impact of the reactants and products

Particle-phase emission component	Atmospheric reaction products	Biological impact
Elemental carbon	—	Nuclei adsorb organic compounds; size permits transport deep into the lungs (alveoli)
Inorganic sulfate and nitrate	—	Respiratory tract irritation
Hydrocarbons (C_{14}-C_{35})	Little information; possibly aldehydes, ketones, and alkyl nitrates	Unknown
PAHs (≥4 rings) (e.g., pyrene, benzo[a]pyrene)	Nitro-PAHs (≥4 rings)[a] Nitro-PAH lactones	Larger PAHs are major contributors of carcinogens in combustion emissions. Many nitro-PAHs are potent mutagens and carcinogens.
Nitro-PAHs (≥3 rings) (e.g., nitropyrenes)	Hydroxylated-nitro derivatives	Many nitro-PAHs are potent mutagens and carcinogens. Some reaction products are mutagenic in bacteria (Ames assay).

[a]Nitro-PAHs with more than two rings will partition into the particle phase.
Source: Health Effects Institute, 1995.

composition of an organic layer on the aerosol seems to influence the rate of PAH photolysis (Jang and McDow, 1995; McDow et al., 1994; Odum et al., 1994).

Because of limited understanding of the mechanisms of these complex heterogeneous reactions, it is currently impossible to draw any firm conclusion concerning the photostability of particle-bound PAHs in the atmosphere. Because DPM contains a relatively high quantity of EC, it is reasonable to speculate that PAHs adsorbed onto these particles might be relatively stable under standard atmospheric conditions, leading to an anticipated half-life of 1 or more days.

2.3.2.2. *Particle-Associated PAH Nitration*

Since 1978, when Pitts et al. (1978) first demonstrated that B[*a*]P deposited on glass-fiber filters exposed to air containing 0.25 ppm NO_2 with traces of HNO_3 formed nitro-B[*a*]P, numerous studies of the heterogeneous nitration reactions of PAHs adsorbed on a variety of substrates in different simulated atmospheres have been carried out (Finlayson-Pitts and Pitts, 1986). PAHs deposited on glass-fiber and Teflon-impregnated glass-fiber filters react with gaseous N_2O_5, yielding their nitro derivatives (Pitts et al., 1985b,c). The most abundant isomers formed were 1-NP from pyrene, 6-nitro-B[*a*]P from B[*a*]P, and 3-nitroperylene from perylene.

The formation of nitro-PAHs during sampling may be an important consideration for DPM collection because of the presence of NO_2 and HNO_3 (Feilberg et al., 1999). However, Schuetzle (1983) concluded that the artifact formation of 1-NP was less than 10% to 20% of the 1-NP present in the diesel particles if the sampling time was less than 23 min (one FTP cycle) and if the sampling temperature was not higher than 43 °C. The formation of nitroarenes during ambient high-volume sampling conditions has been reported to be minimal, at least for the most abundant nitropyrene and nitrofluoranthene isomers (Arey et al., 1988).

DPM contains a variety of nitroarenes, with 1-NP being the most abundant among identified nitro-PAHs. The concentration of 1-NP was measured in the extract of particulate samples collected at the Allegheny Mountain Tunnel on the Pennsylvania Turnpike as 2.1 ppm and ~5 ppm by mass of the extractable material from diesel and SI vehicle PM, respectively. These values are much lower than would be predicted on the basis of laboratory measurements for either diesel or SI engines (Gorse et al., 1983). Several nitroarene measurements have been conducted in airsheds heavily affected by motor vehicle emissions (Arey et al., 1987; Atkinson et al., 1988; Zielinska et al., 1989a,b; Ciccioli et al., 1989, 1993). Ambient PM samples were collected at three sites in the Los Angeles Basin during two summertime periods and one wintertime period. Concentrations of 1-NP ranged from 3 pg/m^3, to 60 pg/m^3, and 3-nitrofluoranthene was also present in DPM at concentrations ranging from not detectable to 70 pg/m^3.

2.3.2.3. *Particle-Associated PAH Ozonolysis*

Numerous laboratory studies have shown that PAHs deposited on combustion-generated fine particles and on model substrates undergo reaction with O_3 (Katz et al., 1979; Pitts et al., 1980, 1986; Van Vaeck and Van Cauwenberghe, 1984; Finlayson-Pitts and Pitts, 1986). The dark reaction toward O_3 of several PAHs deposited on model substrates has been shown to be relatively fast under simulated atmospheric conditions (Katz et al., 1979; Pitts et al., 1980, 1986). Half-lives on the order of 1 to several hours were reported for the more reactive PAHs, such as B[*a*]P, anthracene, and benz[a]anthracene (Katz et al., 1979).

The reaction of PAHs deposited on diesel particles with 1.5 ppm O_3 under high-volume sampling conditions has been shown to be relatively fast, and half-lives on the order of 0.5 to 1 hour have been reported for most PAHs studied (Van Vaeck and Van Cauwenberghe, 1984). The most reactive PAHs include B[*a*]P, perylene, benz[a]anthracene, cyclopenta[cd]pyrene, and benzo[ghi]perylene. The benzofluoranthene isomers are the least reactive of the PAHs studied, and benzo[e]perylene is less reactive than its isomer B[*a*]P. The implications of this study for the high-volume sampling ambient POM are important: reaction of PAHs with O_3 could possibly occur under high-volume sampling conditions during severe photochemical smog

episodes, when the ambient level of O_3 is high. However, the magnitude of this artifact is difficult to assess from available data.

2.3.2.4. *Atmospheric Transport of DE Particulate Matter*

Ultrafine particles emitted by diesel engines undergo nucleation, coagulation, and condensation to form fine particles. DPM can be removed from the atmosphere by dry and wet deposition. Particles of small diameter (<1 μm), such as DPM, are removed less efficiently than larger particles by wet and dry deposition and thus have longer atmospheric residence times. Dry deposition rates vary depending on the particle size. Because of their small size, DE particles have residence times of several days (dry deposition velocities of approximately 0.01 cm/sec) (Winer and Busby, 1995). Diesel particulates may be removed by wet deposition if they serve as condensation nuclei for water vapor deposition or are scavenged by precipitation in- or below-cloud.

In a study designed to assess the atmospheric concentrations and transport of DE particles, Horvath et al. (1988) doped the sole source of diesel fuel in Vienna with an organometallic compound of the heavy earth element dysprosium. The authors found that in some of the more remote sampling areas, DPM composed more than 30% of the particulate mass, indicating that DPM can be dispersed widely.

2.3.3. Diesel Exhaust Aging

Primary DE is considered "fresh," whereas "aged" DE is considered to have undergone chemical and physical transformation and dispersion over a period of a day or two. Laboratory dilution tunnel measurements represent a homogeneous environment compared to the complex and dynamic system into which real-world DE is emitted. The physical and chemical transformation of DE will vary depending on the environment into which it is emitted. In an urban or industrial environment, DE may enter an atmosphere with high concentrations of oxidizing and nitrating radicals, as well as nondiesel organic and inorganic compounds that may influence the toxicity, chemical stability, and atmospheric residence time.

In general, secondary pollutants formed in an aged aerosol mass are more oxidized, and therefore have increased polarity and water solubility (Finlayson-Pitts and Pitts, 1986). Kamens et al. (1988) reported that photooxidation of particle-bound PAH is enhanced as relative humidity is increased. Weingartner et al. (1997a) and Dua et al. (1999) have reported that unlike many other types of particles, diesel particles do not appear to undergo hygroscopic growth once emitted to the atmosphere and may even shrink in size to some extent under increasing relative humidity conditions. Weingartner et al. (1997a) evaluated the hygroscopic growth of diesel particles and found that freshly emitted diesel particles demonstrated minimal hygroscopic

growth (2.5%), whereas aged particles subjected to UV radiation and ozonolysis exhibited somewhat greater but still minimal hygroscopic growth. An increase in the sulfur content of diesel fuel has also been observed to result in somewhat greater water condensation onto diesel particles. To the extent that DE components are oxidized or nitrated in the atmosphere, they may be removed at rates different from their precursor compounds and may exhibit different biological reactivities. Data suggesting that minimal hygroscopic growth of DPM occurs also has implications for the dosimetry of these particles in the lung because the smaller particles will reach the lowest airways of the lung, whereas growth of the particle would result in deposition in the upper airways. The dosimetry of DPM is discussed in Chapter 3.

In a recent experiment, the biological activity of DPM exposed to 0.1 ppm ozone for 48 hours was compared with that of DPM not exposed to ozone (Ghio et al., 2000). Instillations of the ozonated DPM in rat lung resulted in an increase in biological activity (neutrophil influx, increased protein, and lactate dehydrogenase activity) compared with DPM that had not been treated with ozone. These data suggest that ambient levels of ozone can alter DPM constituents causing an increase in toxicity compared with nonozonated DPM.

In addition to changes in particle composition with aging, particle size distributions may vary depending on aggregation and coagulation phenomena in the aging process. People in vehicles, near roadways (e.g., cyclists, pedestrians, people in nearby buildings), and on motorcycles will be exposed to more fresh exhaust than the general population. In some settings where emissions are entrained for long periods through meteorological or other factors, exposures would be expected to include both fresh and aged DE. The complexities of transport and dispersion of emission arising from motor vehicles have been the subject of extensive modeling and experimental studies over the past decades and have been summarized by Sampson (1988); exposures to DPM are discussed in the next section of this chapter.

The major organic constituents of DE and their potential degradation pathways described above provide evidence for (1) direct emission of PAHs, (2) secondary formation of nitroarenes, and (3) secondary sulfate and nitrate formation. Because nitro-PAH products are often more mutagenic than their precursors, the formation, transport, and concentrations of these compounds in an aged aerosol mass are of significant interest.

2.4. AMBIENT DIESEL EXHAUST CONCENTRATIONS AND EXPOSURES

2.4.1. Diesel Exhaust Gases in the Ambient Atmosphere

Although emissions of several DE components have been measured, few studies have attempted to elucidate the contribution of diesel-powered engines to atmospheric concentrations of these components. The emission profile of gaseous organic compounds is different for diesel and SI vehicles; the low-molecular-weight aromatic HCs and alkanes ($<C_9$) are more

characteristic of SI engine emissions, whereas the heavier alkanes (>C_{10}) and aromatic HCs (such as naphthalene, methyl- and dimethyl- naphthalenes, methyl- and dimethyl-indans) are more characteristic of diesel engine emissions. These differences were the basis for apportionment of gasoline- and diesel-powered vehicle emissions to ambient nonmethane hydrocarbon (NMHC) concentrations in the Boston and Los Angeles (South Coast Air Basin) urban areas.

The chemical mass balance receptor model (described below) was applied to ambient samples collected in these areas, along with appropriate fuel, stationary, and area source profiles (Fujita et al., 1997). The average of the sum of NMHC attributed to DE, gasoline-vehicle exhaust, liquid gasoline, and gasoline vapor was 73% and 76% for Boston and the South Coast Air Basin (SoCAB), respectively. The average source contributions of DE to NMHC concentrations were 22% and 13% for Boston and the SoCAB, respectively. Diesel vehicles emit lower levels of NMHC in the exhaust compared with gasoline vehicles. The relative contribution of DE clearly depends on several factors, including fleet composition, sampling location (e.g., near a bus station vs. near a highway or other sources), and the contribution from point and area sources. The contribution of DE to ambient NMHC showed large variations among sampling sites in the Boston area. The source apportionment in the Fujita et al. (1997) study indicates that mobile vehicle-related emissions account for the majority of ambient NMHC in the two urban areas studied, and the results can likely be extrapolated to other urban areas with similar source compositions. Other source apportionment methods such as those used by Henry et al. (1994) have been applied to speciated HC data to separate the mobile source direct emission from gasoline evaporative emissions. This method uses a combination of graphical analysis (Graphical Ratio Analysis for Composition Estimates, GRACE) and multivariate receptor modeling methods (Source Apportionment by Factors with Explicit Restrictions, SAFER) and was not used to identify the diesel engine contribution to the HCs measured.

2.4.2. Ambient Concentrations of DPM

Because DPM is chemically complex, an assessment of ambient DPM concentrations relies primarily on (1) studies that collect ambient samples and adequately characterize their chemical composition, or (2) modeling studies that attempt to recreate emissions and atmospheric conditions. Ambient concentrations of DPM also have been reported from studies using surrogate species. The results of these studies are summarized below. Studies conducted in Europe and Japan were reviewed, but for the most part were not included because of questions surrounding the applicability of measurements in locations that use different diesel technology and control measures from those in the United States.

2.4.2.1. *Source Apportionment Studies*

Receptor models are used to infer the types and relative contributions of sources to pollutant measurements made at a receptor site. Receptor models assume that the mass is conserved between the source and receptor site and that the measured mass of each pollutant is a sum of the contributions from each source. Receptor models are referred to as "top-down" in contrast to "bottom-up" methods, which use emission inventory data, activity patterns, and dispersion modeling from the source to predict concentrations at a receptor site.

The most commonly used receptor model for quantifying concentrations of DPM at a receptor site is the chemical mass balance (CMB) model. Input to the CMB model includes measurements of PM mass and chemistry made at the receptor site as well as measurements made of each of the source types suspected to impact the site. Because of problems involving the elemental similarity between diesel and gasoline emission profiles and their co-emission in time and space, chemical molecular species that provide markers for separation of these sources have been identified (Lowenthal et al., 1992). Recent advances in chemical analytical techniques have facilitated the development of sophisticated molecular source profiles, including detailed speciation of PM-associated organic compounds that allow the apportionment of PM to gasoline and diesel sources with increased confidence. CMB analysis that uses speciation of organic compounds in the source profiles is typically referred to as extended species CMB. Older studies that made use of only EC, total OC, trace elements, and major ions in the source profiles (conventional CMB) have been published and are summarized here, but they are subject to more uncertainty. It should be noted that because receptor modeling is based on the application of source profiles to ambient measurements, estimates of DPM concentration generated by this method include the contribution from on-road and nonroad sources to the extent the source profiles are similar (which would include military sources depending on the sampling locations and fleet composition). In addition, this method identifies sources of primary emissions of DPM only, and the contribution of secondary aerosols is not attributed to sources.

The CMB model has been used to assess concentrations of DPM in areas of California, Phoenix, Denver, and Manhattan (Table 2-23). DPM concentrations reported by Schauer et al. (1996) for samples collected in California in 1982 ranged from 4.4 $\mu g/m^3$ in west Los Angeles to 11.6 $\mu g/m^3$ in downtown Los Angeles. The average contribution of DPM to total $PM_{2.5}$ mass ranged from 13% in Rubidoux to 36% in downtown Los Angeles. As mentioned above, this model accounts for primary emissions of DPM only; the contribution of secondary aerosol formation (both acid and organic aerosols) is not included. In sites downwind from urban areas, such as Rubidoux in this study, secondary nitrate formation can account for a substantial fraction of the mass (25% of the fine mass measured in Rubidoux was attributed to secondary nitrate), a portion of which comes from DE (Gray and Kuklin, 1996).

Table 2-23. Ambient DPM concentrations reported from chemical mass balance modeling

Reference	Location	Year of sampling	Location type	Diesel $PM_{2.5}$ $\mu g/m^3$ mean, (range)	Average DPM % of total PM (range)	Source profile used
Schauer et al., 1996	West LA, CA	1982, annual average (~60 samples at each site)	Urban	4.4	18	EC, OCS, elements
	Pasadena, CA		Urban	5.3	19	
	Rubidoux, CA		Urban	5.4	13	
	Los Angeles, CA		Urban	11.6	36	
Chow et al., 1991	West Phoenix, AZ	1989-90, winter 11 days at each site	Urban	13 (max. 22)	18	EC, OCT, MI, elements
	Central Phoenix, AZ		Urban	13 (max. 16)	20	
	South Scottsdale, AZ		Urban	10 (max. 12)	17	
	Estrella Park, AZ		Nonurban	5	9	
	Gunnery Park, AZ		Nonurban	3	10	
	Pinnacle Peak, AZ		Nonurban	2	12	
California EPA, 1998a	California, 6 air basins	1988-92, annual	Urban[c]	1.8–3.6[a]	[b]	EC, OCT, MI, elements
	California, 9 air basins		Nonurban[c]	0.2–2.6[a]	[b]	EC, OCT, MI, elements
Wittorff et al., 1994	Manhattan, NY	1993, spring 3 days	Urban	29.2(13.2–46.7)[a]	53 (31–68)	EC, OCT, MI, elements
Maricopa Association of Governments, 1999	Phoenix, AZ	1994–95, winter 12 days	Urban	2.4 (0–5.3)	15 (0–27)	EC, OCS, MI, elements
Fujita et al., 1998	Welby, CO	1996–97, winter 60 days	Urban	1.7 (0–7.3)	10 (0–26)	EC, OCS, MI, elements
	Brighton, CO		Suburban	1.2 (0–3.4)	10 (0–38)	

[a]PM_{10}.
[b]Not available.
[c]Urban air basins are qualitatively defined as those areas that are moderately or largely urbanized, and nonurban air basins are those areas that are largely nonurban, but may have one or more densely populated areas.
Abbreviations: EC: Elemental carbon; OCT: OC total; OCS: OC species; MI: Major ions including nitrate, sulfate, chloride and, in some cases, ammonium, sodium, potassium.

The California Environmental Protection Agency (Cal EPA) reported ambient DPM concentrations for 15 air basins in California based on ambient measurements taken statewide from 1988 to 1992 (Cal EPA, 1998a). Cal EPA used CMB analysis of ambient measurements from the San Joaquin Valley (1988-89), South Coast (1986), and San Jose (winters for 1991–92 and 1992–93) to determine mobile source contributions and then applied the California 1990 PM_{10} emissions inventory to determine the fraction of mobile source PM_{10} attributable to diesel emissions. The results of this analysis indicate that annual average basin-wide levels of direct DPM may be as low as 0.2 $\mu g/m^3$ and may range up to 2.6 $\mu g/m^3$ for basins that are largely nonurban but may have one or more densely populated areas (such as Palm Springs in the Salton Sea basin). DPM concentrations for air basins that are moderately or largely urbanized ranged from 1.8 $\mu g/m^3$ to 3.6 $\mu g/m^3$.

Two studies using CMB analysis that report DPM concentrations have been conducted in the Phoenix area. A wintertime study in 1989–90 reported DPM concentrations for nonurban areas ranging from 2 $\mu g/m^3$ to 5 $\mu g/m^3$ and DPM concentrations for central and south Phoenix urban areas ranging from 10 $\mu g/m^3$ to 13 $\mu g/m^3$ (Chow et al., 1991). Chow et al. (1991) reported that DPM levels on single days can range up to 22 $\mu g/m^3$ at the central Phoenix site. A more recent study conducted from November 1994 through March 1995 reported DPM concentrations for Phoenix averaging 2.4 $\mu g/m^3$ and reaching 5.3 $\mu g/m^3$ (Maricopa Association of Governments, 1999). The extended species CMB was used for this study, providing a more confident identification of DPM separate from gasoline PM emissions than the earlier Phoenix study. DPM accounted for an average 15% of ambient $PM_{2.5}$, and gasoline PM accounted for an average of 52% of ambient $PM_{2.5}$ in the 1994–95 Phoenix study.

In a recently published study designed to investigate the ability of a new type of factor analysis, positive matrix factorization, to separate sources contributing to the urban aerosol in Phoenix, Ramadan et al. (2000) report their success in separating the DE PM from other motor vehicle PM. Fine PM samples were collected by two different types of samplers in Phoenix, one set collected from March 1995 through June 1998 and a second set from June 1996 through June 1998. Elemental and OC were analyzed using TOT. Particles of DE origin were identified by their high EC content in addition to specific trace elements, including manganese, sulfur, and iron. DPM concentrations exceeding 5 $\mu g/m^3$ were reported for winter months during the study period. The investigators concluded that motor vehicles, vegetative burning, and HD DE were the three major sources contributing to ambient fine PM in Phoenix, with higher contributions in the winter than in summer.

During the winter of 1997, a study assessed DPM concentrations at two urban sites in the Denver area (Fujita et al., 1998). The Northern Front Range Air Quality Study (NFRAQS), initiated to assess the sources of the "brown cloud" observed along Colorado's Front Range,

conducted air quality sampling during the winter of 1996, summer of 1996, and winter of 1997. For a 60-day period from December 1996 through January 1997, ambient samples collected at two urban Denver sites were analyzed for OC species for use in the extended-species CMB. The average DPM concentrations reported for the urban site at Welby, CO, and the suburban site at Brighton, CO, were 1.7 $\mu g/m^3$ and 1.2 $\mu g/m^3$, respectively. During the study period, DPM concentrations exceeded 5 $\mu g/m^3$ on two occasions in Welby, with reported DPM concentrations of 5.7 $\mu g/m^3$ and 7.3 $\mu g/m^3$. DPM accounted for an average of 10% of ambient $PM_{2.5}$, and gasoline PM accounted for an average of 27% of ambient $PM_{2.5}$.

One of the major claims from the NFRAQS was a substantial contribution of EC from gasoline-powered vehicles, mainly from cold-start and high-emitting vehicles. At the Welby site, the contribution of diesel and gasoline emissions to EC measurements was 52% and 42%, respectively. At the Brighton site, the contribution of diesel and gasoline emissions to EC measurements was 71% and 26%, respectively. The findings from the NFRAQS are compelling and suggest the need for further investigations to quantify the contribution from cold-start and high-emitting vehicle emissions for both gasoline and diesel vehicles. Geographical, temporal, and other site-specific parameters that influence PM concentrations, such as altitude, must be considered when extrapolating the NFRAQS findings to other locations.

In addition to the need for urban and rural average DPM concentrations, an assessment of potential health effects resulting from DPM exposure includes an assessment of people in environments with potentially elevated levels of DPM. Limited data are available to allow a characterization of DPM concentrations in "hotspots" such as near heavily traveled roadways, bus stations, train stations, and marinas. Only one CMB study has attempted to apportion PM measured in an urban hotspot. Wittorff et al. (1994) reported results of conventional CMB performed on PM samples collected in the spring of 1993 over a 3-day period at a site adjacent to a major bus stop on Madison Avenue in midtown Manhattan. Buses in this area idle for as long as 10 minutes, and PM emissions are augmented by the elevated levels of DPM emitted during acceleration away from the bus stop (discussed in Section 2.2.5). DPM concentrations reported from this study ranged from 13.0 $\mu g/m^3$ to 46.7 $\mu g/m^3$. This study attributed, on average, 53% of the PM_{10} to DE. The DPM concentrations resulting from the source apportionment method used in this study require some caution because the CMB model overpredicted PM_{10} concentrations by an average 30%, which suggests that additional sources of the mass were not accounted for in the model. The relevance of the Manhattan bus stop concentrations and potential exposure for large urban populations provide strong motivation for further studies in the vicinity of such hotspots.

In summary, source apportionment studies of ambient samples collected before 1990 suggest that seasonal and annual average DPM concentrations for nonurban areas ranged from 2

$\mu g/m^3$ to 5 $\mu g/m^3$. DPM concentrations reported from CMB studies for urban areas in the pre-1990 timeframe ranged from 4.4 $\mu g/m^3$ to 13 $\mu g/m^3$, with concentrations on individual days ranging up to 22 $\mu g/m^3$. Source apportionment applied to ambient measurements taken in 1990 or later suggest that seasonal or annual average DPM levels in suburban/nonurban locations can range from 0.2 $\mu g/m^3$ to 2.6 $\mu g/m^3$, with maximum reported values ranging up to 3.4 $\mu g/m^3$. DPM concentrations reported from CMB studies in urban areas during 1990 or later range from 1.7 $\mu g/m^3$ to 3.6 $\mu g/m^3$, with maximum concentrations up to 7.3 $\mu g/m^3$. The highest DPM concentrations reported from CMB analysis of ambient measurements were those in the vicinity of a bus stop in midtown Manhattan, which ranged from 13.2 $\mu g/m^3$ to 46.7 $\mu g/m^3$.

2.4.2.2. *EC Surrogate for DPM*

EC is a major component of DE, contributing approximately 50% to 85% of diesel particulate mass, depending on engine technology, fuel type, duty cycle, engine lubrication oil consumption, and state of engine maintenance (Graboski et al., 1998b; Zaebst et al., 1991; Pierson and Brachaczek, 1983; Warner-Selph and Dietzmann, 1984). In urban ambient environments, DE is one of the major contributors to EC, with other potential sources including spark-engine exhaust; combustion of coal, oil, or wood; charbroiling; cigarette smoke; and road dust. Although cold-start emissions from gasoline combustion vehicles were reported to be an important source of EC in wintertime samples collected in two cities in the Denver area (Fujita et al., 1998), it is currently unclear to what extent these results are transferable to other locations. It is noteworthy that the EC content of the cold-start emissions from gasoline combustion vehicles was lower than that from diesel combustion engines in the same study by almost a factor of 2.

Fowler (1985) evaluated several components of DE and concluded that EC is the most reliable overall measure of ambient DE exposure. Because of the large portion of EC in DPM, and the fact that DE is one of the major contributors to EC in many ambient environments, DPM concentrations can be bounded using EC measurements. Surrogate calculations of DPM have been based on the fraction of ambient EC measured in a sample that is attributable to diesel engine exhaust and the fraction of the diesel particle mass accounted for by EC. In the recent Multiple Air Toxics Exposure Study in the South Coast Air Basin (MATES-II, SCAQMD, 2000), EC measurements were used to estimate DPM concentrations by the following relationship: approximately 67% of fine EC in the ambient air in the Los Angeles area originates from diesel engine exhaust (Gray, 1986), and the average EC fraction of diesel particles measured was 64%. Therefore, in the MATES-II study, the South Coast Air Quality Management District calculated DPM concentrations from EC measurements by multiplying a measured EC concentration by 67% and dividing by the fraction of DPM mass accounted for by EC of 64%, for example, DPM concentration = (EC * 0.67)/0.64, or DPM = EC * 1.04 (not

appreciably different from EC≈DPM). This calculation, used in the MATES-II study, relies on data collected in the 1982 timeframe and may not accurately represent the current day contributions of diesel engines to the ambient EC inventory. Using a 1998 emissions inventory for the South Coast Air Basin, it is now estimated that a more appropriate conversion from EC to DPM is to multiply EC by 1.24 (MATES-II, SCAQMD, 2000).

An alternative calculation can be derived using data from recent studies in Colorado and Arizona (Fujita et al., 1998; Maricopa Association of Governments, 1999). The fraction of EC attributable to DE can be estimated from detailed source profiles applied to a CMB model as discussed above. The contribution of diesel engines to EC averaged 68% ± 20% for Brighton, CO, and 49% ± 26% at Welby, CO, as part of the winter 1996-1997 NFRAQS. In Phoenix, diesel engine exhaust was estimated to account for approximately 46% ± 22% of the ambient EC. For some environments, such as certain occupational settings in which diesel engines are in proximity to workers, all the EC may realistically be attributed to DE as a reasonable upper bound estimate of DPM concentrations.

As discussed in Section 2.2, the EC content of DPM can vary widely depending on engine type, load conditions, and the test cycle. However, typical profiles for HD and LD diesel engines have been determined and the typical EC fraction of DPM ranges from approximately 52% to 75%.

Ambient EC attributed to DE in the studies described above ranges from 46% to 68%. A lower-bound estimate of DPM from ambient EC measurements in areas with similar source contributions to those in the Phoenix and Denver areas can be derived using the equation:

$$DPM = (EC * 0.46)/0.75 \text{ or } DPM = EC * 0.62$$

An upper-bound estimate uses the equation:

$$DPM = (EC * 0.68)/0.52 \text{ or } DPM = EC * 1.31$$

Using the average of the ranges provides the equation:

$$DPM = EC * 0.89.$$

Clearly the choice of a point estimate can provide a surrogate calculation of DPM that can vary by at least a factor of two. Although a recommended surrogate DPM calculation method is not provided here, the surrogate DPM calculation is used to illustrate the usefulness of

this approach for estimating DPM in the absence of a more sophisticated receptor modeling analysis for locations where fine PM EC concentrations are available.

One source of variability in EC concentrations reported for ambient studies is the measurement method used to quantify EC. As discussed in Section 2.2.8.1, EC and OC are operationally defined. Ambient samples are typically analyzed for EC using thermal optical reflectance or thermal optical transmittance. The measurement technique used in the NFRAQS and Phoenix studies was TOR, which, as discussed in Section 2.2.8.2, often results in higher EC levels compared to TOT analyses.

Table 2-24 provides a lower- and upper-bound DPM estimate from annual average EC concentrations for three urban areas, in addition to DPM concentrations reported from EC measurements for the MATES- II (SCAQMD, 2000). Under an EPA research grant with the Northeastern States for Coordinated Air Use Management (NESCAUM), $PM_{2.5}$ samples were collected every 6 days for 1 year (1995) in Boston (Kenmore Square), MA, and Rochester, NY, and were analyzed for EC using TOT (Salmon et al., 1997). DPM concentrations were estimated to be in the range from 0.8 $\mu g/m^3$ to 1.7 $\mu g/m^3$ in Boston, and from 0.4 $\mu g/m^3$ to 0.8 $\mu g/m^3$ in Rochester (Table 2-24).

Table 2-24. Ambient diesel particulate matter concentrations from elemental carbon measurements in urban locations

Reference	Year of sampling	Location	$DPM_{2.5}$ $\mu g/m^3$ lower-upper bound range (point estimate)[a]	DPM % of total PM
Salmon et al., 1997	1995, annual	Boston, MA	0.8–1.7 (1.1)	6-12
		Rochester, NY	0.4-0.8 (0.5)	3-6
Sisler, 1996	1992-1995, annual	Washington, DC	0.9-2.2 (1.5)	4-12
		MATES II [c]	Diesel $PM_{2.5}$ $\mu g/m^3$ avg± std dev.	
South Coast Air Quality Management District, 1999	1995-6, annual	Anaheim, CA	2.4 ± 1.8	[b]
		Burbank, CA	3.3 ± 1.9	[b]
		Los Angeles, CA	3.5 ± 1.9	[b]
		Fontanta, CA	3.4 ± 2.3	[b]
		Huntington Park, CA	4.5 ± 2.4	[b]
		Long Beach, CA	2.5 ± 1.7	[b]
		Pico Rivera, CA	4.4 ± 2.2	[b]
		Rubidoux, CA	3.4 ± 2.0	[b]

[a] Lower-bound range: DPM=EC*0.62; upper-bound range: DPM=EC*1.31; point estimate: DPM=EC*0.89.
[b] Not available.
[c]The Multiple Air Toxics Exposure Study in the South Coast Air Basin reported DPM calculated from EC concentrations as DPM=EC*1.04. Standard deviations are reported.

The Interagency Monitoring of Protected Visual Environments (IMPROVE) project being conducted by the National Park Service includes an extensive aerosol monitoring network mainly in rural or remote areas of the country (national parks, national monuments, wilderness areas, national wildlife refuges, and national seashores), and also in Washington, DC (Sisler, 1996). $PM_{2.5}$ samples, collected from March 1992 through February 1995 twice weekly for 24-hour duration at 43 sites (some co-located in the same rural park area), were analyzed for a suite of chemical constituents, including EC (using TOR). EC concentrations in these rural locations may have EC source contributions quite different from those in the urban areas in which the fraction of EC attributable to DE has been reported. The lack of information regarding EC sources in these rural locations makes the application of the EC surrogate highly uncertain. It is noteworthy that annual average EC concentrations in the rural and remote regions reported as part of the IMPROVE network range from 0.1 $\mu g/m^3$ for Denali National Park, AK, to 0.9 $\mu g/m^3$ for the Lake Tahoe, CA, area. In Washington, DC, the annual average EC concentration of 1.7 $\mu g/m^3$ is estimated as an annual average DPM concentration of 1.4 $\mu g/m^3$.

The annual average EC measurements in Washington, DC, suggest that the DPM concentrations are in the range from 1.0 $\mu g/m^3$ to 2.2 $\mu g/m^3$, accounting for 5% to 12% of ambient $PM_{2.5}$. Seasonally averaged data for the Washington, DC, site indicate that EC concentrations and, by extension, DPM concentrations peak in the autumn and winter (2.0 $\mu g/m^3$ and 0.9 $\mu g/m^3$ EC, respectively).

DPM concentrations reported recently as part of the MATES-II study at eight locations ranged from 2.4 $\mu g/m^3$ to 4.5 $\mu g/m^3$. DPM concentrations at Huntington Park and Pico Rivera, CA, were higher than other DPM concentrations in the South Coast Air Basin, perhaps because of higher diesel truck traffic, proximity to nonroad diesel sources, or nondiesel sources of EC, including gasoline vehicle traffic.

In a recent study of the trends in fine particle and EC concentrations in Southern California, Christoforou et al. (2000) report that EC concentrations measured in 1993 were 29%-40% of EC concentrations measured in 1982 at four urban Los Angeles sites. The authors credit lower PM emission rates from on-road diesel engines as well as cleaner-burning diesel fuel for the observed EC decrease. The extent to which nonroad diesel equipment impacts a given site will influence the trend in ambient EC concentrations because fewer regulations have been promulgated to control the PM emissions from these engines.

2.4.2.3. *Dispersion Modeling Results*

Dispersion models estimate ambient levels of PM at a receptor site on the basis of emission factors for the relevant sources and parameters that simulate atmospheric processes such as the advection, mixing, deposition, and chemical transformation of compounds as they are

transported from the source to the receptor site(s). Cass and Gray (1995), Gray and Cass (1998), and Kleeman and Cass (1998) have applied dispersion models to the South Coast Air Basin to estimate DPM concentrations. The models used by these investigators applied emission factors from 1982 and consequently are representative of concentrations prior to the implementation of DPM emission controls. In addition to offering another approach for estimating ambient DPM concentrations, dispersion models can provide the ability to distinguish on-highway from nonroad diesel source contributions and have presented an approach for quantifying the concentrations of secondary aerosols from DE.

Cass and Gray (1995) used a Lagrangian particle-in-cell model to estimate the source contributions to atmospheric fine carbon particle concentrations in the Los Angeles area, including diesel emission factors from on-highway and off-highway sources. Their dispersion model indicates that for 1982, the annual average ambient concentrations of DPM ranged from 1.9 $\mu g/m^3$ in Azusa, CA, to 5.6 $\mu g/m^3$ in downtown Los Angeles (Table 2-25). The contribution of on-highway sources to DPM ranged from 63.3% in downtown Los Angeles to 89% in west Los Angeles. Of the on-highway diesel contribution, the model predicted that for southern California, HD trucks made up the majority (85%) of the DPM inventory, and overall they contributed 66% of the DPM in the ambient air. Nonroad sources of DE include pumping stations, construction sites, shipping docks, railroad yards, and heavy equipment repair facilities. Cass and Gray (1995) also report that wintertime peaks in DPM concentrations can reach 10 $\mu g/m^3$.

Table 2-25. Ambient diesel particulate matter concentrations from dispersion modeling

Reference	Location	Year of sampling	Location type	$DPM_{2.5}$ g/m^3 (mean)	DPM % of total PM
Cass and Gray, 1995	Azusa, CA	1982, annual	Nonurban	1.4[a]	5
	Lennox, CA	1982, annual	Nonurban	3.8[a]	13
	Anaheim, CA	1982, annual	Urban	2.7[a]	12
	Pasadena, CA	1982, annual	Urban	2.0[a]	7
	Long Beach, CA	1982, annual	Urban	3.5[a]	13
	Downtown LA, CA	1982, annual	Urban	3.5[a]	11
	West LA, CA	1982, annual	Urban	3.8[a]	16
Kleeman and Cass, 1998	Claremont, CA	18-19 Aug 1987	Nonurban	2.4 (4.0)[a,b]	8 (6)[b]
Kleeman et al., 2000	Long Beach, CA	24 Sept 1996	Urban	1.9(2.6)[b]	8 (7)[b]
	Fullerton, CA	24 Sept 1996	Nonurban	2.4(3.9)[b]	9 (8)[b]
	Riverside, CA	25 Sept 1996	Suburban	4.4(13.3)[b]	12 (13)[b]

[a] On-road diesel vehicles only; all other values are for on-road plus nonroad diesel emissions.
[b] Value in parentheses includes secondary DPM (nitrate, ammonium, sulfate and hydrocarbons) attributable to atmospheric reactions of primary diesel emissions of NO_x, SO_2 and hydrocarbons. For the fraction of ambient PM attributable to DPM, the value in parenthesis reports total DPM (primary plus secondary) as a fraction of total ambient PM (primary plus secondary).

Kleeman and Cass (1998) developed a Lagrangian model that examines the size and chemical evolution of aerosols, including gas-to-particle conversion processes during transport. This model was applied to one well-characterized episode in Claremont, CA, on August 27-28, 1987. The model provided reasonable predictions of PM_{10} (overpredicting PM_{10} by 13%), EC, and OC, and it adequately reconstructed the size distribution of the aerosols. The model indicated that on August 27-28, 1987, the $PM_{2.5}$ concentration was 76.7 $\mu g/m^3$, 13.2% (10.1 $\mu g/m^3$) of which was attributable to diesel engine emissions. This estimate includes secondary aerosol formation for sulfate, ammonium, nitrate, and organic compounds, which accounted for 4.9 $\mu g/m^3$ of the total estimated DPM mass. The secondary organic aerosol was estimated to be 1.1 $\mu g/m^3$, or 31% of the total secondary aerosol mass, with the remainder composed of nitrate, ammonium, and sulfate aerosols.

Dispersion modeling estimates of diesel PM concentrations from on-highway and nonroad sources have recently been developed as part of the EPA National Air Toxics Assessment (NATA) National Scale Assessment. This assessment uses the Assessment System for Population Exposure Nationwide (ASPEN) dispersion model to estimate ambient concentrations for the year 1996. The NATA national scale assessment reports concentrations of DPM and 32 additional urban air toxic compounds at the county, State, and national level (NATA, 2001).

ASPEN makes a number of simplifying assumptions in order to model concentrations on a nationwide scale. For instance, concentration estimates at the census tract level were estimated using modeling assumptions to allocate emissions from the county level, and the model is very sensitive to the assumptions used. In addition, dispersion of emissions from nonpoint sources (e.g., on-highway and nonroad vehicles) was treated simplistically. For resident tracts that have radii greater than 0.3 km, non-point-source ambient concentrations are estimated on the basis of five pseudo-point sources. The average concentration for the census tract is determined by spatially averaging the ambient concentrations associated with the receptors defined for the five pseudosources that fall within the bounds of the tract. Other limitations include the following: terrain impacts on dispersion were not included; the study relied on long-term climate summary data, and no long-range transport was included for DPM (medium-range transport for DPM, within 300 km, was included). Because of the limitations, the results are most meaningfully interpreted when viewed over large geographic areas. The 1996 results from ASPEN compare well (generally within a factor of 1.5) with estimated concentrations from EC measurements and receptor modeling, as well as data from other dispersion modeling studies. The complete results of the assessment are available at http://www.epa.gov/ttn/uatw/nata.

Table 2-26 presents 25th percentile, average, and 75th percentile nationwide concentrations from the 1996 National-Scale Assessment as well as the contribution of on-road and nonroad DE the sources to the nationwide average. The national average DPM concentration reported in the National-Scale Assessment is 2.1 $\mu g/m^3$, of which nonroad sources are estimated to contribute 67% and on-road sources contribute the remainder. Less than 2% of the nationwide DE inventory is attributed to point sources, and these were not included in the modeling as part of National-Scale Assessment. A wide range in average State-specific ambient DPM concentrations was reported by the National-Scale Assessment with the lowest values for mainly rural States with few DE sources, such as Wyoming (annual average of 0.2 $\mu g/m^3$), and the highest values for States with large urban centers such as New York (annual average of 5.4 $\mu g/m^3$).

Table 2-26. Nationwide ambient diesel particulate matter concentrations for 1996 from the National Air Toxics Assessment National-Scale Assessment dispersion modeling

Location	25th percentile, DPM_{10} mg/m^3	Average, DPM_{10} mg/m^3	75th percentile, DPM_{10} mg/m^3	Contribution to average from on-road sources, DPM_{10} mg/m^3	Contribution to average from nonroad sources, DPM_{10} mg/m^3
Nationwide	0.9	2.1	2.5	0.6	1.4
All urban counties	1.2	2.4	2.7	0.7	1.7
All rural counties	0.4	0.7	1.0	0.3	0.5

Source: NATA, 2001. Data available at http://www.epa.gov/ttn/uatw/nata.

2.4.3. Exposures to Diesel Exhaust

Ultimately, it is personal exposure that determines health impacts. In the following sections, modeled average exposures and some information reflecting potential exposures for those who spend a large portion of their time outdoors are presented. Occupational exposures to DPM are summarized for the variety of workplaces in which diesel engines are used. These occupational exposures are placed into context with equivalent environmental exposures to understand the potential for overlap in average occupational and average ambient exposures. Because DE is a mixture of particles and gases, one must choose a measure of exposure (i.e., dosimeter); $\mu g/m^3$ of DPM has historically been used in many studies as the dosimeter for the entire DE mixture.

2.4.3.1. *Occupational Exposure to DE*

The National Institute for Occupational Safety and Health (NIOSH, 1988) estimates that approximately 1.35 million workers are occupationally exposed to DE emissions. Such workers emissions include mine workers, railroad workers, bus and truck drivers, truck and bus maintenance garage workers, loading dock workers, firefighters, heavy equipment operators, and farm workers.

Measurements of DPM exposure in occupational environments have included respirable particulate (<3.5 μm), smoking-corrected respirable particulate, combustible respirable particulate, and EC, among other methods. The measurement method used in each of the studies discussed below is listed in Table 2-27. Occupational exposures to DPM as well as breathing zone concentrations of DPM have been described in some detail by Watts (1995), Groves and Cain (2000), Hammond (1998), the World Health Organization (1996), and Birch and Cary (1996) and are briefly, but not comprehensively, summarized here.

The highest occupational exposures to DPM are for workers in coal mines and noncoal mines using diesel-powered equipment. These exposures, reported by several investigators, range from approximately 10 $\mu g/m^3$ to 1,280 $\mu g/m^3$ (Table 2-27). Rogers and Whelan (1999) report exposures to specific DPM-associated PAHs (including naphthalene, fluorene, phenanthrene, pyrene, and benz[a]anthracene) for mine workers using diesel fuels containing low and high levels of sulfur, aliphatic, and aromatic compounds. Results of this study indicate that the composition of DPM to which workers were exposed varies considerably based on engine condition, fuel, and other operating parameters. Mine worker exposures to PAH compounds were highest for naphthalene, ranging from 1,312 μg/g to 3,228 μg/g of organics, and exposures were lowest for benz[a]anthracene, ranging from less than 3 μg/g up to 18 μg/g of organics.

Other investigators have reported DPM-associated PAH concentrations that do not necessarily represent personal exposures but are a snapshot of short periods of elevated concentration that make up a portion of a worker's daily exposure. Bagley et al. (1991, 1992) reported levels of B[*a*]P ranging from below the detection limit of 0.05 ng/m^3 to 61 ng/m^3 collected only during periods of mining activity. Watts (1995) reported DPM concentrations in four mines collected during significant diesel activity, ranging from 850 $\mu g/m^3$ to 3,260 $\mu g/m^3$. Heino (1978) reports DPM concentrations for locomotive engineers reaching 2,000 $\mu g/m^3$.

In a study of four railroads, Woskie et al. (1988) reported concentrations of respirable dust (corrected for cigarette smoke particulate) that ranged from 39 $\mu g/m^3$ for engineers/firers to 134 $\mu g/m^3$ for locomotive shop workers and 191 $\mu g/m^3$ for hostlers. Woskie et al. (1988) also reported smoking-corrected respirable dust for railroad clerks (17 $\mu g/m^3$), who are considered to be not exposed to DE. Although these exposures may have included nondiesel PM (background

Table 2-27. Occupational exposure to DPM

Author	Year of sample	Location/job type, typical work schedule of 8 hours	n	Sample type	Range in DPM, μg/m³
Gangal and Dainty, 1993[a]	NA	Noncoal mine workers	~200	RCD	100–900
Säverin, 1999	1992	Noncoal mine workers	255[b]	RTC	38–1,280
Rogers and Whelan, 1999	1990-99	Coal mine workers	>1,300	DPSMM	10–640
Haney, 1990[a]	1980s	Coal mine workers (five mines)	NA	SJI	180–1,000
Ambs, 1991a[a]	NA	Coal mine workers (four mines)	NA	PDEAS	750–780
Woskie et al., 1988	3-years in mid-1980s	Railroad engineer/frier	128	ARP	39–73
		Railroad braker/conductor	158	ARP	52–191
		Railroad shop workers	176	ARP	114–134
Groves and Cain, 2000	NA	Railway repair	64	EC(U)	7-50
Froines et al., 1987	1985	Firefighters (two stations)	238	TSP	63–748
NIOSH, 1992[a]	NA	Firefighters (three stations)	18	EC(T)	6–70
Birch and Cary, 1996	NA	Firefighters	NA	EC(U)	20–79
	NA	Fire station employees (four stations)	NA	EC(U)	4–52
Birch and Cary, 1996	NA	Airport ground crew	NA	EC(U)	7–15
	NA	Public transit workers	NA	EC(U)	15–98
NIOSH, 1990	1990	Diesel forklift dockworkers	24	EC(T)	12–61
Zaebst et al., 1991	1990	Dockworkers	75	EC(T)	9–20
		Mechanics	80	EC(T)	5–28
		Long- and short-haul truckers	128	EC(T)	2–7
Groves and Cain, 2000	NA	Bus garage/repair	53	EC(U)	7-217
		Forklift trucks	27	EC(U)	7-403
Kittelson et al., 2000	1999-2000	Bus drivers	39	EC(T)	1–3
		Parking ramp attendants	12	EC(T)	2 ± 0.4

[a] Cited in Watts (1995). NA: not available.
[b] Personal exposure and area samples were not reported separately for this study.
RCD: respirable combustible dust; RTC: respirable total carbon SPM: submicrometer PM; DPSMM: diesel particulate submicron mass (two-stage impaction sampler used to separate PM by size); EC(T): elemental carbon analyzed by TOT; EC(R) elemental carbon analyzed by TOR; EC(U) elemental carbon analyzed by colouremetric method or method not reported; SJI: single-jet impactor agreed within 10% with simultaneous PDEAS measurements; PDEAS: personal DE aerosol sampler collects DPM <0.8 μm, SPM: particulate matter; ARP: respirable particulate adjusted to remove the influence of cigarette smoke; TSP: total suspended particulate matter.

respirable dust levels have been estimated to have contributed approximately 10 μg/m^3 to 33 μg/m^3 for this study), the majority of the respirable PM is believed to have originated from diesel locomotive emissions. Groves and Cain (2000) reported EC exposures among railway repair workers averaging 21 μg/m^3 with a range from 7-50 μg/m^3. DPM exposures reported for firefighters operating diesel engine vehicles range from 4 μg/m^3 to 748 μg/m^3, which also encompasses the range of DPM exposures reported for airport ground crew and public transportation system personnel (7 μg/m^3 to 98 μg/m^3).

Studies reporting DE exposure among fire station employees typically report particulate levels below 100 μg/m^3 (ranging from 4 μg/m^3 to 79 μg/m^3) (NIOSH, 1992; Birch and Cary, 1996). In a study by Froines et al. (1987), DPM exposures for firefighters in two stations ranged from 39 μg/m^3 to 73 μg/m^3. Birch and Cary (1996) also reported DPM exposures for airport ground crew and public transit workers, ranging from 7 μg/m^3 to 15 μg/m^3 for airport ground crews and 15 μg/m^3 to 98 μg/m^3 for public transit workers. Dock workers using diesel-powered forklifts have been reported to have DPM exposures ranging from 6 μg/m^3 to 403 μg/m^3 (NIOSH, 1990; Zaebst et al., 1991; Groves and Cain, 2000). In studies by NIOSH (1990) and Fowler (1985), the organic material measured accounted for about one-half to almost all of the carbonaceous DPM exposures, providing evidence that some pieces of nonroad equipment (forklifts and construction equipment) emitted DPM with a significant OC fraction in the 1980s and early 1990s.

Zaebst et al. (1991) also reported DPM exposures for mechanics, road drivers, and local drivers for 8-hour shifts at each of six large hub truck terminals. Residential background and highway background samples at fixed sites were also collected during warm-weather and cold-weather periods, and the geometric mean for DPM concentrations ranged from 1 μg/m^3 to 5 μg/m^3. DPM exposures for road and local truckers in warm- and cold-weather periods ranged from 2 μg/m^3 to 7 μg/m^3, whereas exposure levels for mechanics were reported between 5 μg/m^3 and 28 μg/m^3 (geometric means).

Kittelson et al. (2000) are measuring DPM exposures for bus drivers, parking garage attendants, and mechanics using TOT to quantify EC. Personal exposures for bus drivers on four different routes range from 1 μg/m^3 to 3 μg/m^3 and exposure among parking ramp attendants averaged 2 μg/m^3. These results are preliminary, and data for the mechanics have not yet been analyzed. This study will also characterize PAH compounds to which these workers are exposed.

Bus garage workers have also been assessed for exposure to DE using urinary excretion of 8-oxo-2'-deoxyguanosine (Loft et al., 1999). Other biomarkers of DE exposure in occupational workers have included measurements of urinary 1-hydroxypyrene, adducts of DNA

and hemoglobin, and 8-hydroxyguanosine in lung tissue (Nielsen et al., 1996; Tokiwa et al., 1999; Zwirner-Baier and Neumann, 1999; Hara et al., 1997).

To estimate an environmental exposure that is equivalent to an occupational lifetime exposure, the fraction of lifetime worker inhalation exposure (calculated as the amount of air breathed on the job multiplied by the typical amount of time spent on the job) is calculated relative to 70-year lifetime inhalation exposure: (10 m^3/shift/20 m^3/day) * (5 days/7 days) * (48 weeks/52 weeks) * (45-year career/70-year lifetime) = 0.21. Using this calculation, 21% of an annual average occupational lifetime exposure is roughly equivalent to a 70-year annual average lifetime environmental exposure. The equivalent environmental exposures for the occupational exposures presented in Table 2-28 range from 0.6 μg/m^3 to 14 μg/m^3 for truckers, dock workers, and mechanics, and from 2 μg/m^3 to 269 μg/m^3 for miners. The low end of the range of environmental equivalent exposures for several of the occupational settings overlaps with average modeled exposures and with ambient concentrations of DPM in urban areas in the 1990–1996 timeframe. The overlap between some occupational exposures and environmental exposures, as well as the small difference between occupational environmental equivalent exposures and environmental exposures, is a significant concern and suggests the potential for significant risk in the general population. The possible magnitude of the cancer risk in the general population is discussed in Chapter 8, Section 8.3.

Table 2-28. Ranges of occupational exposure to DPM by job category with estimates of equivalent environmental exposures

Year of sampling	Occupations	Occupational DPM, μg/m^3	Environmental equivalent[a] exposure, μg/m^3
1980s and 1990s	Miners	10–1,280	2–269
1980s	Railroad workers	39–191	8–40
1985 and later	Firefighters	4–748	1–157
NA	Airport crew, public transit workers	7–98	2–21
1990	Dockworkers, mechanics	5–61	1–13
1990	Long- and short-haul truckers	2–7	0.4–2

[a]Environmental equivalent exposure is calculated as the occupational exposure * (10 m^3/shift / 20 m^3/day)* (5 days / 7days) * (48 weeks / 52 weeks) * (45 year career / 70 year lifetime), or occupational exposure * 0.21 (discussed in section 2.4.3.1.

2.4.3.2. *Ambient Exposure to DE*

Modeled estimates of population exposures to DPM integrate exposure in various indoor and outdoor environments and also account for the demographic distribution, time-activity

patterns, and DPM concentrations in various environments, including job-related exposures. Two modeling efforts have been developed to determine DPM exposures in the general population: the Hazardous Air Pollutant Exposure Model for Mobile Sources, version 3 (HAPEM-MS3) and the California Population Indoor Exposure Model (CPIEM). EPA has also developed version 4 of the HAPEM, which provides State-specific average exposures for DPM and 32 other urban air toxic compounds. The draft exposure assessment using HAPEM version 4 (HAPEM4) has been conducted as part of the National Air Toxics Assessment National-Scale Analysis described in Section 2.4.2.3 above and results are provided here.

2.4.3.2.1. ***The Hazardous Air Pollutant Exposure Model.*** To estimate population exposures to DPM, EPA has used HAPEM-MS3 (U.S. EPA, 1999b). This model provides national and urban-area-specific exposures to DPM from on-road sources only. HAPEM-MS3 is based on the CO probabilistic National Ambient Air Quality Standards (NAAQS) exposure model (pNEM/CO), which is used to estimate the frequency distribution of population exposure to CO and the resulting carboxyhemaglobin levels (Law et al., 1997). HAPEM simulates the CO exposure scenario of individuals in 22 demographic groups for 37 microenvironments. CO concentrations are based on ambient measurements made in 1990 and are related to exposures of individuals in a 10-km radius around the sampling site. DPM exposures are calculated as in Equation 2-5, using a ratiometric approach to CO.

$$DPM_{\mu g/m^3} = (CO_{\mu g/m^3} / CO_{g/mi}) \times DPM_{g/mi} \qquad (2\text{-}5)$$

Data provided to the model include CO monitoring data for 1990; time-activity data collected in Denver, Washington, DC, and Cincinnati from 1982 to 1985; microenvironmental data; and 1990 census population data. Motor vehicle DPM and CO emission rates reported by EPA (1999c) are used to calculate mobile-source DPM exposures, and exposures in future years are projected based on the increase in vehicle miles traveled. EPA's PART5 model is used to estimate DPM emission rates (g/mi) for the fleet as a whole in any given calendar year. PART5 is currently being modified to account for deterioration, actual in-use emissions, poor maintenance, and tampering effects, all of which increase emission factors. As a result, HAPEM-MS3 exposure estimates based on PART5 emission factors may underestimate true exposures from on-road sources. A comparison of PART5 HD diesel vehicle emission factors with those presented earlier in this chapter suggests that PART5 may underestimate HD diesel vehicle emissions by up to 50%.

HAPEM-MS3 assumes that the highway fleet (gasoline plus diesel) emissions ratio of CO to DPM can be used as an adjustment factor to convert estimated CO personal exposure to

DPM exposure estimates. This assumption is supported by the observation that even though gasoline vehicles emit the large majority of CO, gasoline and diesel highway vehicles travel on the same roadways. DPM and CO are both relatively long-lived atmospheric species (1–3 days) except under certain conditions (Seinfeld and Pandis, 1998); therefore, the model does not account for chemical and physical differences between the DPM and CO, and the model assumes that for the average person in a modeled air district, CO and DPM are well mixed. Exposure in microscale environments in which these assumptions may not be valid were not modeled.

A validation study conducted for the pNEM/CO model on which HAPEM-MS3 is based indicates that CO exposures for the population in the 5th percentile were overestimated by approximately 33%, whereas those with exposures in the 98th percentile were underestimated by about 30%. This validation study is considered applicable to the HAPEM-MS3 model. To address the underestimate of exposures for the most highly exposed, Brodowicz (1999) used CO concentrations relevant to the most highly exposed populations to determine DPM exposures for different demographic groups within this population; the results are discussed below.

Annual average DPM exposures from on-road vehicles and nonroad sources nationwide for the general population, rural and urban population, outdoor workers, and urban children are reported in Tables 2-29 and 2-30. The modeled annual average DPM exposure nationwide (urban and rural areas) in 1996 from on-road sources only was 0.8 $\mu g/m^3$. The modeled annual average exposure in urban areas for the same year was 0.8 $\mu g/m^3$, and the modeled exposure for rural areas was 0.4 $\mu g/m^3$. Among the demographic groups modeled, urban outdoor workers in general were found to have the highest average exposure to DPM, averaging 1.0 $\mu g/m^3$ from on-road sources in 1996. DPM exposures attributable to on-road sources are projected to decrease until approximately 2007 because of fleet turnover and the full implementation of Federal regulations that are currently in place. Full implementation of the recently finalized Heavy-Duty Engine and Vehicle Standards and Highway Diesel Fuel Sulfur Control Requirements would significantly lower DPM exposures from on-road sources in the post-2007 timeframe (U.S. EPA, 2000b).

Because diesel vehicle traffic, and therefore exposure to DPM, varies for different urban areas, HAPEM-MS3 was used to estimate annual average population exposures for 10 urban areas. Modeled 1996 DPM exposures in the cities ranged from 0.6 $\mu g/m^3$ in Chicago and St. Louis to 1.3 $\mu g/m^3$ in Phoenix (Table 2-31). In 1996, estimated average DPM exposure from on-road sources was higher than the national average in five cities: Atlanta, Minneapolis, New York, Phoenix, and Spokane. Nationally in 1996, 97% of DPM exposure from on-road vehicles was attributable to HD diesel vehicles, and the rest was generated mainly by LD diesel trucks.

Table 2-29. Annual average nationwide DPM exposure estimates (μg/m³) from on-road sources for rural and urban demographic groups in 1990, 1996, and 2007 using HAPEM-MS3

Demographic group	1990	1996	2007
50-State population	0.8	0.8	0.4
Rural population	0.5	0.4	0.2
Urban population	0.9	0.8	0.4
Urban outdoor workers	1.1	1.0	0.5
Urban children (0-17)	0.9	0.8	0.4

Source: U.S. EPA, 1999b, adjusted to reflect HDDV VMT described in U.S. EPA, 2000b.

Table 2-30. Draft annual average, 25th, and 75th percentile nationwide DPM exposure estimates (μg/m³) from on-road and nonroad sources for rural and urban counties in 1996 using HAPEM4

Demographic group	25th Percentile, DPM_{10} mg/m³	Average, DPM_{10} mg/m³	75th Percentile, DPM_{10} mg/m³	Contribution to average from on-road sources, DPM_{10} mg/m³	Contribution to average from nonroad sources, DPM_{10} mg/m³
Nationwide	0.6	1.4	1.8	0.5	0.9
Rural population	0.3	0.6	0.7	0.2	0.3
Urban population	0.8	1.6	2.0	0.5	1.1

Source: NATA, 2001. Data available at http://www.epa.gov/ttn/uatw/nata.

Because HAPEM-MS3 is suspected to underestimate exposures in highly exposed populations, 1990 CO concentrations relevant to the most highly exposed populations were used to determine 1990 DPM exposures for different demographic groups in this population. The highest DPM exposures ranged from 0.8 μg/m³ for outdoor workers in St. Louis to 2.0 μg/m³ for outdoor workers in Spokane and up to 4.0 μg/m³ for outdoor children in New York (Table 2-31). The highest exposed demographic groups were those who spend a large portion of their time outdoors. It is important to note that these exposure estimates are lower than the total exposure to DPM because they reflect only DPM from on-road sources and not exposure to nonroad DPM emissions.

Table 2-31. Annual average DPM exposures for 1990 and 1996 in the general population and among the highest exposed demographic groups in nine urban areas and nationwide from on-road sources only using HAPEM-MS3

Urban area	1990 Population average exposure, μg/m³	1996 Population average exposure, μg/m³	Highest DPM exposure in 1990, μg/m³ (demographic group experiencing this exposure)
Nationwide	*0.8*	*0.8*	*NA*
Atlanta, GA	0.8	0.9	NA
Chicago, IL	0.8	0.6	1.3 (outdoor workers)
Denver, CO	0.7	0.8	1.2 (outdoor workers)
Houston, TX	0.6	0.9	0.8 (outdoor workers)
Minneapolis, MN	1.0	1.0	1.5 (outdoor workers)
New York, NY	1.6	1.2	4.0 (outdoor children)
Philadelphia, PA	0.7	0.7	1.2 (outdoor children)
Phoenix, AZ	1.4	1.3	2.4 (nonworking men 18-44)
Spokane, WA	1.3	1.1	2.0 (outdoor workers)
St. Louis, MO	0.6	0.6	0.8 (outdoor workers)

NA - Not available.
Source: U.S. EPA, 1999b, adjusted to reflect HDDV VMT described in U.S. EPA, 2000b.

The HAPEM4 modeling approach provides exposure estimates from on-road and nonroad sources as well as point and area sources for pollutants other than DPM. In addition, HAPEM4 incorporates technical advancements over previous Agency exposure assessments. Instead of using a surrogate pollutant such as CO to estimate exposure, HAPEM4 uses census tract DPM concentrations provided by the ASPEN dispersion model described in Section 2.4.2.3 to estimate DPM exposure for individuals in each census tract in the United States. The exposure modeling results are aggregated to provide county, State, and nationwide exposure estimates. HAPEM4 also incorporates the latest data regarding time-activity patterns from the Consolidated Human Activity Database and the latest data available regarding penetration of PM to indoor environments. The results of this modeling approach are currently undergoing peer review and are therefore considered a draft and subject to change.

Nationwide exposure estimates from HAPEM4 are provided in Table 2-30. The draft National-Scale Assessment 1996 national average estimate of DPM exposure attributable to on-road and nonroad sources is 1.4 μg/m³. On-road sources are estimated to account for 0.5 μg/m³ and nonroad sources 0.9 μg/m³. The HAPEM-MS3 1996 exposure value of 0.8 μg/m³ and the

most recent draft National-Scale Assessment value of 0.5 μg/m^3 differ slightly as a result of the different modeling approaches. Both the HAPEM-MS3 and HAPEM4 exposure results support the risk perspective provided in Chapter 8, Section 8.3.

2.4.3.2.2. ***Personal exposures: microenvironments/hotspots.*** Personal monitoring for DPM exposure has focused on occupationally exposed groups, including railroad workers, mine workers, mechanics, and truck drivers. Although some studies have measured personal exposures to ambient PM, none have conducted detailed chemical analysis to quantify the portion of PM attributable to DE (e.g., using extended species CMB, discussed above). EC concentrations have been reported for some microenvironments and are discussed in this section. Microenvironmental exposures of significant concern include in-vehicle exposures such as school buses and passenger cars as well as near highways and in urban canyons. Because DPM from mobile sources is emitted into the breathing zone of humans, this source has a greater potential for human exposure (per kg of emissions) compared to combustion particulates emitted from point sources.

Recent EC measurements reported for enclosed vehicles driving on Sacramento roadways ranged from below detection limits up to 10 μg/m^3 and from 3 μg/m^3 to 40 μg/m^3 on Los Angeles roadways. Elevated levels of $PM_{2.5}$ and EC were observed when the vehicle being followed was powered by a HD diesel truck or bus (Cal EPA, 1998b). EC is also present in the exhaust of gasoline vehicles, so these measurements are likely to include some EC from gasoline vehicles. The SHEDS (Stochastic Human Exposure and Dose Simulation) model for PM predicts that although the typical person spends only about 5% of his or her time in a vehicle, this microenvironment can contribute on average 20% and as much as 40% of a person's total PM exposure (Burke et al., 2000).

The California Air Resources Board also collected EC near the Long Beach Freeway for 4 days in May 1993 and 3 days in December 1993 (Cal EPA, 1998a). Using emission estimates from their EMFAC7G model and EC and OC composition profiles for diesel and gasoline exhaust, tire wear, and road dust, CARB estimated the contribution of the freeway to DPM concentrations. For the 2 days of sampling in December 1993, DE from vehicles on the nearby freeway was estimated to contribute from 0.7 μg/m^3 to 4.0 μg/m^3 excess DPM above background concentrations, with a maximum of 7.5 μg/m^3.

In 1986, EC concentrations were measured in Glendora, CA, during a carbonaceous aerosol intercomparison study (Cadle and Mulawa, 1990; Hansen and Novakov, 1990). One technique used during the study reported EC concentrations in 1-minute intervals, reflecting the impact from diesel vehicles 50 m from the study site. The diesel vehicles were estimated to contribute up to 5 μg/m^3 EC above the background concentration.

In a study designed to investigate relationships between DE exposure and respiratory health of children in the Netherlands, EC measurements were collected in 23 schools located from 47 m to 377 m from a freeway and in 8 schools located at a distance greater than 400 m from a freeway (Brunekreef, 1999). EC concentrations in schools near freeways ranged from 1.1 $\mu g/m^3$ to 6.3 $\mu g/m^3$, with a mean of 3.4 $\mu g/m^3$, and EC concentrations in schools more than 400 m from freeways ranged from 0.8 $\mu g/m^3$ to 2.1 $\mu g/m^3$, with a mean of 1.4 $\mu g/m^3$. Brunekreef et al. (2000), using a reflectance method to report "soot" or carbonaceous particulate concentrations as a surrogate for EC, found a statistically significant increase in carbonaceous particle concentrations inside and outside of the schools with increasing truck traffic (predominantly diesel), with decreasing distance between the school and the highway, and with an increase in the percent of time the school was downwind of the highway. In additional studies in elderly subjects in Helsinki and Amsterdam, Janssen et al. (2000) reported that outdoor measurements of EC were highly correlated with indoor and personal exposure measurements of EC, supporting the position that short-term increases in outdoor EC concentrations are reflected in increased personal exposures even for those who spend much of their time indoors.

Although there is little quantitative information regarding personal exposure to DPM, certain exposure situations are expected to result in higher than average exposures. Those in the more highly exposed categories would generally include people living in urban areas in which diesel delivery trucks, buses, and garbage trucks frequent the roadways, but also included would be people living near freeways, bus stations, construction sites, train stations, marinas frequented by diesel-powered vessels, and distribution hubs using diesel truck transport. One study using the 1-hydroxypyrene biomarker of DE exposure reported exposure among most (76%) of the 26 adolescents sampled in Harlem (Northridge et al., 1999). In a follow-on study, Kinney et al. (2000) reported EC concentrations from personal monitors worn by study staff on sidewalks at four Harlem intersections that ranged from 1.5 $\mu g/m^3$ to 6 $\mu g/m^3$. The EC concentrations were found to be associated with diesel bus and truck counts such that spatial variations in sidewalk concentrations of EC were attributed to local diesel sources in Harlem.

In any situation in which diesel engines operate and a majority of time is spent outdoors, personal exposures to DE are expected to exceed average exposures. Because a large but currently undefined portion of DPM is emitted during acceleration, those living and working in the vicinity of sources operating in this transient mode could experience highly elevated levels of DPM. DPM enriched in soluble organic material (as opposed to EC) is emitted from LD vehicles, some nonroad equipment, on-road diesel engines during cold-start and motoring conditions, and poorly maintained vehicles. The potential health effects of acute exposures to elevated DPM levels as well as health effects resulting from chronic exposures are discussed in subsequent chapters in this document.

2.4.3.2.3. ***The California Population Indoor Exposure Model.*** CPIEM, developed under contract to the CARB, estimates Californians' exposure to DPM using distributions of input data and a Monte Carlo approach (Cal EPA, 1998a). This model uses population-weighted outdoor DPM concentrations in a mass balance model to estimate DPM concentrations in four indoor environments: residences, office buildings, schools, and stores/retail buildings. The model takes into account air exchange rates, penetration factors, and a net loss factor for deposition/removal. In four additional environments (industrial plants, restaurants/lounges, other indoor places, and enclosed vehicles), assumptions were made about the similarity of each of these spaces to environments for which DPM exposures had been calculated. Industrial plants and enclosed vehicles were assumed to have DPM exposures similar to those in the outdoor environment; restaurants/lounges were assumed to have DPM concentrations similar to stores; and other indoor places were assumed to have DPM concentrations similar to offices. The estimated DPM concentrations in the indoor and outdoor environments range from 1.6 $\mu g/m^3$ to 3.0 $\mu g/m^3$ (Table 2-32).

Table 2-32. Modeled and estimated concentrations of DPM in microenvironments for California for all sources

Microenvironment	Estimated mean DPM (stdev), $\mu g/m^3$
Residences	1.9 (0.9)
Offices	1.6 (0.7)
Schools	1.9 (0.8)
Stores/public/retail bldgs	2.1 (0.9)
Outdoor places	3.0 (1.1)
Industrial plants[a]	3.0 (1.1)
Restaurants/lounges[a]	2.1 (0.9)
Other indoor places[a]	1.6 (0.7)
Enclosed vehicles[a]	3.0 (1.1)

[a]Concentrations assumed based on similarity with modeled environments.
Source: California EPA, 1998a.

The DPM concentrations reported in Table 2-32 were used as input to CPIEM, and time-activity patterns for children and adults were used to estimate total indoor and total air exposures to DPM. Overall, total indoor exposures were estimated to be 2.0 ± 0.7 μg/m^3, and total air exposures (indoor and outdoor exposures) were 2.1 ± 0.7 μg/m^3 (Table 2-33). The South Coast Air Basin and the San Francisco Bay Area were also modeled using CPIEM, where total air exposures to DPM were estimated to be 2.5 ± 0.9 μg/m^3 and 1.7 ± 0.9 μg/m^3, respectively.

Table 2-33. Estimated indoor air and total air exposures to DPM in California in 1990

Exposed population	Total indoor exposure (stdev), μg/m^3	Total air exposure, (stdev), μg/m^3
All Californians	2.0 (0.7)	2.1 (0.8)
South Coast Air Basin	2.4 (0.9)	2.5 (0.9)
San Francisco Bay Area	1.7 (0.9)	1.7 (0.9)

Source: California EPA, 1998a.

Exposure estimates were also made by Cal EPA (1998a) for 1995, 2000, and 2010 using a ratiometric approach to 1990 exposures. Total air exposures reported for 1995 and projected for 2000 and 2010 were 1.5 μg/m^3, 1.3 μg/m^3, and 1.2 μg/m^3, respectively.

2.5. SUMMARY AND DISCUSSION

This chapter summarizes information regarding the history of the use of diesel engines, technological developments and their impact on emissions over time, Federal standards on DE, the chemical and physical character of DE, atmospheric transformations of DE, and ambient DE concentrations and exposures. The aspects of each of these topics that are most relevant to the discussion of health effects in later chapters of this document are summarized here. Because the majority of information regarding the chemical composition and historical changes in DE pertains to on-road diesel engines, these data are discussed in greater detail than diesel emissions from nonroad equipment. Where possible, nonroad emissions were discussed in Chapter 2 and are briefly summarized here.

2.5.1. History of Diesel Engine Use, Standards, and Technology

The use of diesel engines in the trucking industry began in the 1940s, and diesel engines slowly displaced gasoline engines among HD trucks, accounting for 36% of new HD truck sales in 1960, 85% of sales in 1970, and almost 100% of sales in 1997. It is estimated that in 2000, HD diesel vehicles will travel more than 224 billion miles (U.S. EPA, 2000b). In 1997, on-highway HD diesel engines contributed 66% of the $PM_{2.5}$ emitted by on-highway vehicles.

To understand changes in emissions over time, it is important to note the difference between model year emission trends and calendar year emission trends. Emission trends by model year refer to the year in which an engine was made; the emission rate is specific to the technology and regulations in effect for that year. Emissions in a specific calendar year refer to aggregate emissions due to the mix of model year engines on the road. Because of the time required for fleet turnover, emission rates for the on-road fleet in any calendar year are not as low as the most recent model year emission rate. In 1997, 40% of the HD vehicles on the road were at least 10 years old and traveled approximately 17% of total HD vehicle miles.

EPA set a smoke standard for on-road HD diesel engines beginning with the 1970 model year. In the ensuing years, standards for PM from diesel engines for on-road applications decreased from 0.6 g/bhp-hr in 1988 to 0.1 g/bhp-hr for trucks in 1994-1995 and 0.05 g/bhp-hr for buses in 1996-1997. Calendar year emission contributions of PM from diesel engines to national PM_{10} inventories reflect decreases expected to result from Federal regulations, because the emission factor models (MOBILE5 and PART5) used to provide emission estimates for mobile sources largely use engine test data required for certification. The U.S. EPA Trends Report estimates that PM_{10} emissions attributable to on-road diesel vehicles decreased 27% between 1980 and 1998. DPM emission factors (g/mi by model year) measured from in-use vehicles decreased on average by a factor of six from the mid-1970s to the mid-1990s.

It is important to note that in spite of the decreasing trend in DPM emission factors by model year, a wide range in emission factors from in-use testing is reported, even for newer model year HD vehicles (from less than 0.1 g/mi to more than 1 g/mi for model year 1996 vehicles). The high variability in DPM emissions within one model year has been attributed to deterioration[3] and differences in measurement methods and test conditions at the various testing facilities. Studies in which consistent testing methods were used suggest that deterioration (even for newer model year engines) causes some of the variability in emission factors, whereas other

[3]Deterioration includes increases in emission rates (g/bhp hr) due to normal wear as well as manufacturing defects and malfunctions such as retarded timing, fuel injector malfunction, smoke limiting mechanism problems, clogged air filter, wrong or worn turbocharger, clogged intercooler, engine mechanical failure, excess oil consumption, and electronics that have been tampered with or have failed.

studies clearly demonstrate the important influence of test conditions and driving protocols (e.g., aggressive driving) on DPM emission factors.

Even though significant reductions in DPM from diesel vehicle emissions for on-road applications have been realized, diesel engines (nonroad and on-road combined) are still significant contributors to 1998 inventories of particulate matter, contributing approximately 23% of $PM_{2.5}$ emissions (not including the contribution from natural and miscellaneous sources).

Technology innovations that impact diesel engine emissions have occurred in the years since 1960, in particular the advent of turbocharging with charge air cooling and direct-injection engines. The use of these new technologies tends to lower emissions from on-road diesel engines; until the late 1970s, however, engines were optimized for performance rather than emissions, so the effect on emissions prior to this time was small. The limited amount of data available indicates that on-road engines in the 1950 to 1975 timeframe had DPM emissions similar to, and in some cases higher than, those of the mid-1970 engines that were not yet controlled for particulates.

Few data are available to assess the changes in emission rates from locomotive, marine, or other nonroad diesel engine sources over time. It is expected that because the typical lifespan of a locomotive engine is at least 40 years and PM regulations for these engines do not take effect until 2000, PM emission rates by model year from locomotives are not likely to have changed substantially since the introduction of the diesel engine into the railroad industry in the early 1950s.

Particulate matter regulations for nonroad diesel equipment are not as stringent as PM regulations for on-road diesel engines. Although PM emissions have declined for on-road trucks, it is estimated that PM_{10} emissions from nonroad diesel engines increased 17% between 1980 and 1998. DPM emissions from nonroad diesel engines are expected to continue to increase from current levels in the absence of new regulations. No information is available regarding changes in the chemical composition of nonroad engine emissions over time.

2.5.2. Physical and Chemical Composition of Diesel Exhaust

Complete and incomplete combustion of fuel in the diesel engine results in the formation of a complex mixture of hundreds of organic and inorganic compounds in the gas and particle phases. Among the gaseous components of DE, the aldehydes are particularly important because of their health effects and because they are an important fraction of the gaseous emissions. Formaldehyde makes up a majority of the aldehyde emissions (65%-80%) from diesel engines, with the next most abundant aldehydes being acetaldehyde and acrolein. Other gaseous components of DE that are notable for their health effects include benzene, 1,3-butadiene, PAH, and nitro-PAH. Dioxin compounds have also been detected in trace quantities in DE and

currently account for 1.2% of the national inventory. Dioxin compounds are known to accumulate in certain foods, such as beef, poultry, and dairy products. It is unknown whether deposition of DE emissions has an impact on food chains in local areas.

DPM contains EC, OC, and small amounts of sulfate, nitrate, metals, trace elements, water, and unidentified compounds. DPM is typically composed of more than 50% to approximately 75% EC depending on the age of the engine, deterioration, HD versus LD, fuel characteristics, and driving conditions. The OC portion of DPM originates from unburned fuel, engine lubrication oil, and low levels of partial combustion and pyrolysis products and typically ranges from approximately 19% to 43%, although the range can be broader depending on many of the same factors that influence the EC content of DPM. Polyaromatic hydrocarbons generally constitute less than 1% of the DPM mass. Metal compounds and other elements in the fuel and engine lubrication oil are exhausted as ash and typically make up 1%-5% of the DPM mass. Elements and metals detected in DE include barium, calcium, chlorine, chromium, copper, iron, lead, manganese, mercury, nickel, phosphorus, sodium, silicon, and zinc. The composition of DPM contrasts strongly with the typical chemical composition of ambient $DPM_{2.5}$ that is dominated by sulfate for aerosols measured in the eastern United States and by nitrate, ammonium, and OC in the western United States.

Approximately 1% to 20% of the mass of DPM in DE is in the ultrafine size range (nuclei-mode), with the majority of particles ranging in size from 0.005 to 0.05 microns and having a mean diameter of about 0.02 microns. These particles account for 50%-90% of the number of particles. These ultrafine particles are largely composed of sulfate and/or sulfate with condensed OC.

Evidence regarding an increase in the number of ultrafine particles from new HD engines is inconclusive. The dilution conditions used to measure the size distribution of DE have a large impact on the number of ultrafine particles quantified. To understand the size distribution of DPM to which people are exposed will require measurements under conditions that more closely resemble ambient conditions.

Approximately 80%-95% of the mass of particles in DE is in the size range from 0.05-1.0 microns, with a mean particle diameter of about 0.2 microns, and therefore in the fine PM size range. Diesel particles in the 0.05-1.0 micron range are aggregates of primary spherical particles consisting of an EC core, adsorbed organic compounds, sulfate, nitrate, and trace elements. These particles have a very large surface area per gram of mass, which makes them an excellent carrier for adsorbed inorganic and organic compounds and, due to their small size, they can effectively reach the lower portions of the respiratory tract. The EC core has a high specific surface area of approximately 30-90 m^2/g.

Because of the potential toxicological significance of the organic components associated with DPM, it is important to understand, to the extent possible, the historical changes in the amount and composition of the DPM-associated organic fraction. The organic component of DPM has typically been characterized by extraction with organic solvents, although other techniques such as thermogravimetric methods have also been used. Results from studies using similar extraction methods were compared to characterize historical changes in the SOF emission rates, the percentage of DPM comprised by SOF, and the composition of SOF. Data from both engine and chassis dynamometer tests suggest that SOF emission rates have decreased by model year from 1975 to 1995. When expressed as a percentage of total DPM, the contribution of SOF to total DPM demonstrates a wide range of variability that may be attributed to different test cycles, different engine types, and different deterioration rates among the vehicles tested. Currently, LD diesel engines emit DPM with a higher fraction of SOF than do HD engines.

Chassis dynamometer tests demonstrate an overall decrease in the mass percentage contribution of SOF to DPM, ranging from 10% to 60% in the 1980s and ~5% to 20% in the 1990s. In contrast, engine dynamometer tests demonstrate that typically 10%-50% of DPM mass is soluble organic matter for engines in model years 1980-1995. The higher SOF fraction of DPM from 1990s model year engine dynamometer tests is attributed primarily to the differences in the engine and chassis dynamometer driving cycles. The engine dynamometer testing includes high- speed and low-load or low-speed lugging test modes in the engine Federal Test Procedure that produce DPM with a high SOF fraction.

The chassis dynamometer data are considered to reflect real-world trends in emissions from heavy HD vehicles by model year because vehicles from different model years, with different mileage and different levels of deterioration, are represented. Thus, it is expected that the percentage of SOF from new (1990 or later) model year heavy HD diesel vehicles is lower than that from older vehicles. This expectation is supported by data demonstrating an overall increase in the fraction of EC in the carbonaceous component of DPM. The important observation from the engine test data is that some driving modes occurring in real-world applications even with new (post-1990) engines may produce DPM with a high SOF component (up to 50%).

PAH and nitro-PAH are present in DPM from both new and older engine exhaust. There is no information to suggest that the overall PAH composition profile for DPM has changed. There are too few data to speculate on the changes in emissions of total PAH, nitro-PAH, or PAH and nitro-PAH components such as BaP and 1-NP. The data suggest that differences in a vehicle's engine type and make, general engine condition, fuel composition, and test conditions can influence the emissions levels of PAH. Some studies suggest that fuel composition is the most important determinant of PAH emissions. There is limited evidence that gas-phase PAH

emission rates increase with higher fuel PAH content and that some particle-phase PAH emission rates increase with higher fuel PAH content. These data suggest that during the period from 1960 to 1986, when the aromatic content of fuel increased, PAH emissions may have increased until the aromatic content of diesel fuel was capped in 1993. The aromatic content of nonroad diesel fuel is not federally regulated and is typically greater than 30%. PAH emissions from nonroad equipment would also be expected to vary with the PAH content of the fuel.

Currently, information regarding emission rates, chemical composition, and relative contribution of DPM from high-emitting HD diesel vehicles is not available and may significantly change the understanding of DPM composition to which people are exposed. Some studies have reported a substantial number of smoking diesel trucks in the in-use fleet. Although the correlation between smoke and particulate concentration varies with the driving cycle and measurement method, the results of smoke opacity tests suggest that high-emitting HD diesel vehicles may be important contributors to ambient DE and DPM concentrations.

The chemical composition of DPM to which people are currently exposed is determined by a combination of older and newer technology on-road and nonroad engines. Consequently, the decrease in the SOF of DPM by model year does not directly translate into a proportional decrease in DPM-associated organic material to which people are currently exposed. In addition, the impact from high-emitting and/or smoking diesel engines is not quantified at this time. Because of these uncertainties, the changes in DPM composition over time cannot presently be quantified. The data clearly indicate that toxicologically significant organic components of DE (e.g., PAHs, PAH derivatives, nitro-PAHs) were present in DPM and DE in the 1970s and are still present in DPM and DE as a whole.

Although a significant fraction of ambient DPM (over 50% is possible) is also emitted by nonroad equipment, there are no data available to characterize changes in the chemical composition of DPM from nonroad equipment over time.

Some analysts project that diesel engines will increase substantially in the LD fleet in coming years. Although LD engines currently emit DPM with higher SOF than HD engines of the same model year, recently promulgated Tier 2 standards will require control measures in the 2004-2007 timeframe that will reduce PM emissions from these vehicles. These control measures provide some assurance that even if LD diesel use increases, DPM emitted from these vehicles will likely have a smaller SOF component than such engines currently emit.

2.5.3. Atmospheric Transformation of Diesel Exhaust

An understanding of the physical as well as chemical transformations of DE in the atmosphere is necessary to fully understand the impact of this complex chemical mixture on human health. In the past two decades, data acquired from laboratory and ambient experiments

have provided information regarding the atmospheric loss processes and transformation of DE, but knowledge concerning the products of these chemical transformations is still limited. A recent study has suggested that DPM exposed to ambient levels of ozone is sufficiently altered to increase the rat lung inflammatory effect compared with DPM not exposed to ozone.

Studies investigating the chemical and physical changes of DE emissions suggest that there is little or no hygroscopic growth of primary diesel particles. This observation suggests that the small size of DPM particles might be maintained upon inhalation, particularly near the emission source, allowing these particles to reach the lower portions of the respiratory tract. Increased solubility can increase the removal efficiency of secondary diesel particles compared with their precursor compounds. Secondary aerosols from DE may also exhibit different biological reactivities from the primary particles. For example, there is evidence for nitration of some PAH compounds resulting in the formation of nitroarenes that are often more mutagenic than their precursors.

2.5.4. Ambient Concentrations and Exposure to Diesel Exhaust

Because of changes in engine technology and DPM emissions over time, ambient concentrations reported from studies before 1990 are compared here to those reported after 1990. There are no studies in which direct comparisons can be made because of different analytical and modeling tools used to assess DPM ambient levels.

DPM concentrations reported from CMB and dispersion modeling studies in the 1980s suggest that in urban and suburban areas (Phoenix, AZ, and Southern California), annual average DPM concentrations ranged from 2 to 13 $\mu g/m^3$, with possible maximum daily values in Phoenix of 22 $\mu g/m^3$. In these studies, the average contribution of DPM in urban areas to total ambient PM ranged from 7% in Pasadena, CA, to 36% in Los Angeles.

In the 1990 timeframe, annual or seasonal average DPM concentrations reported in CMB studies and from EC measurements for urban and suburban areas range from 1.2 to 4.5 $\mu g/m^3$. The contribution of DPM to ambient PM at these sites averaged 10%-15% on a seasonal or annual basis, with contributions up to 38% on individual days (Brighton, CO). Dispersion modeling on individual days in Southern California in the 1990s predicts DPM concentrations ranging from 1.9 to 4.4 $\mu g/m^3$ (8%-12% of ambient PM). On individual days at a major bus stop in New York City, DPM concentrations were reported to reach 46.7 $\mu g/m^3$ and averaged 53% of ambient PM, highlighting the important influence of diesel bus traffic in an urban street canyon.

In nonurban and rural areas in the 1980s, DPM concentrations reported range from 1.4 to 5 $\mu g/m^3$ and on average comprised 5%-12% of the ambient aerosol. In the 1990s, nonurban air basins in California were reported to have DPM concentrations ranging from 0.2-2.6 $\mu g/m^3$.

Although estimates from emissions models suggest that DPM emissions from on-road sources decreased during the 1990s, the atmospheric data available do not provide a clear indication of trends in DPM concentrations but are likely to be more a reflection of the choice in sampling sites, source apportionment methods, and modeling techniques. In general, from the limited number of studies available it appears that DPM concentrations averaged over at least a season in the 1990s typically ranged from 1-4 $\mu g/m^3$. These data can be used in model-monitor comparisons and to provide an indication of long-term average exposures in some urban areas. Additional work is needed to assess ambient DPM and DE concentrations in several urban environments, to assess microenvironments, and to evaluate the relative impact of nonroad and on-road sources on concentrations.

A comprehensive exposure assessment cannot currently be conducted because of the lack of data. Information regarding DPM in occupational environments suggests that exposure ranges up to approximately 1,280 $\mu g/m^3$ for miners, with lower exposure measured for railroad workers (39-191 $\mu g/m^3$), firefighters (4-748 $\mu g/m^3$), public transit personnel who work with diesel equipment (7-98 $\mu g/m^3$), mechanics and dockworkers (5-65 $\mu g/m^3$), truck drivers (2-7 $\mu g/m^3$), and bus drivers (1-3 $\mu g/m^3$). Work area concentrations at fixed sites are often higher than measured exposures, especially for mining operations or other enclosed spaces. For several occupations involving DE exposure, an increased risk of lung cancer has been reported by epidemiologic studies (discussed in Chapter 7). An estimate of the 70-year lifetime environmental exposure equivalent to these occupational exposures provides one means of comparing the potential overlap between occupational exposures and exposures modeled for the general public. The estimated 70-year lifetime exposures equivalent to those for the occupational groups discussed above range from 0.4-2 $\mu g/m^3$ on the low end to 2-269 $\mu g/m^3$ on the high end.

The EPA has performed a national-scale exposure assessment for DPM from on-road sources. Current national exposure modeling using the HAPEM-MS3 model suggests that in 1996, annual average DPM exposure from on-road DE sources in urban areas was 0.8 $\mu g/m^3$, whereas in rural areas, exposures were 0.4 $\mu g/m^3$. Among 10 urban areas in which DPM exposures were modeled, 1996 annual average exposure from on-road DE sources ranged from 0.6 $\mu g/m^3$ to 1.2 $\mu g/m^3$. Outdoor workers and children who spent a large amount of time outdoors were estimated to have elevated DPM exposures in 1990, ranging up to 4.0 $\mu g/m^3$ from on-road sources only. Based on the national inventory, nonroad emission sources could contribute at least twofold more DPM than that emitted by on-road sources. Results of the draft National-Scale Assessment for 1996 indicate that national average exposure to DPM, including nonroad sources, is 1.4 $\mu g/m^3$, with 0.9 $\mu g/m^3$ of that average attributed to emissions from nonroad sources.

Low-end exposures for many of the occupational groups overlap 1990 and 1996 exposures from on-road sources modeled for the general population (0.8 $\mu g/m^3$) and for the more highly exposed groups. This potential overlap, or small difference between occupational and ambient exposures, presents a concern that health effects observed in occupational groups may also be evidenced in the general population. The potential magnitude of this risk is discussed in Chapter 8.

In different exposure environments, the types of diesel vehicles, their mode of operation, maintenance, atmospheric transformation, and many additional factors influence the chemical nature and quantity of DPM to which people are exposed. The potential health consequences of both short- and long-term exposures to DE are discussed in the following chapters of this document.

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3. DOSIMETRY OF DIESEL PARTICULATE MATTER

3.1. INTRODUCTION

Animals and humans receive different internal doses when breathing the same external concentrations of airborne materials such as diesel particulate matter (DPM) (Brain and Mensah, 1983; Schlesinger, 1985). The dose received in different species differs from the aspects of the total amount deposited within the respiratory tract, the relative distribution of the dose to specific regions in the respiratory tract, and the residence time of these materials within the respiratory tract, i.e., clearance. Using an external concentration breathed by laboratory animals as a basis for any guidance for human exposure to DPM would then be an inadequate approximation of the total and regional dose that humans may receive.

The reason for the existence of this chapter and for consideration about interspecies dosimetry is the lack of human health effect data on DPM and the concomitant need to be able to evaluate existing animal data from the aspect of an equivalent human dose. The objective of this chapter is to evaluate and address this issue of interspecies dosimetric differences through:

- A general overview of what is known about how particles like DPM are deposited, transported to, and cleared from the respiratory tract. Information on both laboratory animals (mainly rodents) and humans will be considered and interspecies similarities and differences highlighted.
- An overview of what is known about the bioavailability of the organic compounds adsorbed onto DPM from information in humans, animals, and in vitro studies, and from model predictions.
- An evaluation of the suitability of available dosimetric models and procedures for DPM to estimate interspecies extrapolations whereby an exposure scenario, conditions, and outcome in laboratory animals are adjusted to an equivalent outcome in humans via calculation of an internal dose.

The focus in this chapter will be on the particulate fraction of diesel emissions, i.e, DPM. Although diesel engine exhaust consists of a complex mixture of typical combustion gases, vapors, low-molecular-weight hydrocarbons, and particles, it is the particle phase that is considered to be of major health concern. The major constituents of diesel engine exhaust (DE) and their atmospheric reaction products are described in Chapter 2.

As will be deduced in Chapter 5, pulmonary toxicity and carcinogenicity are the major focal points of diesel toxicity and of DPM deposition. Therefore, dosimetric considerations are limited to the lung although DPM deposition would occur throughout the respiratory tract, from

the nares to the alveoli. Aspects of respiratory tract dosimetry to be considered in this chapter include the characteristics of DPM, deposition of DPM throughout the respiratory tract, the conducting airways and alveolar regions, normal DPM clearance mechanisms and rates of clearance in both these regions, clearance rates during lung overload (in rats), elution of organics from DPM, transport of DPM to extra-alveolar sites, and the interrelationships of these factors.

The overall goal in this chapter follows from the objective—to judge the feasibility and suitability of procedures allowing for derivation of an internal dose estimate of DPM for humans, i.e., of a human equivalent concentration to exposure concentrations and conditions used in animal studies. This goal is of significance especially in the quantitative dose-response analysis of DPM effects in laboratory animals proposed in Chapter 6.

3.2. CHARACTERISTICS OF INHALED DIESEL PARTICULATE MATTER

The formation, transport, and characteristics of DPM are among the subjects considered in detail in Chapter 2. DPM consists of aggregates of spherical carbonaceous particles (typically about 0.2 μm mass median aerodynamic diameter [MMAD] or, more appropriately, mass median thermodynamic diameter [MMTD]) to which significant amounts of higher-molecular-weight organic compounds are adsorbed. DPM has an extremely large surface area that allows for the adsorption of organic compounds (see Chapter 2, Section 2.2.2). The organic carbon portion of DPM can range from at least 19% to 43% from highway diesel engines; no data are available to characterize the organic content of DPM from nonroad engines. The toxicologically relevant organic chemicals include high-molecular-weight hydrocarbons such as the polycyclic aromatic hydrocarbons (PAHs) and their derivatives (Chapter 2, Section 2.2.8).

3.3. REGIONAL DEPOSITION OF INHALED DIESEL PARTICULATE MATTER

This section discusses the major factors controlling the disposition of inhaled particles. Note that disposition is defined as encompassing the processes of deposition, absorption, distribution, metabolism, and elimination. The regional deposition of particulate matter in the respiratory tract is dependent on the interaction of a number of factors, including respiratory tract anatomy (airway dimensions and branching configurations), ventilatory characteristics (breathing mode and rate, ventilatory volumes and capacities), physical processes (diffusion, sedimentation, impaction, and interception), and the physicochemical characteristics (particle size, shape, density, and electrostatic attraction) of the inhaled particles. Regional deposition of particulate material is usually expressed as deposition fraction of the total particles or mass inhaled and may be represented by the ratio of the particles or mass deposited in a specific region to the number or mass of particles inspired. The factors affecting deposition in these various regions and their importance in understanding the fate of inhaled DPM are discussed in the following sections.

It is beyond the scope of this document to present a comprehensive account of the complexities of respiratory mechanics, physiology, and toxicology, and only a brief review will be presented here. The reader is referred to publications that provide a more in-depth treatment of these topics (Weibel, 1963; Brain and Mensah, 1983; Raabe et al., 1988; Stöber et al., 1993; U.S. EPA, 1996).

The respiratory tract in both humans and experimental mammals can be divided into three general regions on the basis of structure, size, and function: the extrathoracic (ET), the tracheobronchial (TB), and the alveolar (A). In humans, inhalation can occur through the nose or mouth or both (oronasal breathing). Animal models used in respiratory toxicology studies, particularly the rat, however, are obligate nose breathers.

3.3.1. Deposition Mechanisms

This section provides an overview of the basic mechanisms by which inhaled particles deposit within the respiratory tract. Details concerning the aerosol physics that explain both how and why particle deposition occurs as well as data on total human respiratory tract deposition are presented in detail in the earlier PM Criteria Document (U.S. EPA, 1996) and will only be briefly summarized here. For more extensive discussions of deposition processes, refer to reviews by Morrow (1966), Raabe (1982), U.S. EPA (1982), Phalen and Oldham (1983), Lippmann and Schlesinger (1984), Raabe et al. (1988), and Stöber et al. (1993).

As pictorially represented in Figure 3-1, particles may deposit by five major mechanisms (inertial impaction, gravitational settling, Brownian diffusion, electrostatic attraction, and interception). The relative contribution of each deposition mechanism to the fraction of inhaled particles deposited varies for each region of the respiratory tract.

It is important to appreciate that these processes are not necessarily independent but may, in some instances, interact with one another such that total deposition in the respiratory tract may be less than the calculated probabilities for deposition by the individual processes (Raabe, 1982). Depending on the particle size and mass, varying degrees of deposition may occur in the ET (or nasopharyngeal), TB, and A regions of the respiratory tract.

Upon inhalation of particulate matter such as that found in DE, particle deposition will occur throughout the respiratory tract. Because of high airflow velocities and abrupt directional changes in the ET and TB regions, inertial impaction is a primary deposition mechanism, especially for particles ≥ 2.5 µm d_{ae} (aerodynamic equivalent diameter). Although inertial impaction is a prominent process for deposition of larger particles in the tracheobronchial region, it is of considerably less significance as a determinant of regional deposition patterns for

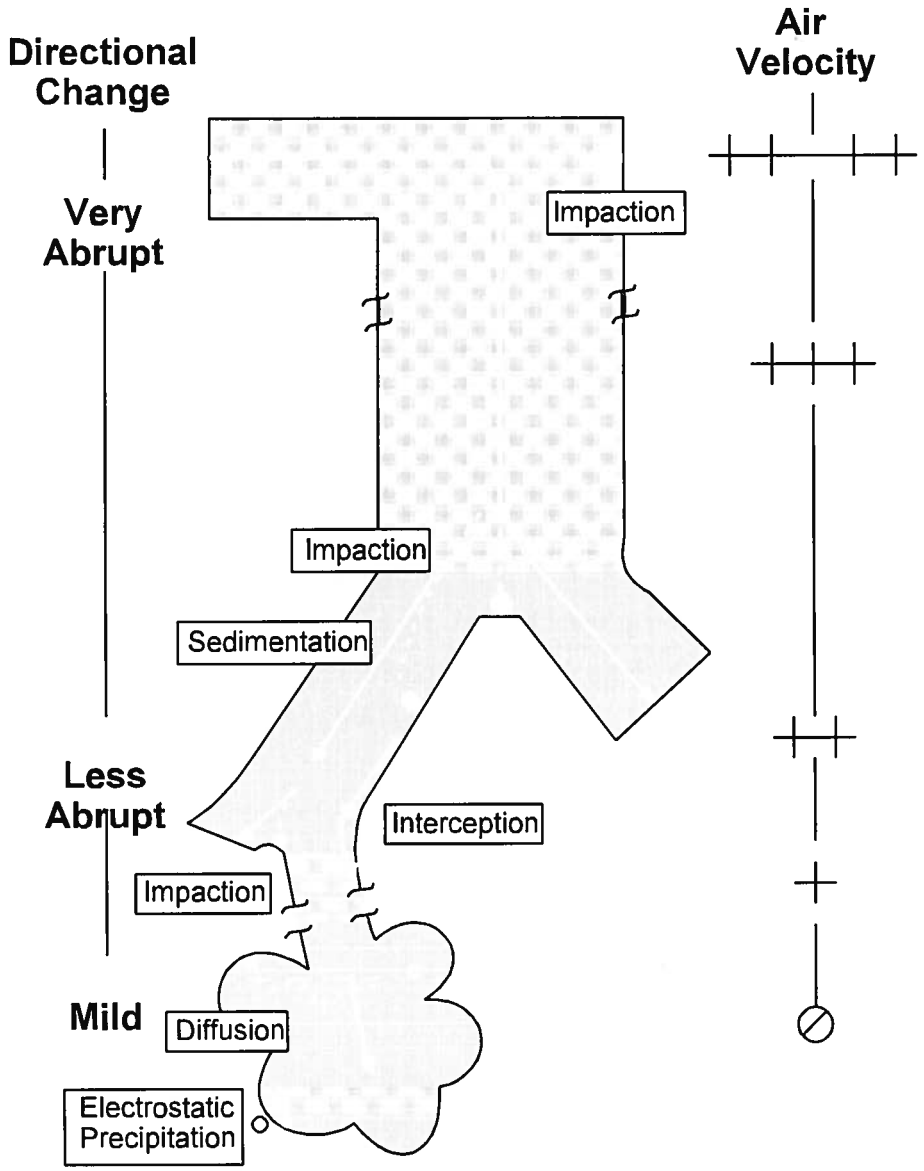

Figure 3-1. Schematic representation of major mechanisms, including diffusion, involved in particle deposition. Airflow is signified by the arrows and particle trajectories by the dashed line.

DPM, which have a $d_{ae} \leq 0.2$ μm and may be considered a rather polydisperse distribution with sigma g values of 2.4 and greater.

All aerosol particles are continuously influenced by gravity, but particles with a $d_{ae} > 0.5$ μm are affected to the greatest extent. A spherical compact particle will acquire a terminal settling velocity when a balance is achieved between the acceleration of gravity acting on the particle and the viscous resistance of the air; it is this velocity that brings the particle into contact with airway surfaces. Both sedimentation and inertial impaction cause the deposition of many particles within the same size range. These deposition processes act together in the ET and TB regions, with inertial impaction dominating in the upper airways and sedimentation becoming increasingly dominant in the lower conducting airways, especially for the largest particles that can penetrate into the smaller bronchial airways.

As particle diameters become <1 μm, the particles are increasingly subjected to diffusive deposition because of random bombardment by air molecules, which results in contact with airway surfaces. A d_{ae} of 0.5 μm is often considered a boundary between diffusion and aerodynamic (sedimentation and impaction) mechanisms of deposition. Thus, instead of having a d_{ae}, diffusive particles of different shapes can be related to the diffusivity of a thermodynamic equivalent size based on spherical particles (Heyder et al., 1986). Diffusive deposition of particles is favored in the A region of the respiratory tract as particles of this size are likely to penetrate past the ET and TB regions.

Electrostatic precipitation is deposition related to particle charge. The electrical charge on some particles may result in an enhanced deposition over what would be expected from size alone. This is due to image charges induced on the surface of the airway by these particles, or to space-charge effects whereby repulsion of particles containing like charges results in increased migration toward the airway wall. The effect of charge on deposition is inversely proportional to particle size and airflow rate. A recent study employing hollow airway casts of the human tracheobronchial tree that assessed deposition of ultrafine (0.02 μm) and fine (0.125 μm) particles found that deposition of singly charged particles was 5-6 times that of particles having no charge, and 2-3 times that of particles at Boltzmann equilibrium (Cohen et al., 1998). This suggests that within the TB region of humans, electrostatic precipitation may be a significant deposition mechanism for ultrafine and some fine particles, the latter of which are inclusive of DPM. Thus, although electrostatic precipitation is generally a minor contributor to overall particle deposition, it may be important for DPM.

Interception is deposition by physical contact with airway surfaces and is most important for fiber deposition (U.S. EPA, 1996).

Figure 3-2 shows the regional (ET, TB, A) deposition in the human respiratory tract as influenced by particle size. Keeping in mind that DPM is a polydisperse distribution with 0.2 μm

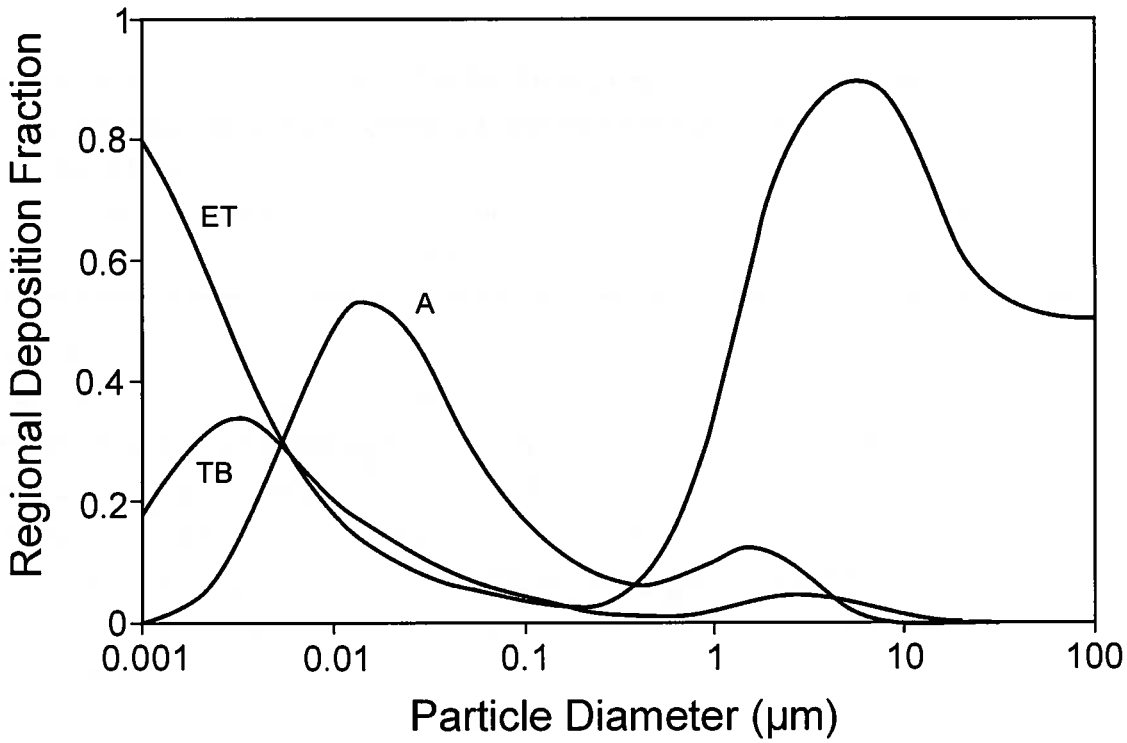

Figure 3-2. Generalized regional deposition fractions of various sized particles in the human respiratory tract. (Adapted from the International Commission on Radiological Protection (ICRP) Publication 66 (1994) model. For unit density, spherical particles inhaled through the nose by an adult male with a tidal volume of 1250 mL, respiratory frequency of 20 min^{-1}, and functional residual capacity (FRC) of 3300 mL.) ET, extrathoracic; TB, tracheobronchial; A, alveolar.

being only the median diameter, it can be seen that principal fraction particles sized from < 0.2 down to around 0.002 µm would, as predicted based on their size and the expected mechanism of diffusion, deposit in the alveolar region. Particles below this size range (and above around 4 µm) tend to deposit in the ET region. Specific modeling results for deposition of DPM particles inclusive of their distribution (i.e., σ_g) are presented in Section 3.6.

3.3.1.1. *Biological Factors Modifying Deposition*

The available experimental deposition data in humans are commonly derived using healthy adult Caucasian males. Various factors can act to alter deposition patterns from those obtained in this group. The effects of different biological factors, including gender, age, and respiratory tract disease, on particle deposition have been reviewed previously (U.S. EPA, 1996, Section 10.4.1.6). In general, there appears to be an inverse relationship between airway resistance and total deposition.

Differences in patterns of deposition between humans and animals have been summarized (U.S. EPA, 1996; Schlesinger, 1985) and show clearly that when exposed to the same aerosol or gas, humans and animals receive doses that may differ in both total and regional (i.e., ET, TB, or A) deposition from a number of variables including particle size, especially for larger sized particles, i.e. $d_{ae} \geq 1$ μm. Such interspecies differences are important because the adverse toxic effect is likely more related to the quantitative pattern of deposition within the respiratory tract than to the exposure concentration; this pattern determines not only the initial respiratory tract tissue dose but also the specific pathways by which the inhaled material is cleared and redistributed (Schlesinger, 1985). Such differences in initial deposition must be considered when relating biological responses obtained in laboratory animal studies to effects in humans.

The deposition patterns of inhaled diesel particles in the respiratory tract of humans and mammalian species has been reviewed (Health Effects Institute, 1995). Schlesinger (1985) showed that physiological differences in the breathing mode for humans (nasal or oronasal breathers) and laboratory rats (obligatory nose breathers), combined with different airway geometries, resulted in significant differences in lower respiratory tract deposition patterns for larger sized particles (>1 μm d_{ae}) in that a much lower fraction of inhaled larger particles is deposited in the alveolar region of the rat compared with humans. However, alveolar deposition of the much smaller DPM (around 0.2 μm d_{ae}) was not affected as much by the differences among species, as was demonstrated in model calculations by Xu and Yu (1987). These investigators modeled the deposition efficiency of inhaled DPM in rats, hamsters, and humans on the basis of calculations of the models of Schum and Yeh (1980) and Weibel (1963). These simulations (Figure 3-3) indicate relative deposition patterns in the lower respiratory tract (trachea = generation 1; alveoli = generation 23) and are similar among hamsters, rats, and humans. Variations in alveolar deposition of DPM over one breathing cycle in these different species were predicted to be within 30% of one another (Xu and Yu, 1987). Xu and Yu (1987) note that this similarity is concordant with the premise that deposition of the submicron diesel particles is dominated by diffusion rather than sedimentation or impaction. Although these data assumed nose-breathing by humans, the results would not be very different for mouth-breathing because of the low filtering capacity of the nose for particles in the 0.1 to 0.5 μm range (see Figure 3-2).

The preceding discussion addresses deposition patterns and deposition efficiencies of DPM in the respiratory tract of various species including humans. The alveolar region was focused upon primarily because, as shown in Chapter 5, this region is where adverse effects from long-term DPM exposure are typically observed. For dosimetric calculations and modeling, however, it would be of much greater importance to consider the actual deposited dose. Table 3-1 presents the analysis of Xu and Yu (1987) on prediction of the deposited doses of DPM

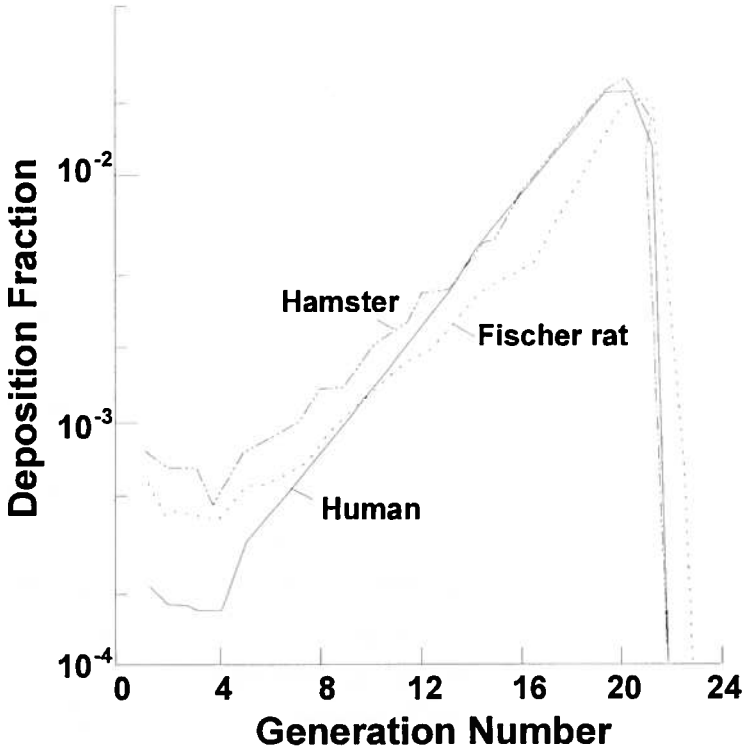

Figure 3-3. Modeled deposition distribution patterns of inhaled DE particles in the airways of different species. Generation 1-18 are TB; >18 are A.

inhaled in 1 min in the lungs of humans, rats, and hamsters on three different bases: the total lung volume (M), the surface area of all lung airways (M_1), or the surface area of the epithelium of the alveolar region only (M_2). According to this analysis, the deposited dose is lower in humans than in the two rodent species regardless of how the deposited dose is expressed. These results are most certainly due predominately to the greater respiratory exchange rate in rodents and smaller size of the rodent lung. Table 3-1 also indicates that the differences (between humans to animals) are less on a surface area basis (≈3-fold) than on a lung volume basis (≈14-fold). This is due to larger alveolar diameters and concomitant lower surface area per unit of lung volume in humans. Such differences in the deposited dose in relevant target areas such as the alveolar region are important and have to be considered when extrapolating the results from DPM exposure studies in animals to humans. As will be discussed elsewhere in this document, procedures for dose extrapolation from animals to humans includes considering the process of clearance, with clearance measurements being in relation to surface area rather than to volume. Thus predicted doses of particulates would be based on surface areas, such as M_1 andM_2 in Table 3-1, rather than on volume, M.

Table 3-1. Predicted doses of inhaled DPM per minute based on total lung volume (M), total airway surface area (M_1), or surface area in alveolar region (M_2)

Species	M (10^{-3} μg/min/cm^3)	M_1 (10^{-6} μg/min/cm^2)	M_2 (10^{-6} μg/min/cm^2)
Hamster	3.548	3.088	2.382
Fischer rat	3.434	3.463	2.608
Human	0.249	1.237	0.775

$$M = \frac{\text{mass DPM deposited in lung per minute}}{\text{total lung volume}}$$

$$M_1 = \frac{\text{mass DPM deposited in lung per minute}}{\text{total airway surface area}}$$

$$M_2 = \frac{\text{mass DPM deposited on the unciliated airways per minute}}{\text{surface area of the unciliated airways}}$$

Based on the following conditions: (1) mass median aerodynamic diameter (MMAD) = 0.2 μm; geometric standard deviation (σ_g) = 1.9; packing density (ϕ) = 0.3; and particle mass density (ρ) = 1.5 g/cm^2; (2) particle concentration = 1 mg/m^3; and (3) nose-breathing. For humans, total lung volume = 3200 cm^2, total airway surface area = 633,000 cm^2, surface area of the unciliated airways = 627,000 cm^2. Corresponding values for Fisher rats are 418cm^2, 412cm^2, and 409cm^2; for hamsters, 282cm^2, 262cm^2, and 261cm^2. Tidal volumes (in cm^2) and respiratory frequency (per min) used for humans were 500 and 14; for Fisher rats, 1.6 and 98; for hamsters, 67 and 1.0.

Source: Xu and Yu, 1987.

Particle deposition will initiate particle redistribution processes (e.g., clearance mechanisms, phagocytosis) that transfer the particles to various subcompartments, including the alveolar macrophage pool, pulmonary interstitium, and lymph nodes. Over time, therefore, only small amounts of the original particle intake would be associated with the alveolar surface areas.

3.3.2. Particle Clearance and Translocation Mechanisms

This section provides an overview of the mechanisms and pathways by which particles are cleared from the respiratory tract. The mechanisms of particle clearance as well as clearance routes from the various regions of the respiratory tract have been considered in the PM Criteria Document (U.S. EPA, 1996) and reviewed by Schlesinger et al. (1997).

Particles that deposit upon airway surfaces may be cleared from the respiratory tract completely, or be translocated to other sites within this system, by various regionally distinct processes. These clearance mechanisms can be categorized as either absorptive (i.e., dissolution) or nonabsorptive (i.e., transport of intact particles) and may occur simultaneously or with

temporal variations. Particle solubility in terms of clearance refers to solubility within the respiratory tract fluids and cells. Thus, a poorly soluble particle is one whose rate of clearance by dissolution is insignificant compared to its rate of clearance as an intact particle (as is the case with DPM). The same clearance mechanisms act on different particles to different degrees, with their ultimate fate being a function of deposition site, physicochemical properties (including any toxicity), and sometimes deposited mass or number concentration. However, the duration of clearance for poorly soluble particles such as DPM as it exists between species, months for rats vs. years or even decades for humans, can make dissolution of DPM a significant contributor for humans (Kreyling, 1992).

Figure 3-4 outlines many of the known and suspected clearance pathways for poorly soluble particles, such as DPM, that deposit in the alveolar region. Included are the representations of the translocation pathways from the alveolar epithelium through the insterstitium and on through the lymph nodes; this latter path will be referred to frequently later in this chapter.

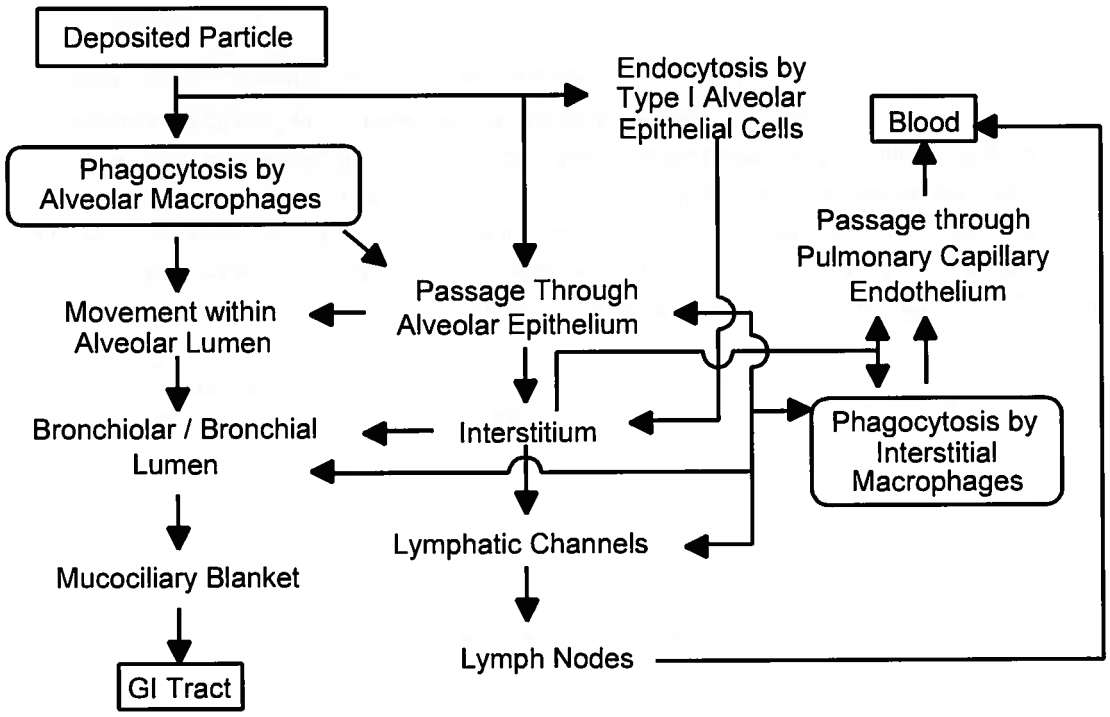

Figure 3-4. Diagram of known and suspected clearance pathways for poorly soluble particles depositing in the alveolar region. (Modified from Schlesinger, 1995).

3.3.2.1. *Extrathoracic Region*

The clearance of poorly soluble particles deposited in the nasal passages occurs via mucociliary transport, and the general flow of mucus is backwards, i.e., towards the nasopharynx. Mucus flow in the most anterior portion of the nasal passages is forward, clearing deposited particles to the vestibular region where removal is by sneezing, wiping, or blowing.

Soluble material deposited on the nasal epithelium is accessible to underlying cells via diffusion through the mucus. Dissolved substances may be subsequently translocated into the bloodstream. The nasal passages have a rich vasculature, and uptake into the blood from this region may occur rapidly.

Clearance of poorly soluble particles deposited in the oral passages is by expectoration or by swallowing into the gastrointestinal tract.

3.3.2.2. *Tracheobronchial Region*

The dynamic relationship between deposition and clearance is responsible for determining lung burden at any point in time. Clearance of poorly soluble particles from the TB region is mediated primarily by mucociliary transport, a more rapid process than those operating in alveolar regions. Mucociliary transport (often referred to as the mucociliary escalator) is accomplished by the rhythmic beating of cilia that line the respiratory tract from the trachea through the terminal bronchioles. This movement propels the mucous layer containing deposited particles (or particles within alveolar macrophages [AMs]) toward the larynx. Clearance rate by this system is determined primarily by the flow velocity of the mucus, which is greater in the proximal airways and decreases distally. These rates also exhibit interspecies and individual variability. Considerable species-dependent variability in tracheobronchial clearance has been reported, with dogs generally having faster clearance rates than guinea pigs, rats, or rabbits (Felicetti et al., 1981). The half-time ($t_{1/2}$) values for tracheobronchial clearance of relatively insoluble particles are usually on the order of hours, as compared to alveolar clearance, which is on the order of hundreds of days in humans and dogs. The clearance of particulate matter from the tracheobronchial region is generally recognized as being biphasic or multiphasic (Raabe, 1982). Some studies have shown that particles are cleared from large, intermediate, and small airways with $t_{1/2}$ of 0.5, 2.5, and 5 h, respectively. However, reports have indicated that clearance from airways is biphasic and that the long-term component for humans may take much longer for a significant fraction of particles deposited in this region, and may not be complete within 24 h as generally believed (Stahlhofen et al., 1990; ICRP, 1994).

Although most of the particulate matter will be cleared from the tracheobronchial region towards the larynx and ultimately swallowed, the contribution of this fraction relative to carcinogenic potential is unclear. With the exception of conditions of impaired bronchial

clearance, the desorption $t_{1/2}$ for particle-associated organics is generally longer than the tracheobronchial clearance times, thereby making uncertain the importance of this fraction relative to toxicity in the respiratory tract (Pepelko, 1987). However, Gerde et al. (1991a) showed that for low-dose exposures, particle-associated PAHs were released rapidly at the site of deposition indicating that they would be available for involvement in postulated carcinogenic processes. The relationship between the early clearance of poorly soluble particles of 4 µm aerodynamic diameter from the tracheobronchial regions and their longer-term clearance from the alveolar region is illustrated in Figure 3-5, clearly showing the rapid depuration from the TB region compared with the A region. This relationship, although demonstrated with 4 µm particles, is probably relevant and applicable to DPM-sized particles (i.e., 0.2 µm) as clearance mechanisms are believed not to be particularly particle-sized dependent (Morrow et al., 1967a,b; Snipes et al., 1983).

Cuddihy and Yeh (1986) reviewed respiratory tract clearance of particles inhaled by humans. Depending on the type of particle (ferric oxide, Teflon discs, or albumin microspheres), the technique employed, and the anatomic region (midtrachea, trachea, or main bronchi), particle

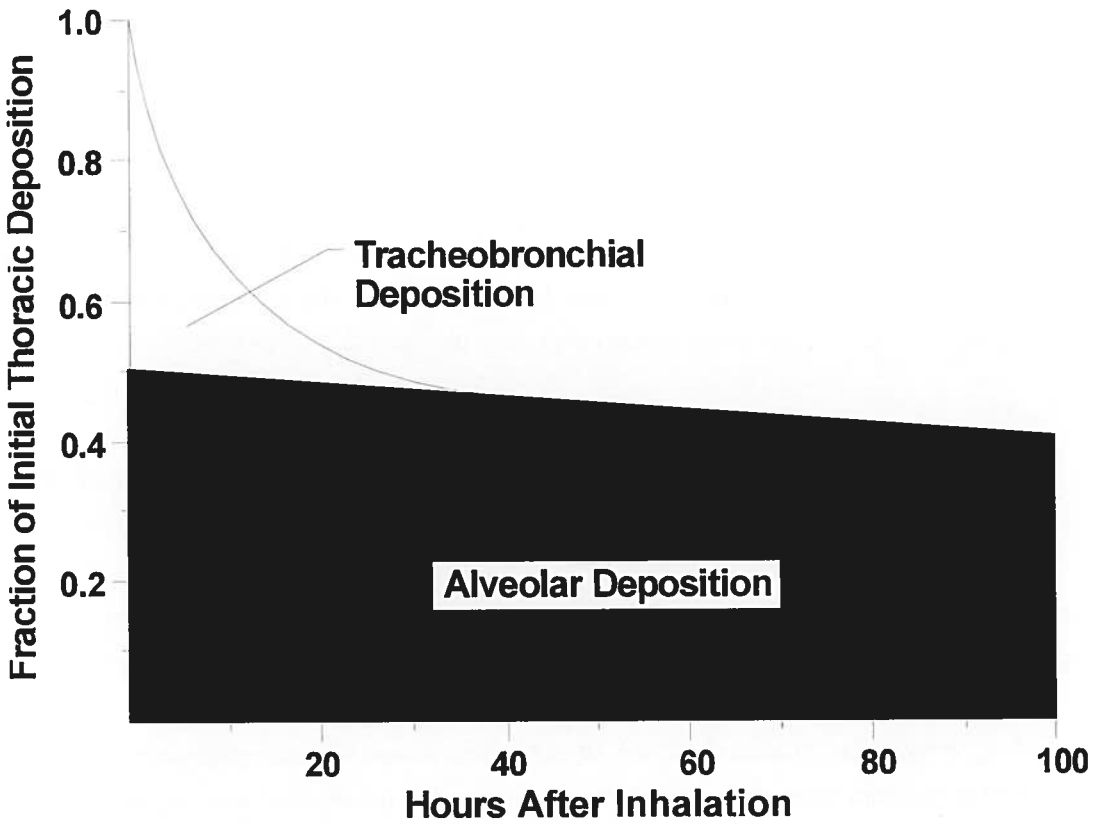

Figure 3-5. Modeled clearance of poorly soluble 4-µm particles deposited in tracheobronchial and alveolar regions in humans.

velocity (moved by mucociliary transport) ranged from 2.4 to 21.5 mm/min. The highest velocities were recorded for midtracheal transport, and the lowest were for main bronchi.

Cuddihy and Yeh (1986) described salient points to be considered when estimating particle clearance velocities from tracheobronchial regions: these include respiratory tract airway dimensions, calculated inhaled particle deposition fractions for individual airways, and thoracic (A + TB) clearance measurements. Predicted clearance velocities for the trachea and main bronchi were found to be similar to those experimentally determined for inhaled radiolabeled particles, but not those for intratracheally instilled particles. The velocities observed for inhalation studies were generally lower than those of instillation studies. Figure 3-6 illustrates a comparison of the short-term clearance of inhaled particles by human subjects and the model predictions for this clearance. However, tracheobronchial clearance via the mucociliary escalator is of limited importance for long-term clearance.

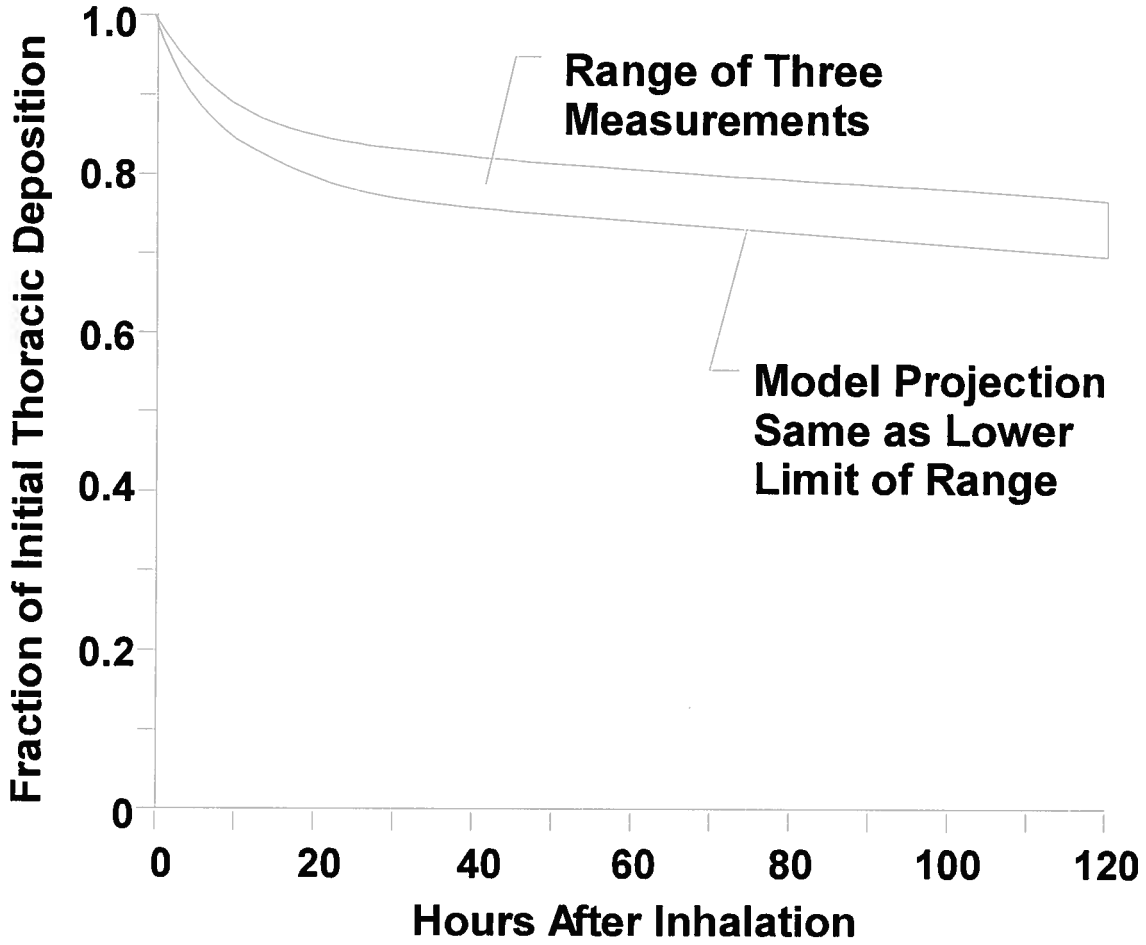

Figure 3-6. Short-term thoracic clearance of inhaled particles as determined by model prediction and experimental measurement.

Source: Cuddihy and Yeh, 1986 (from Stahlhofen et al., 1980).

Exposure of F344 rats to whole exhaust containing DPM at concentrations of 0.35, 3.5, or 7.1 mg/m^3 for up to 24 mo did not significantly alter tracheal mucociliary clearance as assessed by clearance of ^{99m}Tc-macroaggregated albumin instilled into the trachea (Wolff et al., 1987). The authors stated that measuring retention would yield estimates of clearance efficiency comparable to measuring the velocity for transport of the markers in the trachea. The results of this study were in agreement with similar findings of unaltered tracheal mucociliary clearance in rats exposed to DPM (0.21, 1.0, or 4.4 mg/m^3) for up to 4 mo (Wolff and Gray, 1980). However, the 1980 study by Wolff and Gray, as well as an earlier study by Battigelli et al. (1966), showed that acute exposure to high concentrations of DE soot (1.0 and 4.4 mg/m^3 in the study by Wolff and Gray [1980] and 8 to 17 mg/m^3 in the study by Battigelli et al. [1966]) produced transient reductions in tracheal mucociliary clearance. Battigelli et al. (1966) also noted that the compromised tracheal clearance was not observed following cessation of exhaust exposure.

That tracheal clearance does not appear to be significantly impaired or is impaired only transiently following exposure to high concentrations of DPM is consistent with the absence of pathological effects in the tracheobronchial region of the respiratory tract in experimental animals exposed to DPM. The apparent retention of a fraction of the deposited dose in the airways could be cause for some concern regarding possible effects in this region, especially in light of the results from simulation studies by Gerde et al. (1991b) suggesting that release of PAHs from particles may occur within minutes and therefore at the site of initial deposition. However, the absence of effects in the TB areas in long-term DPM studies and experimental evidence that particle-associated PAHs are released at the site of particle deposition together suggest that these PAHs and other organics may be of lesser importance in tumorigenic responses of rats than originally suspected. On the other hand, the data of Nikula et al. (1997a,b) could be interpreted to suggest that a larger fraction of particles are translocated to the interstitium of the respiratory tract in primates that are heavily exposed (and therefore presumably in humans) than in rats that are heavily exposed, including the interstitium of the respiratory bronchioles, an anatomical site absent in rats (Section 3.6). Moreover, eluted PAHs in the TB region are retained longer than those in the alveoli (Gerde et al., 1999), allowing time for activation. Also, the results of Kreyling (1992) indicate that appreciable dissolution of even poorly soluble particles may occur as a consequence of long absolute duration of clearance, such as years or decades, in humans. Thus PAHs may have a role in human response to DE that cannot be evaluated with the rat model.

Also, impairment of mucociliary clearance function as a result of exposure to occupational or environmental respiratory tract toxicants or to cigarette smoke may significantly enhance the retention of particles in the TB region. For example, Vastag et al. (1986) demonstrated that not only smokers with clinical symptoms of bronchitis but also symptom-free

smokers have significantly reduced mucociliary clearance rates. Although impaired tracheobronchial clearance could conceivably have an impact on the effects of deposited DPM in the conducting airways, it does not appear to be relevant to the epigenetic mechanism likely responsible for DE-induced rat pulmonary tumors as the tumors observed in these studies were all or nearly all of A vice TB origin.

Poorly soluble particles such as DPM that are deposited within the TB region are cleared predominantly by mucociliary transport towards the oropharynx, followed by swallowing. Poorly soluble particles may also be cleared by traversing the epithelium by endocytotic processes, and enter the peribronchial region. Clearance may occur following phagocytosis by airway macrophages, located on or beneath the mucous lining throughout the bronchial tree, or via macrophages that enter the airway lumen from the bronchial or bronchiolar mucosa (Robertson, 1980).

3.3.2.3. *A Region*

A number of investigators have reported on the alveolar clearance kinetics of human subjects. Bohning et al. (1980) examined alveolar clearance in eight humans who had inhaled <0.4 mg of ^{85}Sr-labeled polystyrene particles (3.6 ± 1.6 μm diam.). A double-exponential model best described the clearance of the particles and provided $t_{1/2}$ values of 29 ± 19 days and 298 ± 114 days for short-term and long-term phases, respectively. It was noted that of the particles deposited in the alveolar region, 75% ± 13% were cleared via the long-term phase. Alveolar retention $t_{1/2}$ values of 330 and 420 days were reported for humans who had inhaled aluminosilicate particles of MMAD 1.9 and 6.1 μm (Bailey et al., 1982). In a comprehensive study Bailey et al. (1985) followed the long-term retention of inhaled particles in a human respiratory tract. The retention of 1 and 4 μm fused aluminosilicate particles labeled with strontium-85 and yttrium-88, respectively, was followed in male volunteers for about 533 days. Approximately 7% of the initial lung deposit of 1 μm particles and 40% of the 4 μm particles were associated with a rapid clearance phase corresponding to the calculated tracheobronchial deposits. Retention of the remaining material followed a two-component exponential function, with phases having half-times of the order of tens of days and several hundred days, respectively.

Quantitative data on clearance rates in humans having large lung burdens of particulate matter are lacking. Bohning et al. (1982) and Cohen et al. (1979), however, did provide evidence for slower clearance in smokers, and Freedman and Robinson (1988) reported slower clearance rates in coal miners who had mild pneumoconiosis with presumably high lung burdens of coal dust. Although information on particle burden and particle overload relationships in humans is much more limited than in experimental animal models, inhibition of clearance does seem to occur. Stöber et al. (1967) estimated a clearance $t_{1/2}$ of 4.9 years in coal miners with nil or slight

silicosis, based on postmortem lung burdens. The lung burdens and estimated exposure histories ranged from 2 to 50 mg/g of lung or more, well above the value at which clearance impairment is observed in the rat. Furthermore, impaired clearance resulting from smoking or exposure to other respiratory toxicants may increase the possibility of an enhanced particle accumulation effect resulting from exposure to other particle sources such as DPM.

Normal alveolar clearance rates in laboratory animals exposed to DPM have been reported by a number of investigators (Table 3-2). Because the rat is, historically, the species for which experimentally induced lung cancer data are available and for which most clearance data exist, it is the species most often used for assessing human risk, and reviews of alveolar clearance studies have been generally limited to this species.

Chan et al. (1981) subjected 24 male F344 rats to nose-only inhalation of diluted DE generated from a diesel engine (6 mg/m^3) labeled with ^{131}Ba or ^{14}C for 40 to 45 min and assessed total lung deposition, retention, and elimination. Based on radiolabel inventory, the deposition efficiency in the respiratory tract was 15% to 17%. Measurement of ^{131}Ba label in the feces during the first 4 days following exposure indicated that 40% of the deposited DPM was eliminated via mucociliary clearance. Clearance of the particles from the lower respiratory tract followed a two-phase elimination process consisting of a rapid ($t_{1/2}$ of 1 day) elimination by mucociliary transport and a slower ($t_{1/2}$ of 62 days) macrophage-mediated alveolar clearance. This study provided data for normal alveolar clearance rates of DPM not affected by prolonged exposure or particle overloading.

Several studies have investigated the effects of exposure concentration on the alveolar clearance of DPM by laboratory animals. Wolff et al. (1986, 1987) provided clearance data ($t_{1/2}$) and lung burden values for F344 rats exposed to DE for 7 h/day, 5 days/week for 24 mo. Exposure concentrations of 0.35, 3.5, and 7.1 mg of DPM/m^3 were employed in this whole body-inhalation exposure experiment. Intermediate (hours-days) clearance of $^{67}Ga_2O_3$ particles (30 min, nose-only inhalation) was assessed after 6, 12, 18, and 24 mo of exposure at all of the DPM concentrations. A two-component function described the clearance of the administered radiolabel:

$$F_{(t)} = A\exp(-0.693\ t/\tau_1) + B\exp(-0.693\ t/\tau_2), \qquad (3\text{-}1)$$

where $F_{(t)}$ was the percentage retained throughout the respiratory tract, A and B were the magnitudes of the two components (component A included nasal, lung, and gastrointestinal clearance, while component B represented intermediate lung clearance) and τ_1 and τ_2 were the

Table 3-2. Alveolar clearance in laboratory animals exposed to DPM in whole exhaust

Species/sex	Exposure technique	Exposure duration	Particles mg/m^3	Observed effects	Reference
Rats, F-344, M	Nose only; Radiolabeled DPM	40-45 min	6	Four days after exposure, 40% of DPM eliminated by mucociliary clearance. Clearance from lower RT was in 2 phases. Rapid mucociliary ($t_{1/2}$ = 1 day); slower macrophage-mediated ($t_{1/2}$ = 62 days).	Chan et al. (1981)
Rats, F-344	Whole body; assessed effect on clearance of $^{67}Ga_2O_3$ particles	7 h/day 5 days/week 24 mo	0.35 3.5 7.1	τ_1 significantly higher with exposure to 7.1 mg/m^3 for 24 mo; τ_2 significantly longer after exposure to 7.1 mg/m^3 for 6 mo and to 3.5 mg/m^3 for 18 mo.	Wolff et al. (1986, 1987)
Rats	Whole body	19 h/day 5 days/week 2.5 years	4	Estimated alveolar deposition = 60 mg; particle burden caused lung overload. Estimated 6-15 mg particle-bound organics deposited.	Heinrich et al. (1986)
Rats, F-344, MF	Whole body	7 h/day 5 days/week 18 mo	0.15 0.94 4.1	Long-term clearance was 87 ± 28 and 99 ± 8 days for 0.15 and 0.94 mg/m^3 groups, respectively; $t_{1/2}$ = 165 days for 4.1 mg/m^3 group.	Griffis et al. (1983)
Rats, F-344;	Nose-only; Radiolabeled ^{14}C	45 min 140 min	7 2	Rats demonstrated 3 phases of clearance with $t_{1/2}$ = 1, 6, and 80 days, representing tracheobronchial, respiratory bronchioles, and alveolar clearance, respectively. Guinea pigs demonstrated negligible alveolar clearance from day 10 to 432.	Lee et al. (1983)
Guinea pigs, Hartley		45 min	7		
Rats, F-344		20 h/day 7 days/week 7-112 days	0.25 6	Monitored rats for a year. Proposed two clearance models. Clearance depends on initial particle burden; $t_{1/2}$ increases with higher exposure. Increases in $t_{1/2}$ indicate increasing impairment of AM mobility and transition into overload condition.	Chan et al. (1984)

RT = respiratory tract.
AM = alveolar macrophage.
τ_1 = clearance from primary, ciliated airways.
τ_2 = clearance from nonciliated passages.

half-times for the *A* and *B* components, respectively. The early clearance half-times (τ_1), were similar for rats in all exposure groups at all time points except in the high-exposure (7.1 mg/m^3) group following 24 mo of exposure, which was faster than the controls. Significantly longer *B* component retention half-times, representing intermediate clearance probably from nonciliated structures such as alveolar ducts and alveoli, were noted after as little as 6 mo exposure to DPM at 7.1 mg/m^3 and 18 mo exposure to 3.5 mg/m^3.

Nose-only exposures to ^{134}Cs fused aluminosilicate particles (FAP) were used to assess long-term (weeks-months) clearance. Following 24-mo exposure to DPM, long-term clearance of ^{134}Cs-FAP was significantly ($p<0.01$) altered in the 3.5 (cumulative exposure [C × T] of 11,760 mg·h/m^3) and 7.1 mg/m^3, C × T = 23,520 mg·h/m^3) exposure groups ($t_{1/2}$ of 264 and 240 days, respectively) relative to the 0.35 mg/m^3 and control groups ($t_{1/2}$ of 81 and 79 days, respectively). Long-term clearance represents the slow component of particle removal from the alveoli. The decreased clearance correlated with the greater particle burden in the lungs of the 3.5 and 7.1 mg/m^3 exposure groups. Based on these findings, the cumulative exposure of > 11,760 mg·h/m^3 (or 3.5 mg/m^3 for a lifetime exposure) represented a particle overload condition resulting in compromised alveolar clearance mechanisms; the clearance rate at the lowest concentration (0.35 mg/m^3; cumulative exposure of 118 mg·h/m^3) was not different from control rates (Figure 3-7).

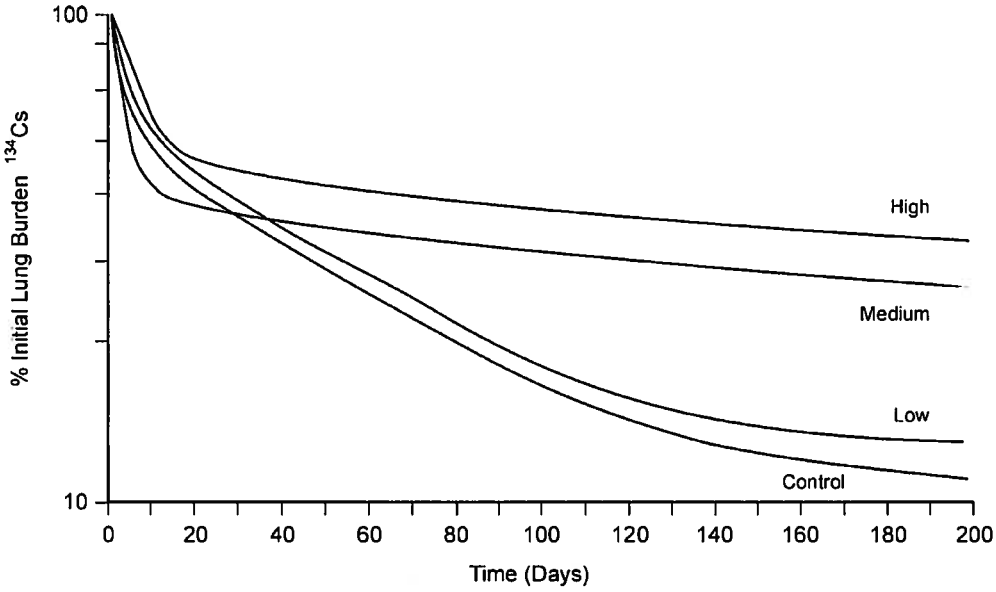

Figure 3-7. Clearance from lungs of ^{134}Cs-FAP fused aluminosilicate tracer particles inhaled after 24 months of DE exposure at concentrations of 0 (control), 0.35 (low), 3.5 (medium), and 7.1 (high) mg DPM/m^3.

Heinrich et al. (1986) exposed rats 19 h/day, 5 days/week for 2.5 years to DPM at a particle concentration of about 4 mg/m^3, equal to a "C × T" of 53,200 mg·h/m^3. The deposition in the alveolar region was estimated to equal 60 mg. The lung particle burden was apparently sufficient to result in a "particle overload" condition (Section 3.4). With respect to the organic matter adsorbed onto the particles, the authors estimated that over the 2.5-year period, 6-15 mg of particle-bound organic matter had been deposited and was potentially available for biological effects. This estimation was based on the analysis of the DE used in the experiments, values for rat ventilatory functions, and estimates of deposition and clearance.

Accumulated burden of DPM in the lungs following an 18-mo, 7 h/day, 5 days/week exposure to whole DE was reported by Griffis et al. (1983). Male and female F344 rats exposed to 0.15, 0.94, or 4.1 mg DPM/m^3 were sacrificed at 1 day and 1, 5, 15, 33, and 52 weeks after exposure, and DPM was extracted from lung tissue dissolved in tetramethylammonium hydroxide. Following centrifugation and washing of the supernatant, DPM content of the tissue was quantitated using spectrophotometric techniques. The analytical procedure was verified by comparing results to recovery studies using known amounts of DPM with lungs of unexposed rats. Lung burdens were 0.035, 0.220, and 1.890 mg/g lung tissue, respectively, in rats exposed to diluted whole exhaust at 0.15, 0.94, and 4.1 mg DPM/m^3. Long-term retention for the 0.15 and 0.94 mg/m^3 groups had estimated half-times of 87 ± 28 and 99 ± 8 days, respectively. The retention $t_{1/2}$ for the 4.1-mg/m^3 exposure group was 165 ± 8 days, which was significantly (p<0.0001) greater than those of the lower exposure groups. The 18-mo exposures to 0.15 or 0.96 mg/m^3 levels of DPM [C × T] equivalent of 378 and 2,368 mg·h/m^3, respectively) did not affect clearance rates, whereas the exposure to the 4.1 mg/m^3 concentration C × T = 10,332 mg·h/m^3) resulted in impaired clearance.

Lee et al. (1983) described the clearance of DPM (7 mg/m^3 for 45 min or 2 mg/m^3 for 140 min) by F344 rats (24 per group) and Hartley guinea pigs exposed by nose-only inhalation to diluted whole exhaust with no apparent particle overload in the lungs as being in three distinct phases. The exposure protocols provided comparable total doses based on a ^{14}C radiolabel. $^{14}CO_2$ resulting from combustion of ^{14}C-labeled diesel fuel was removed by a diffusion scrubber to avoid erroneous assessment of ^{14}C intake by the animals. Retention of the radiolabeled particles was determined up to 335 days after exposure and resulted in a three-phase clearance with retention $t_{1/2}$ values of 1, 6, and 80 days. The three clearance phases are taken to represent removal of tracheobronchial deposits by the mucociliary escalator, removal of particles deposited in the respiratory bronchioles, and alveolar clearance, respectively. Species variability in clearance of DPM was also demonstrated because the Hartley guinea pigs exhibited negligible alveolar clearance from day 10 to day 432 following a 45-min exposure to a DPM concentration

of 7 mg/m^3. Initial deposition efficiency (20% ± 2%) and short-term clearance were, however, similar to those for rats.

Lung clearance in male F344 rats preexposed to diluted whole DE containing DPM at 0.25 or 6 mg/m^3 20 h/day, 7 days/week for periods lasting from 7 to 112 days was studied by Chan et al. (1984). Following this preexposure protocol, rats were subjected to 45-min nose-only exposure to ^{14}C-DE, and alveolar clearance of radiolabel was monitored for up to 1 year. Two models were proposed: a normal biphasic clearance model and a modified lung retention model that included a slow-clearing residual component to account for sequestered aggregates of macrophages. The first model described a first-order clearance for two compartments: $R(t) = Ae^{-u1t} + Be^{-u2t}$. This yielded clearance $t_{1/2}$ values of 166 and 562 days for rats preexposed to 6.0 mg/m^3 for 7 and 62 days, respectively. These values were significantly ($p<0.05$) greater than the retention $t_{1/2}$ of 77 ± 17 days for control rats. The same retention values for rats of the 0.25 mg/m^3 groups were 90 ± 14 and 92 ± 15 days, respectively, for 52- and 112-day exposures and were not significantly different from controls. The two-compartment model represents overall clearance of the tracer particles, even if some of the particles were sequestered in particle-laden macrophages with substantially slower clearance rates. For the second model, which excluded transport of the residual fractions in sequestered macrophage aggregates, slower clearance was observed in the group with a lung burden of 6.5 mg (exposed to 6.0 mg/m^3 for 62 days), and no clearance was observed in the 11.8 mg group (exposed to 6.0 mg/m^3 for 112 days). Clearance was shown to be dependent on the initial burden of particles, and therefore the clearance $t_{1/2}$ would increase in higher exposure scenarios. This study emphasizes the importance of particle overloading of the lung and the ramifications on clearance of particles; the significant increases in half-times indicate an increasing impairment of the alveolar macrophage mobility and subsequent transition into an overload condition as is discussed further in Section 3.4.

Long-term alveolar clearance rates of particles in various laboratory animals and humans have been reviewed by Pepelko (1987). Although retention $t_{1/2}$ varies both among and within species and is also dependent on the physicochemical properties of the inhaled particles, the retention $t_{1/2}$ for humans is much longer (>8 mo) than the average retention $t_{1/2}$ of 60 days for rats.

Clearance from the A region occurs via a number of mechanisms and pathways, but the relative importance of each is not always certain and may vary between species. Particle removal by macrophages comprises the main nonabsorptive clearance process in this region. Alveolar macrophages reside on the epithelium, where they phagocytize and transport deposited material, which they contact by random motion or via directed migration under the influence of local chemotactic factors (Warheit et al., 1988).

Particle-laden macrophages may be cleared from the A region along a number of pathways (U.S. EPA, 1996). Uningested particles or macrophages in the interstitium may

traverse the alveolar-capillary endothelium, directly entering the blood (Raabe, 1982; Holt, 1981); endocytosis by endothelial cells followed by exocytosis into the vessel lumen seems, however, to be restricted to particles <0.1 μm diameter, and may increase with increasing lung burden (Lee et al., 1985; Oberdörster, 1988). Once in the systemic circulation, transmigrated macrophages, as well as uningested particles, can travel to extrapulmonary organs.

Alveolar macrophages constitute an important first-line cellular defense mechanism against inhaled particles that deposit in the alveolar region of the lung. It is well established that a host of diverse materials, including DPM, are phagocytized by AMs shortly after deposition (White and Garg, 1981; Lehnert and Morrow, 1985) and that such cell-contained particles are generally rapidly sequestered from both the extracellular fluid lining in the alveolar region and the potentially sensitive alveolar epithelial cells. In addition to this role in compartmentalizing particles from other lung constituents, AMs are prominently involved in mediating the clearance of relatively insoluble particles from the air spaces (Lehnert and Morrow, 1985). Although the details of the actual process have not been delineated, AMs with their particle burdens gain access and become coupled to the mucociliary escalator and are subsequently transported from the lung via the conducting airways. Although circumstantial, numerous lines of evidence indicate that such AM-mediated particle clearance is the predominant mechanism by which relatively insoluble particles are removed from the alveolar region of the lungs (Gibb and Morrow, 1962; Ferin, 1982; Harmsen et al., 1985; Lehnert and Morrow, 1985; Powdrill et al., 1989).

The removal characteristics for particles deposited in the alveolar region of the lung have been descriptively represented by numerous investigators as a multicompartment or multicomponent process in which each component follows simple first-order kinetics (Snipes and Clem, 1981; Snipes et al., 1988; Lee et al., 1983). Although the various compartments can be described mathematically, the actual physiological mechanisms determining these differing clearance rates have not been well characterized.

Lehnert et al. (1988, 1989) performed studies using laboratory rats to examine particle-AM relationships over the course of alveolar clearance of low to high lung burdens of noncytotoxic microspheres (2.13 μm diam.) to obtain information on potential AM-related mechanisms that form the underlying bases for kinetic patterns of alveolar clearance as a function of particle lung burdens. The intratracheally instilled lung burdens varied from 1.6×10^7 particles (about 85 μg) for the low lung burden to 2.0×10^8 particles (about 1.06 mg) for the mid-dose and 6.8×10^8 particles (about 3.6 mg) for the highest lung burden. The lungs were lavaged at various times postexposure and the numbers of spheres in each macrophage counted. Although such experiments provide information regarding the response of the lung to particulate matter, intratracheal instillation is not likely to result in the same depositional characteristics as

inhalation of particles. Therefore, it is unlikely that the response of alveolar macrophages to these different depositional characteristics will be quantitatively similar.

The $t_{1/2}$ values of both the early and later components of clearance were virtually identical following deposition of the low and medium lung burdens. For the highest lung burden, significant prolongations were found in both the early, more rapid, as well as the slower component of alveolar clearance. The percentages of the particle burden associated with the earlier and later components, however, were similar to those of the lesser lung burdens. On the basis of the data, the authors concluded that translocation of AMs from alveolar spaces by way of the conducting airways is fundamentally influenced by the particle burden of the cells so translocated. In the case of particle overload that occurred at the highest lung burden, the translocation of AMs with the heaviest cellular burdens of particles (i.e., greater than about 100 microspheres per AM) was definitely compromised.

On the other hand, analysis of the disappearance of AMs with various numbers of particles indicates that the particles may not exclusively reflect the translocation of AMs from the lung. The observations are also consistent with a gradual redistribution of retained particles among the AMs in the lung concurrent with the removal of particle-containing AMs via the conducting airways. Experimental support suggestive of potential processes for such particle redistribution comes from a variety of investigations involving AMs and other endocytic cells (Heppleston and Young, 1973; Evans et al., 1986; Aronson, 1963; Sandusky et al., 1977; Heppleston, 1961; Riley and Dean, 1978).

3.3.3. Translocations of Particles to Extra-Alveolar Macrophage Compartment Sites

Although the phagocytosis of particles by cells free within the lung and the mucociliary clearance of the cells with their particulate matter burdens represent the most prominent mechanisms that govern the fate of particles deposited in the alveolar region, other mechanisms exist that can affect both the retention characteristics of relatively insoluble particles in the lung and the lung clearance pathways for the particles. One mechanism is endocytosis of particles by alveolar lining (Type I) cells (Sorokin and Brain, 1975; Adamson and Bowden, 1978, 1981) that normally provide >90% of the cell surface of the alveoli in the lungs of a variety of mammalian species (Crapo et al., 1983). This process may be related to the size of the particles that deposit in the lungs and the numbers of particles that are deposited. Adamson and Bowden (1981) found that with increasing loads of carbon particles (0.03 μm diam.) instilled in the lungs of mice, more free particles were observed in the alveoli within a few days; it should be noted, however, that this phenomenon was demonstrated with very high doses given as a bolus such that the mechanism and relevance of this phenomenon at lower concentrations may be different or even unrelated to what may happen at much lower concentrations. The relative abundance of particles

endocytosed by Type I cells also increased with increasing lung burdens of the particles, but instillation of large particles (1.0 μm) rarely resulted in their undergoing endocytosis. A 4 mg burden of 0.1 μm diameter latex particles is equivalent to 8×10^{12} particles, whereas a 4 mg burden of 1.0 μm particles is composed of 8×10^{9} particles. Regardless, DPM with volume median diameters between 0.05 and 0.3 μm (Frey and Corn, 1967; Kittleson et al., 1978) would be expected to be within the size range for engulfment by Type I cells should suitable encounters occur. Indeed, it has been demonstrated that DPM is endocytosed by Type I cells in vivo (White and Garg, 1981).

Unfortunately, information on the kinetics of particle engulfment (endocytosis) by Type I cells relative to that by AMs is scanty. Even when relatively low burdens of particulate matter are deposited in the lungs, some fraction of the particles usually appears in the regional lymph nodes (Ferin and Feldstein, 1978; Lehnert, 1989). As will be discussed, endocytosis of particles by Type I cells is an initial, early step in the passage of particles to the lymph nodes. Assuming particle phagocytosis is not sufficiently rapid or perfectly efficient, increasing numbers of particles would be expected to gain entry into the Type I epithelial cell compartment during chronic aerosol exposures. Additionally, if particles are released on a continual basis by AMs that initially sequestered them after lung deposition, some fraction of the "free" particles so released could also undergo passage from the alveolar space into Type I cells.

The endocytosis of particles by Type I cells represents only the initial stage of a process that can lead to the accumulation of particles in the lung's interstitial compartment and the subsequent translocation of particles to the regional lymph nodes. As suggested by the results of Adamson and Bowden (1981), a vesicular transport mechanism in the Type I cell can transfer particles administered at high concentrations by instillation from the air surface of the alveolar epithelium into the lung's interstitium, where particles may be phagocytized by interstitial macrophages or remain in a "free" state for a poorly defined period that may be dependent on the physicochemical characteristics of the particle. The lung's interstitial compartment accordingly represents an anatomical site for the retention of particles in the lung, although the kinetics on movement into and out of this site remain obscure for both humans and test species. Whether or not AMs, and perhaps polymorphonuclear neutrophils (PMNs) that have gained access to the alveolar space compartment and phagocytize particles there, also contribute to the particle translocation process into the lung's interstitium also remains a controversial issue.

Translocation of particulate matter to the various interstitial spaces within the lung is a prominent phenomenon occurring at least at high (occupational) exposures that has been examined extensively for both DPM and coal dust in a species comparison between rats and primates (Nikula et al., 1997a,b). Detailed pulmonary morphometry conducted on F344 rats and cynomolgus monkeys that had been exposed for 24 months to occupational levels of DPM (1.95

mg/m^3; see Lewis et al., 1989) showed major differences in the pulmonary sites of particulate deposition. In rats, about 73% of DPM was present in the alveolar ducts/alveoli and 27% in interstitial compartments; for monkeys the corresponding figures were markedly different at 43% and 57%. The corresponding pulmonary histopathology confirmed that both species were affected, although rats are more sensitive, as incidence and severity scores for alveolar effects ranged from 15 of 15 with severity scores from 1-4 (minimal to moderate), whereas for monkeys the corresponding values were only 4 of 15 at a range of 0-2 (not observed to minimal). Similarly, both species exhibited histopathology at the interstitial sites of deposition but with effects in monkeys being slightly more severe (1 of 15 graded as slight, 14 of 15 graded as minimal) than those in rats (14 of 15 graded as slight, 1 of 15 graded as minimal). The basis for this interspecies difference may be due to any number of clear contrasts that exist between rat and primate lungs, including anatomical (primates and humans have respiratory bronchioles whereas rats do not), kinetic (primates and human clearance processes allow more residence time of particles in the lung than do those in rats or rats may have faster interstitial to lymph node clearance rates than do humans and primates), or morphological (primates and humans have more interstitial tissue, more and thicker pleura, and wider interstitial spaces than do rats). Aspects of the study itself that may obscure its interpretation include the relative lifespan the exposure represented between the tested species (lifetime for rat vs. about 10% lifetime of primate), that there was only the single time point at which the relative burdens were determined, and that rat lymph node burdens were not included in the analysis. The analysis of Kuempel (2000) using human occupational data clearly showed that models require an interstitialization process to provide adequate fits to the empirical human (miners') lung deposition data discussed in that study. Hypotheses about possible mechanisms for the interstitialization process are scant, although Harmsen et al. (1985) provided some evidence in dogs that migration of AMs may contribute to the passage of particles to the interstitial compartment and also may be involved in the subsequent translocation of particles to draining lymph nodes. Translocation to the extrapulmonary regional lymph nodes apparently can involve the passage of free particles as well as particle-containing cells via lymphatic channels in the lungs (Harmsen et al., 1985; Ferin and Feldstein, 1978; Lee et al., 1985). Further, it has been noted that particles accumulate both more rapidly and more abundantly in lymph nodes that receive lymphatic drainage from the lung (Ferin and Feldstein, 1978; Lee et al., 1985). It should be stressed that further investigation is required to confirm the character and even existence of the interstitialization process in the lungs of humans with exposures to particles at lower environmental concentrations, or to submicrometer particles such as DPM, or to examine the kinetics and time course of the interstitialization process.

3.3.3.1. *Clearance Kinetics*

The clearance kinetics of PM have been reviewed in the PM CD (U.S. EPA, 1996) and by Schlesinger et al. (1997), the results of which indicate that clearance kinetics may be profoundly influenced by several factors. The influence of time, for example, is definitively showed by the work of Bailey et al. (1985; discussed above), who showed that the rate of clearance from the pulmonary region to the GI tract decreased nearly fourfold from initial values to those noted at 200 days and beyond after particle inhalation.

3.3.3.2. *Interspecies Patterns of Clearance*

The inability to study the retention of certain materials in humans for direct risk assessment requires the use of laboratory animals. Adequate toxicological assessment necessitates that interspecies comparisons consider aspects of dosimetry including knowledge of clearance rates and routes. The basic mechanisms and overall patterns of clearance from the respiratory tract are similar in humans and most other mammals. Regional clearance rates, however, can show substantial variation between species, even for similar particles deposited under comparable exposure conditions (U.S. EPA, 1996; Schlesinger et al., 1997; Snipes et al., 1989).

In general, there are species-dependent rate constants for various clearance pathways. Differences in regional and total clearance rates between some species are a reflection of differences in mechanical clearance processes. For consideration in assessing particle dosimetry, the end result of interspecies differences in clearance is that the retained doses in the lower respiratory tract can differ between species, which may result in differences in response to similar particulate exposures.

3.3.3.3. *Clearance Modifying Factors and Susceptible Populations*

A number of host and environmental factors may modify clearance kinetics and may consequently make individuals exhibiting or afflicted with these factors particularly susceptible to the effects resulting from exposure to DPM. These include age, gender, physical activity, respiratory tract disease, and inhalation of irritants (U.S. EPA, 1996, Section 10.4.2.5). Respiratory tract clearance appears to be prolonged in a number of pathophysiological conditions in humans, including chronic sinusitis, chronic bronchitis, asthma, chronic obstructive lung disease, and various acute respiratory infections.

3.3.3.4. *Respiratory Tract Disease*

Earlier studies reviewed in the PM CD (U.S. EPA, 1996) noted that various respiratory tract diseases are associated with alterations in overall clearance and clearance rates. Prolonged

nasal mucociliary clearance in humans is associated with chronic sinusitis or rhinitis, and cystic fibrosis. Bronchial mucus transport may be impaired in people with bronchial carcinoma, chronic bronchitis, asthma, and various acute infections. In certain of these cases, coughing may enhance mucus clearance, but it generally is effective only if excess secretions are present.

The rates of A region particle clearance are reduced in humans with chronic obstructive lung disease and in laboratory animals with viral infections, whereas the viability and functional activity of macrophages are impaired in human asthmatics and in animals with viral-induced lung infections (U.S. EPA, 1996). However, any modification of functional properties of macrophages appears to be injury specific, reflecting the nature and anatomic pattern of disease.

3.4. PARTICLE "OVERLOAD"

3.4.1. Introduction

Some experimental studies using laboratory rodents employed high exposure concentrations of relatively nontoxic, poorly soluble particles. These particle loads interfered with normal clearance mechanisms, producing clearance rates different from those that would occur at lower exposure levels. Prolonged exposure to high particle concentrations is associated with what is termed particle overload. This is defined as the overwhelming of macrophage-mediated clearance by the deposition of particles at a rate exceeding the capacity of that clearance pathway. Aspects and occurrence of this phenomenon have already been alluded to in earlier portions of this chapter on alveolar clearance (Section 3.3.2.3). The relevance of this phenomenon for human risk assessment has long been the object of scientific inquiry. A monograph on this matter and many others relevant to DPM has appeared (ILSI, 2000), and the results, opinions, and judgments put forth therein are used extensively in this chapter and in this assessment.

Wolff et al. (1987) used ^{134}Cs-labeled fused aluminosilicate particles to measure alveolar clearance in rats following 24-mo exposure to low, medium, and high concentrations of DE (targeted concentrations of DPM of 0.35, 3.5 and 7.1 mg/m^3). The short-term component of the multicomponent clearance curves was similar for all groups, but long-term clearance was retarded in the medium- and high-exposure groups (Figure 3-7). The half times of the long-term clearance curves were 79, 81, 264, and 240 days, respectively, for the control, low-, medium-, and high-exposure groups. Clearance was overloaded at the high and medium but not at the low exposure level. Lung burdens of DPM were measured after 6, 12, 18, and 24 mo of exposure. The results (Figure 3-8) indicate that the lung burden of deposited particles was appreciably increased or "overloaded" compared with the low level of exposure in the two highest exposures post 6 months. Figure 3-8 also compares these observational results of lung burden with simulated results where no overload would occur (McClellan, 2000). Comparison

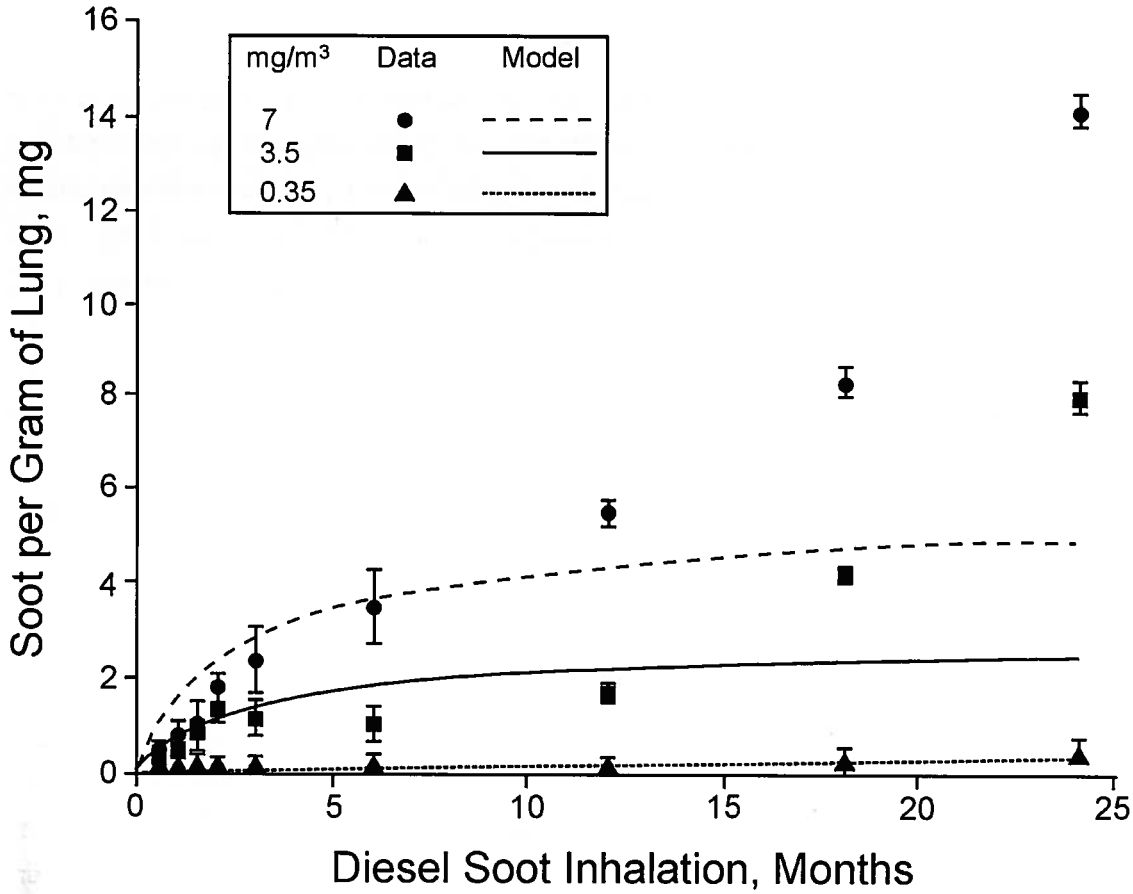

Figure 3-8. Lung burdens (in mg DPM soot/g lung) in rats chronically exposed to DE at 0.35 (low) (●), 3.5 (medium) (▲), and 7.1 (high) mg / m³ (■). The solid figures represent actual data with means and standard errors from animals sacrificed at 6, 12, and 18 months after initiation of exposures. Lines are simulated model results from these same exposure levels, assuming no effect of exposure concentration on deposition or clearance of particles (from Wolff et al., 1987; McClellan, 2000).

of the observed and simulated results clearly shows that the two highest exposure levels resulted in lung burdens that were ever-increasing and not at all concordant with the simulated results, whereas the burdens at the low-exposure level were closely approximated by the simulation. Thus, at the two highest exposure levels, deposition processes were outpacing clearance mechanisms. Results from the low-exposure level indicate that clearance processes were not inhibited, the lung burden remaining the same throughout all time periods examined.

Morrow (1988) has proposed that the condition of particle overloading in the lungs is caused by a loss in the mobility of particle-engorged AMs and that such an impediment is related to the cumulative volumetric load of particles in the AMs. Morrow (1988) has further estimated that the clearance function of an AM may be completely impaired when the particle burden in the AM is of a volumetric size equivalent to about 60% of the normal volume of the AM. Morrow's

hypothesis was the initial basis for the physiology-oriented multicompartmental kinetic (POCK) model derived by Stöber et al. (1989) for estimating alveolar clearance and retention of relatively insoluble, respirable particles in rats.

A revised version of this model refines the characterization of the macrophage pool by including both the mobile and immobilized macrophages (Stöber et al., 1994). Application of the revised version of the model to experimental data suggested that lung overload does not cause a dramatic increase in the total burden of the macrophage pool but results in a great increase in the particle burden of the interstitial space, a compartment that is not available for macrophage-mediated clearance. The revised version of the POCK model is discussed in greater detail in the context of other dosimetry models below.

Oberdörster and co-workers (1992) assessed the alveolar clearance of smaller (3.3 μm diam.) and larger (10.3 μm diam.) polystyrene particles, the latter of which are volumetrically equivalent to about 60% of the average normal volume of a rat AM, after intratracheal instillation into the lungs of rats. Even though both sizes of particles were found to be phagocytized by AMs within a day after deposition, and the smaller particles were cleared at a normal rate, only minimal lung clearance of the larger particles was observed over an approximately 200-day postinstillation period, thus supporting the volumetric AM overload hypothesis.

It has been hypothesized that when the retained lung burden approaches 1 mg particles/g lung tissue, overloading will begin in the rat (Morrow, 1988); at 10 mg particles/g lung tissue macrophage-mediated clearance of particles would effectively cease. Overloading appears to be a nonspecific effect noted in experimental studies, generally in rats, using many different kinds of poorly soluble particles (including TiO_2, volcanic ash, DPM, carbon black, and fly ash) and results in A region clearance slowing or stasis, with an associated inflammation and aggregation of macrophages in the lungs and increased translocation of particles into the interstitium (Muhle et al., 1990a,b; Lehnert, 1990; Morrow, 1994). Following overloading, the subsequent retardation of lung clearance, accumulation of particles, chronic inflammation, and the interaction of inflammatory mediators with cell proliferative processes and DNA may lead to the development of fibrosis, epithelial cell mutations, and fibrosis in rats (Mauderly, 1996). The phenomenon of overload has been discussed in greater detail in the previous PM CD (U.S. EPA, 1996).

3.4.2. Relevance to Humans

The relevance of "lung overload" to humans, and even to species other than laboratory species (rats and mice and hamsters; Muhle et al., 1990a,b), is not clear. Although likely to be of little relevance for most "real world" ambient exposures of humans, this phenomenon is of concern in interpreting some long-term experimental exposure data and perhaps for human

occupational exposure. In addition, relevance to humans is clouded by the fact that macrophage-mediated clearance is slower and perhaps less important in humans than in rats (Morrow, 1994).

Particle overload appears to be an important factor in the pulmonary carcinogenicity observed in rats exposed to DPM. A study by Griffis et al. (1983) demonstrated that exposure (7 h/day, 5 days/week) of rats to diluted whole DE containing DPM at concentrations of 0.15, 0.94, or 4.1 mg/m^3 for 18 mo resulted in lung burdens of 0.035, 0.220, and 1.89 mg/g of lung tissue, respectively. The alveolar clearance of those rats with the highest lung burden (1.89 mg/g of lung) was impaired, as determined by a significantly greater ($p<0.0001$) retention $t_{1/2}$ for DPM. Impaired clearance was reflected in the greater lung burden/exposure concentration ratio at the highest exposure level. Similarly, in the study by Chan et al. (1984), rats exposed for 20 h/day, 7 days/week to diluted whole DE containing DPM (6 mg/m^3) for 112 days had an extraordinarily high lung particle burden of 11.8 mg, with no alveolar particle clearance being detected over 1 year.

Muhle et al. (1990a,b) indicated that overloading of rat lungs occurred when lung particle burdens reached 0.5 to 1.5 mg/g of lung tissue and that clearance mechanisms were totally compromised at lung particle burdens ≥10 mg/g for particles with a specific density close to 1, observations that are concordant with those of Morrow (1988).

Pritchard (1989), utilizing data from a number of DE exposure studies, examined alveolar clearance in rats as a function of cumulative exposure. The resulting analysis noted a significant increase in retention $t_{1/2}$ values at exposures above 10 mg/m^3·h/day and also showed that normal lung clearance mechanisms appeared to be compromised as the lung DPM burden approached 0.5 mg/g of lung.

Animal studies have revealed that impairment of alveolar clearance can occur following chronic exposure to DPM (Griffis et al., 1983; Wolff et al., 1987; Vostal et al., 1982; Lee et al., 1983) or a variety of other diverse poorly soluble particles of low toxicity (Lee et al., 1986, 1988; Ferin and Feldstein, 1978; Muhle et al., 1990). Because high lung burdens of relatively insoluble, biochemically inert particles result in diminution of normal lung clearance kinetics or in what is now called particle overloading, this effect appears to be more related to the mass and/or volume of particles in the lung than to the nature of the particles per se. Particle overload relates only to poorly soluble particles of low toxicity. It must be noted, however, that some types of particles may be cytotoxic and impair clearance at lower lung burdens (e.g., crystalline silica may impair clearance at much lower lung burdens than DPM). Regardless, as pointed out by Morrow (1988), particle overloading in the lung modifies the dosimetry for particles in the lung and thereby can alter toxicologic responses.

Although quantitative data are limited regarding lung overload associated with impaired alveolar clearance in humans, impairment of clearance mechanisms appears to occur, and at a lung burden generally in the range reported to impair clearance in rats, i.e., approximately 1 mg/g lung tissue. Stöber et al. (1967), in their study of coal miners, reported lung particle burdens of 2 to 50 mg/g lung tissue, for which estimated clearance $t_{1/2}$ values were very long (4.9 years). Freedman and Robinson (1988) also reported slower alveolar clearance rates in coal miners, some of whom had a mild degree of pneumoconiosis. It must be noted, however, as has been reported even in some studies with rats exposed lifetime to overload conditions (50 mg/m^3 TiO_2; Lee et al., 1986) that no lung cancer was reported among those miners with apparent particle overload.

Consideration of the above information further clarifies the human relevance of noncancer effects that may be elicited from overload-type conditions in rats studies. Under conditions that would be most likely to elicit overload conditions in humans, such as the excessive dust burdens in the lungs of miners, cancer is not observed although noncancer responses such as fibrosis and macrophage responses are documented (Freedman and Robinson, 1988; Haschek and Witschi, 1991; Oberdörster, 1994). In deliberation on the matter of whether the rat lung nonneoplastic responses to poorly soluble particles (such as DPM) are predictive of a similar hazard in humans, an expert panel (ILSI, 2000) opined that such responses would indeed be a useful predictor for similar responses in humans.

3.4.3. Potential Mechanisms for an AM Sequestration Compartment for Particles During Particle Overload

Several factors may be involved in the particle-load-dependent retardations in the rate of particle removal from the lung and the corresponding functional appearance of an abnormally slow clearing or particle sequestration compartment. As previously mentioned, one potential site for particle sequestration is the containment of particles in the Type I cells. Information on the retention kinetics for particles in the Type I cells is not currently available. Also, no morphometric analyses have been performed to date to estimate what fraction of a retained lung burden may be contained in the Type I cell population of the lung during lung overloading.

Another anatomical region in the lung that may be a slow clearing site is the interstitial compartment (Kuempel, 2000). Little is known about the kinetics of removal of free particles or particle-containing macrophages from the interstitial spaces, or what fraction of a retained burden of particles is contained in the lung's interstitium during particle overload. The gradual accumulation of particles in the regional lymph nodes and the appearance of particles and cells with associated particles in lymphatic channels and in the peribronchial and perivascular

lymphoid tissue (Lee et al., 1985; White and Garg, 1981) suggest that the mobilization of particles from interstitial sites via local lymphatics is a continual process.

Indeed, it is clear from histologic observations of the lungs of rodents chronically exposed to DPM that Type I cells, the interstitium, the lymphatic channels, and pulmonary lymphoid tissues could collectively comprise subcompartments of a more generalized slow clearing compartment.

Although these sites must be considered potential contributors to the increased retention of particles during particle overload, a disturbance in particle-associated AM-mediated clearance is undoubtedly the predominant cause, inasmuch as, at least in rodents, the AMs are the primary reservoirs of deposited particles. The factors responsible for a failure of AMs to translocate from the alveolar space compartment in lungs with high particulate matter burdens remain uncertain, although a hypothesis concerning the process involving volumetric AM burden has been offered (Morrow, 1988).

Other processes also may be involved in preventing particle-laden AMs from leaving the alveolar compartment under conditions of particle overload in the lung. Clusters or aggregates of particle-laden AMs in the alveoli are typically found in the lungs of laboratory animals that have received large lung burdens of a variety of types of particles (Lee et al., 1985), including DPM (White and Garg, 1981; McClellan et al., 1982). The aggregation of AMs may explain, in part, the reduced clearance of particle-laden AM during particle overload. The definitive mechanism(s) responsible for this clustering of AMs has not been elucidated to date. Whatever the underlying mechanism(s) for the AM aggregation response, it is noteworthy that AMs lavaged from the lungs of DE-exposed animals continue to demonstrate a propensity to aggregate (Strom, 1984). This observation could result either from the surface characteristics of AMs being fundamentally altered or from macrophage activation by phagocytized particles that then release chemotactic factors (Bellmann et al., 1990) in a manner that promotes their adherence to one another in the alveolar region. AM aggregation may not simply be directly caused by their abundant accumulation as a result of immobilization by large particle loads. Furthermore, even though overloaded macrophages may redistribute particle burden to other AMs, clearance may remain inhibited (Lehnert, 1988). This may, in part, be because attractants from the overloaded AMs cause aggregation of those that are not carrying a particle burden.

3.5. BIOAVAILABILITY OF ORGANIC CONSTITUENTS PRESENT ON DIESEL EXHAUST PARTICLES

Because it has been shown that DPM extract is not only mutagenic but also contains known carcinogens, the organic fraction was originally considered to be the primary source of carcinogenicity in animal studies. Since then, evidence has been presented that carbon black,

lacking an organic component, is capable of inducing lung cancer at exposure concentrations sufficient to induce lung particle overload. This suggested that the relatively insoluble carbon core of the particle may be of greater importance for the pathogenic and carcinogenic processes observed in the rat inhalation studies conducted at high exposure concentrations. (See Chapter 7 for a discussion of this issue.) However, lung cancer reported in epidemiologic studies was associated with diesel exposure levels far below those inducing particle overload in lifetime studies in rats. It is therefore suggested that compounds in the organic fraction of DPM may have some role in the etiology of human lung cancers. This leads to an interest in characterizing the bioavailability of organics.

The bioavailability of toxic organic compounds adsorbed to DPM can be influenced by a variety of factors. Although the agent may be active while present on the particle, most particles are taken up by AMs, a cell type not generally considered to be a target site. In order to reach the target site, elution from the particle surface is necessary followed by diffusion and uptake by the target cell. Metabolism to an active form by either the phagocytes or the target cells is also required for activity of many of the compounds present.

This section describes only the various manner and mechanisms by which organics adsorbed onto DPM may become bioavailable. In vivo and in vitro results involving various biological extraction media as well as modeled scenarios of bioavailability are presented. Actual estimates of the amount of organics from DPM to which respiratory tract tissues may be exposed are discussed and presented in Section 3.6.2.7.

3.5.1. In Vivo Studies

3.5.1.1. *Laboratory Investigations*

Several studies reported on the retention of particle-adsorbed organics following administration to various rodent species. In studies reported by Sun et al. (1982, 1984) and Bond et al. (1986), labeled organics were deposited on DPM following heating to vaporize away the organics originally present. Sun et al. (1982) compared the disposition of either pure or diesel particle-adsorbed benzo[*a*]pyrene (B[*a*]P) following nose-only inhalation by F344 rats. About 50% of particle-adsorbed B[*a*]P was cleared with a half-time of 1 h, predominantly by mucociliary clearance. The long-term retention of particle-adsorbed ^{3}H-B[*a*]P at 18 days was approximately 230-fold greater than that for pure ^{3}H-B[*a*]P (Sun et al., 1982). At the end of exposure, about 15% of the ^{3}H label was found in blood, liver, and kidney. Similar results were reported in a companion study by Bond et al. (1986), and by Sun et al. (1984) with another PAH, 1-nitropyrene, except the retention half-time was 36 days.

Ball and King (1985) studied the disposition and metabolism of intratracheally instilled ^{14}C-labeled 1-NP (>99.9% purity) coated onto DPM. About 50% of the ^{14}C was excreted within

the first 24 h; 20% to 30% of this appeared in the urine, and 40% to 60% was excreted in the feces. Traces of radiolabel were detected in the trachea and esophagus. Five percent to 12% of the radiolabel in the lung co-purified with the protein fraction, indicating some protein binding. The corresponding DNA fraction contained no ^{14}C above background levels.

Bevan and Ruggio (1991) assessed the bioavailability of B[*a*]P adsorbed to DPM from a 5.7-L Oldsmobile diesel engine. In this study, exhaust particles containing 1.03 μg B[*a*]P/g particles were supplemented with exogenous ^{3}H-B[*a*]P to provide 2.62 μg B[*a*]P/g of exhaust particles. In vitro analysis indicated that the supplemented B[*a*]P eluted from the particles at the same rate as the original B[*a*]P. Twenty-four hours after intratracheal instillation in Sprague-Dawley rats, 68.5% of the radiolabel remained in the lungs. This is approximately a 3.5-fold greater proportion than that reported by Sun et al. (1984), possibly because smaller amounts of B[*a*]P adsorbed on the particles resulted in stronger binding or possibly because of differences between inhalation exposure and intratracheal exposure. At 3 days following administration, more than 50% of the radioactivity remained in the lungs, nearly 30% had been excreted into the feces, and the remainder was distributed throughout the body. Experiments using rats with cannulated bile ducts showed that approximately 10% of the administered radioactivity appeared in the bile over a 10-h period and that less than 5% of the radioactivity entered the feces via mucociliary transport. Results of these studies showed that when organics are adsorbed to DPM the retention of organics in the lungs is increased considerably. Because retention time is very short following exposure to pure compounds not bound to particles, it can be concluded that the increased retention time is primarily the result of continued binding to DPM. The detection of labeled compounds in blood, systemic organs, urine, and bile as well as the trachea, however, provides evidence that at least some of the organics are eluted from the particles following deposition in the lungs and would not be available as a carcinogenic dose to the lung. As discussed above, the results of Gerde (1999a,b) indicate that most of the organics eluted from particles deposited in the alveolar region, especially PAHs, are predicted to rapidly enter the bloodstream and thus not to contribute to potential induction of lung cancer.

3.5.1.2. *Studies in Occupationally Exposed Humans*

DNA adducts in the lungs of experimental animals exposed to DE have been measured in a number of animal experiments (World Health Organization, 1996). Such studies, however, provide limited information regarding bioavailability of organics, as positive results may well have been related to factors associated with lung particle overload, a circumstance reported by Bond et al. (1990), who found carbon black, a substance virtually devoid of organics, to induce DNA adducts in rats at lung overload doses. These authors showed that levels of DNA adducts present in pulmonary type II cells from the lungs of rats (n=15) exposed to equivalent conditions

of either carbon black or DE (each at 6.2 mg/m^3) were nearly the same and 4- to 5-fold more than air-exposed controls. This similarity was noted despite a difference of nearly three orders of magnitude in solvent-extractable organic content between DE (30%) and carbon black (0.04%). None of the DE or carbon black adducts comigrated with B[*a*]P diol epoxide.

On the other hand, DNA adduct formation and/or mutations in blood cells following exposure to DPM, especially at levels insufficient to induce lung overload, can be presumed to be the result of organics diffusing into the blood. Hemminki et al. (1994) reported increased levels of DNA adducts in lymphocytes of bus maintenance and truck terminal workers. Österholm et al. (1995) studied mutations at the hprt-locus of T-lymphocytes in bus maintenance workers. Although they were unable to identify clear-cut exposure-related differences in types of mutations, adduct formation was significantly increased in the exposed workers. Nielsen et al. (1996) reported significantly increased levels of lymphocyte DNA adducts, hydroxyvaline adducts in hemoglobin, and 1-hydroxypyrene in urine of garage workers exposed to DE.

3.5.2. In Vitro Studies

3.5.2.1. *Extraction of Diesel Particle-Associated Organics by Biological Fluids*

In vitro extraction of mutagenic organics by biological fluids can be estimated by measurement of mutagenic activity in the particular fluid. Using this approach, Brooks et al. (1981) reported extraction efficiencies of only 3% to 10% that of dichloromethane following DPM incubation in lavage fluid, serum, saline, albumin, or dipalmitoyl lecithin. Moreover, extraction efficiency did not increase with incubation time up to 120 h. Similar findings were reported by King et al. (1981), who also reported that lung lavage fluid and lung cytosol fluid extracts of DPM were not mutagenic. Serum extracts of DPM did exhibit some mutagenic activity, but considerably less than that of organic solvent extracts. Furthermore, the mutagenic activity of the solvent extract was significantly reduced when combined with serum or lung cytosol fluid, suggesting protein binding or biotransformation of the mutagenic components. Siak et al. (1980) assessed the mutagenicity of material extracted from DPM by bovine serum albumin in solution, simulated lung surfactant, fetal calf serum (FCS), and physiological saline. Only FCS was found to extract some mutagenic activity from the DPM. Keane et al. (1991), however, reported positive effects for mutagenicity in salmonella and sister chromatid exchange in V79 cells exclusively in the supernatant fraction of DPM dispersed in aqueous mixtures of dipalmitoyl phosphatidyl choline, a major component of pulmonary surfactant, indicating that pulmonary surfactant components can extract active components of DPM and result in bioavailability.

The ability of biological fluids to extract organics in vitro and their effectiveness in vivo remains equivocal because of the character of the particular fluid. For example, extracellular

lung fluid is a complex mixture of constituents that undoubtedly have a broad range of hydrophobicity (George and Hook, 1984; Wright and Clements, 1987), which is fundamentally different from serum in terms of chemical composition (Gurley et al., 1988). Moreover, assessments of the ability of lavage fluids, which actually represent substantially diluted extracellular lung fluid, to extract mutagenic activity from DPM clearly do not reflect the in vivo condition. Finally, except under very high exposure concentrations, few particles escape phagocytosis and possible intracellular extraction. In this respect, Hiura et al. (1999) have shown that whole exhaust containing DPM, but not carbon black or diesel particles devoid of organics, induces apoptosis, apparently through generation of oxygen radicals. This study implicates organic compounds present on DPM. It also indicates the bioavailability of organics for generation of radicals from reaction with particle-associated organics or following elution from DPM.

3.5.2.2. *Extraction of DPM-Associated Organics by Lung Cells and Cellular Components*

A more likely means by which organics may be extracted from DPM and metabolized in the lung is either through particle dissolution or extraction of organics from the particle surface within the phagolysosomes of AMs and other lung cells. This mechanism presupposes that the particles are internalized. Specific details about the physicochemical conditions of the intraphagolysosomal environment, where particle dissolution in AMs presumably occurs in vivo, have not been well characterized. It is known that phagolysosomes constitute an acidic (pH 4 to 5) compartment in macrophages (Nilsen et al., 1988; Ohkuma and Poole, 1978). The relatively low pH in the phagolysosomes has been associated with the dissolution of some types of inorganic particles (some metals) by macrophages (Marafante et al., 1987; Lundborg et al., 1984), but few studies provide quantitative information concerning how organics from DPM may be extracted in the phagolysosomes (Bond et al., 1983). Whatever the mechanism, assuming elution occurs, the end result is a prolonged exposure of the respiratory epithelium to DPM organics, which include low concentrations of carcinogenic agents such as PAH.

Early studies by King et al. (1981) found that when pulmonary alveolar macrophages were incubated with DPM, amounts of organic compounds and mutagenic activity decreased measurably from the amount originally associated with the particles, suggesting that organics were removed from the phagocytized particles. Leung et al. (1988) studied the ability of rat lung and liver microsomes to facilitate transfer and metabolism of B[*a*]P from diesel particles. ^{14}C-B[*a*]P coated diesel particles, previously extracted to remove the original organics, were incubated directly with liver or lung microsomes. About 3% of the particle-adsorbed B[*a*]P was transferred to the lung microsomes within 2 h. Of this amount about 1.5% was metabolized, for a total of about 0.05% of the B[*a*]P originally adsorbed to the DPM. Although transformation is

slow, the long retention of particles, including DPM, in humans may cause the fraction eluted and metabolized to be considerably higher than this figure.

In analyzing phagolysosomal dissolution of various ions from particles in the lungs of Syrian golden hamsters, however, Godleski et al. (1988) demonstrated that solubilization did not necessarily result in clearance of the ions (and therefore general bioavailability) in that binding of the solubilized components to cellular and extracellular structures occurred. It is reasonable to assume that phagocytized DPM particles may be subject to similar processes and that these processes would be important in determining the rate of bioavailability of the particle-bound constituents of DPM.

Alveolar macrophages or macrophage cell lines that were exposed to high concentrations of DPM in vitro were observed to undergo apoptosis, which was attributed to the generation of reactive oxygen radicals (ROR) (Hiura et al. 1999). Further experimentation showed that DPM with the organic constituents extracted was no longer able to induce apoptosis or generate ROR. The organic extracts alone, however, were able to induce apoptosis as well as the formation of stress-activated protein kinases that play definitive roles in cellular apoptotic pathways. The injurious effects of nonextracted DPM or of DPM extracts were observed to be reversible by the antioxidant radical scavenger N-acetyl cysteine. These data suggest strongly that, at least at high concentrations of DPM, the organic constituents contained on DPM play a central role in cellular toxicity and that this toxicity may be attributable to the generation of ROR.

3.5.3. Modeling Studies

Gerde et al. (1991a,b) described a model simulating the effect of particle aggregation and PAH content on the rate of PAH release in the lung. According to this model, particle aggregation will occur with high exposure concentrations, resulting in a slow release of PAHs and prolonged exposure to surrounding tissues. However, large aggregates of particles are unlikely to form at doses typical of human exposures. Inhaled particles, at low concentrations, are more likely to deposit and react with surrounding lung medium without interference from other particles. The model predicts that under low-dose exposure conditions, more typical in humans, particle-associated organics will be released more rapidly from the particles because they are not aggregated. Output from this model suggests strongly that sustained exposure of target tissues to PAHs will result from repeated exposures, not from increased retention due to association of PAHs with carrier particles. This distinction is important because at low doses PAH exposure and lung tumor formation would be predicted to occur at sites of deposition rather than retention, as occurs with high doses.

The site of release of PAHs influences effective dose to the lungs because, as noted previously, at least some free organic compounds deposited in the lungs are rapidly absorbed into

the bloodstream. Gerde et al. (1991b) predicted PAHs would be retained in the alveoli less than 1 min, whereas they may be retained in the conducting airways for hours. These predictions were based on an average diffusion distance to capillaries of only about 0.5 μm in the alveoli, as compared to possibly greater than 50 μm in the conducting airways such as the bronchi. An experimental study by Gerde et al. (1999) provided support for this prediction. Beagle dogs were exposed to ^{3}H-B[*a*]P adsorbed on the carbonaceous core of DPM at a concentration of 15 μg B[*a*]P/gm particles. A rapidly eluting fraction from DPM deposited in the alveoli was adsorbed into the bloodstream and metabolized in the liver, whereas the rapidly eluting fraction from DPM deposited in the conducting airways was to a large extent retained and metabolized in situ in the airway epithelium. Thus, organics eluting from DPM depositing in the conducting airways (i.e., the TB region) would have a basis for a longer residence time in the tissues (and for consequent biological activity) than would organics eluting from DPM depositing in the pulmonary parenchyma. And, given the same overall deposited dose of DPM to the total pulmonary system, a deposited dose with a higher proportion in the TB region would incur a higher probability of tissue interactions with any eluted organics. This may be the case when comparing regional doses of DPM to humans as compared to rats for two reasons. First, one deposition model (Freijer et al., 1999) projects that for air concentrations of DPM at either 0.1 or 1.0 mg/m^3, a higher proportion of the total DPM dose to the pulmonary system would be deposited in the TB area for humans at 31% (TB/Total; 0.098 / 0.318) than for rats at only 16% (0.04 / 0.205). Second, comparative morphometry data of DPM from chronically exposed rats and primates showed higher levels of DPM adjacent to conducting airways in primates (i.e., the interstitium of the respiratory bronchioles) than were present in parallel regions in the rat (interstitium of the alveolar ducts) (Nikula et al., 1997a,b). The focal nature of this deposition could give rise to localized high concentrations of any organics eluted.

3.5.4. Summary and Bioavailability

At present, the available data are insufficient to accurately model the effective dose of organics in the respiratory tract of humans or animals exposed to DPM. As mentioned above, though, the following Section (3.6.2.7) does present estimates of the actual amount of organics, including carcinogenic PAH such as B[*a*]P, that are deposited in the lung and could become bioavailable.

Overall, the results of studies presented in Section 3.6 provide evidence that at least some of the organic matter adsorbed to DPM deposited in the respiratory tract is eluted. The percentage taken up and metabolized to an active form by target cells is, however, uncertain. Organics eluted from particles deposited in alveoli are likely to rapidly enter the bloodstream via translocation across endothelial cells, where they may undergo metabolism by enzymes such as

cytochromes P-450 that are capable of producing reactive species. Organics eluted from particles deposited in the conducting airways (the bronchioles, bronchi, and trachea) may also undergo metabolism in other cell types such as the Clara cells with constituent or inducible cytochrome P-450 species. Risk of harmful effects for particles deposited in the conducting airways is predicted to be greater because solubilized organic compounds will be retained in the thicker tissue longer, allowing for metabolism by epithelial cells lining the airways. Furthermore, since some deposition in conducting airways occurs primarily at bifurcations, localized higher concentrations may occur.

3.6. MODELING THE DEPOSITION AND CLEARANCE OF PARTICLES IN THE RESPIRATORY TRACT

3.6.1. Introduction

The biological effects of inhaled particles are a function of their disposition, i.e., their deposition and clearance. This, in turn, depends on their patterns of deposition (i.e., the sites within which particles initially come into contact with airway epithelial surfaces and the amount removed from the inhaled air at these sites) and clearance (i.e., the rates and routes by which deposited materials are removed from the respiratory tract). Removal of deposited materials involves the competing processes of macrophage-mediated clearance and dissolution-absorption. Over the years, mathematical models for predicting deposition, clearance and, ultimately, retention of particles in the respiratory tract have been developed. Such models help interpret experimental data and can be used to make predictions of deposition for cases where data are not available. A review of various mathematical particle deposition models was given by Morrow and Yu (1993) and in U.S. EPA (1996).

Currently available data for long-term inhalation exposures to poorly soluble particles (e.g., TiO_2, carbon black, and DPM) show that pulmonary retention and clearance of these particles are not adequately described by simple first-order kinetics and a single compartment representing the alveolar macrophage particle burden. Several investigators have developed models for deposition, transport, and clearance of poorly soluble particulate matter in the lungs. All of these models identify various compartments and associated transport rates, but empirically derived data are not available to substantiate many of the assumptions made in these models.

3.6.2. Dosimetry Models for DPM

3.6.2.1. *Introduction*

The extrapolation of toxicological results from laboratory animals to humans, the goal of this chapter, requires the use of dosimetry models for both species that include, first, the deposition of DPM in various regions of the respiratory tract, and second, the transport and

clearance of the particles, including adsorbed constituents, from their deposited sites. Therefore the ideal model structure would incorporate both deposition and clearance in animals and humans.

Deposition of particles in the respiratory tract, as described above, can be by impaction, sedimentation, interception, and diffusion, with the contribution from each mechanism a function of particle size, lung structure, and size and breathing parameters. Because of the size of diesel particles, under normal breathing conditions most of this deposition takes place by diffusion, and the fraction of the inhaled mass that is deposited in the thoracic region (i.e., TB plus A regions) is substantially similar for rats and humans.

Among deposition models that include aspects of lung structure and breathing dynamics, the most widely used have been typical-path or single-path models (Yu, 1978; Yu and Diu, 1983). The single-path models are based on an idealized symmetric geometry of the lung, assuming regular dichotomous branching of the airways and alveolar ducts (Weibel, 1963). They lead to modeling the deposition in an average regional sense for a given lung depth. Although the lower airways of the lung may be reasonably characterized by such a symmetric representation, there are major asymmetries in the upper airways of the tracheobronchial tree that in turn lead to different apportionment of airflow and particulate burden to the different lung lobes. The rat lung structure is highly asymmetric because of its monopodial nature, leading to significant errors in a single-path description. This is rectified in the multiple-path model of the lung, which incorporates asymmetry and heterogeneity in lung branching structure and calculates deposition at the individual airway level. This model has been developed for the rat lung (Anjilvel and Asgharian, 1995; Freijer et al., 1999) and, in a limited fashion because of insufficient morphometric data, for the human lung (Subramaniam et al., 1998; Yeh and Schum, 1980). Such models are particularly relevant for fine and ultrafine particles such as occur in DPM. However, models for clearance have not yet been implemented in conjunction with the use of the multiple-path model.

Clearance of particles in the respiratory tract takes place (1) by mechanical processes: mucociliary transport in the ciliated conducting airways and macrophage phagocytosis and migration in the nonciliated airways, and (2) by dissolution. The removal of material such as the carbonaceous core of DPM is largely by mechanical clearance, whereas the clearance of the organics adsorbed onto the carbon core is principally by dissolution.

Several models currently exist that integrate both deposition and clearance, some specific for humans and others specific for laboratory animals. They differ significantly in the level of physiological detail that is captured in the model and in the uncertainties associated with the values of the parameters used. All of these models identify various compartments and associated transport rates, but empirically derived data are not available to validate many of the assumptions

made in the models. A review of the principal human and animal deposition/clearance models, including candidate models for use in animal-to-human extrapolation in this assessment, are considered below.

3.6.2.2. *Human Models*

The International Commission on Radiological Protection (ICRP) recommends specific mathematical dosimetry models as a means to calculate the mass deposition and retention by different parts of the human respiratory tract and, if needed, tissues beyond the respiratory tract. The latest ICRP-recommended model, ICRP66 (1994), considers the human respiratory tract as four general anatomical regions: the ET region, which is divided into two subregions; the TB region, which is also subdivided into two regions; and the gas-exchange tissues, which are further defined as the alveolar-interstitial (AI) region but are exactly comparable to the pulmonary or A region. The fourth region is the lymph nodes. The deposition component of the model for the ET, TB, and A regions is semi-empirical based on equations derived from fitting experimental deposition data. The dimensional model used for the TB and A regions was adopted from several sources (Weibel, 1963; Yeh and Schum, 1980; and Phalen et al., 1985); the physical aspects of the individual airway generations for these regions were all averaged after each source was adjusted to a standard functional residual capacity. The equations for estimating deposition in these areas was empirical, obtained from fitting data obtained from partial human lung casts or from theoretical calculation for these regions. Deposition in the four regions is given as a function of particle size with two different types of particle size parameters: activity median thermodynamic diameter (AMTD) for deposition of particles ranging in size from 0.0005 to 1.0 μm and the activity median aerodynamic diameter (AMAD) for deposition of particles from 0.1 to 100μm. Reference values of regional deposition are provided and guidance is given for extrapolating to specific individuals and populations under different levels of activity. This model also includes consideration of particle inhalability, a measure of the degree to which particles can enter the respiratory tract and be available for deposition. After deposition occurs in a given region, two different intrinsic clearance processes act competitively on the deposited particles: particle transport, including mucociliary clearance from the respiratory tract and physical clearance of particles to the regional lymph nodes; and absorption, including movement of material to blood and both dissolution-absorption and transport of ultrafine particles. Rates of particle clearance derived from studies with human subjects are assumed to be the same for all types of particles. The ICRP model provides average concentration or average number values on a regional basis, i.e., mass or number deposited or retained in the ET, TB, or A regions. Additionally, while the ICRP66 model was developed primarily for use with airborne radioactive

particles and gases in humans, its use for describing the dosimetry of inhaled mass of nonradioactive substances in humans is also appropriate.

The National Council on Radiation Protection (NCRP) has issued a human respiratory tract dosimetry model that was developed concurrently with the ICRP model (NCRP, 1997; Phalen et al.,1991). It addresses (1) inhalability of particles, (2) new subregions of the respiratory tract, (3) dissolution-absorption as an important aspect of the model, and (4) body size (and age). The proposed NCRP model defines the respiratory tract in terms of a naso-oro-pharyngo-laryngeal (NOPL) region, a TB region, a pulmonary (P) region, and the lung-associated lymph nodes (LN). Like the ICRP model, the deposition component of the model for the ET region is semi-empirical, based on equations derived from fitting experimental deposition data. The dimensional model used for the TB and A regions was that of Yeh and Schum (1980). The data from this model were used to estimate physical processes along a typical lung path (vice multiple-path; see MPPDep model description below) on a generation-by-generation basis. The rates of dissolution-absorption of particles and their constituents are derived from clearance data from humans and laboratory animals. The effect of body growth on particle deposition is also considered in the model, although particle clearance rates are assumed to be independent of age. The NCRP model currently available considers deposition only within these regions of the respiratory tract. As with the ICRP model, the NCRP model can be used for evaluating inhalation exposures to all types of particles. Comparison of regional deposition patterns estimated by the ICRP66 and the current NCRP models have been reported (Yeh et al., 1996). One principal difference between the models is the enhanced deposition of ultrafines in the tracheobronchial region predicted by the NCRP model compared with the ICRP model. This effect of enhanced deposition is claimed to be due to the entrance configuration of an airway bifurcation.

The model of Freijer et al. (1999) is a multiple-path particle deposition model (MPPDep) for the human respiratory tract that differs fundamentally from the above two models as described in the Introduction. Calculations from the model may be based on either single-path or multiple-path methods for tracking air flow and calculating aerosol deposition in the lung. The single-path method calculates deposition for a typical path, whereas the multiple-path method is capable of incorporating the asymmetry in lung structure and providing lobar-specific and airway-specific information. Two options are provided for idealizing the geometry of the human lung; one uses a symmetric geometry for the whole lung and the second option captures the asymmetry in the lobar structure, but treats the geometry within each lung lobe in a symmetric fashion. Both models are constructed using morphometric data compiled by Yeh and Schum (1980). Within each airway, deposition is calculated using theoretically derived efficiencies for deposition by diffusion (most relevant to DPM), sedimentation, and impaction within the airway

or airway bifurcation. Filtration of particulate aerosols by the head is determined using empirical efficiency functions. The model calculates deposition of monodisperse and polydisperse aerosols in the respiratory tract of both humans (and rats) for particles ranging from ultrafine (0.01 microns) to coarse (20 microns) sizes. Various breathing patterns may be simulated: endotratracheal, nasal, oral, and combined nasal and oral (oronasal). The exposure scenario may be constant or variable. For the variable scenario, the user may specify different breathing patterns either on an hourly basis during the day or activity patterns for variable time durations. Adjustment for inhalability of the particle is also included as an option. The software in this model provides results for the deposition fraction and mass deposited in the various regions of the respiratory tract in graphical and text formats.

The combined model of Yu et al. (1991) has a human component that will be discussed below.

3.6.2.3. *Animal Models*

Strom et al. (1988) developed a multicompartmental model for particle retention that partitioned the alveolar region into two compartments on the basis of the physiology of clearance. The alveolar region has a separate compartment for sequestered macrophages, corresponding to phagocytic macrophages that are heavily laden with particles and clustered, and consequently have significantly lowered mobility. The model has the following compartments:
(1) tracheobronchial tree, (2) free particulate on the alveolar surface, (3) mobile phagocytic alveolar macrophages, (4) sequestered particle-laden alveolar macrophages, (5) regional lymph nodes, and (6) gastrointestinal tract. The model is based on mass-dependent clearance (the rate coefficients reflect this relationship), which dictates sequestration of particles and their eventual transfer to the lymph nodes. The transport rates between various compartments were obtained by fitting the calculated results to lung and lymph node burden experimental data for both exposure and postexposure periods. Because the number of fitted parameters was large, the model is not likely to provide unique solutions that would simulate experimental data from various sources and for different exposure scenarios. For the same reason, it is not readily possible to use this model for extrapolating to humans.

Stöber and co-workers have worked extensively in developing models for estimating retention and clearance of relatively insoluble respirable particles (as DPM) in the lung. Their most recent work (1994), a revised version of the POCK model, is a rigorous attempt to incorporate most of the physiologically known aspects of alveolar clearance and retention of inhaled relatively insoluble particles. Their multicompartmental kinetics model has five subcompartments. The transfer of particles between any of the compartments within the alveolar region is macrophage mediated. There are two compartments that receive particles cleared from

the alveolar regions: the TB tract and the lymphatic system. The macrophage pool includes both mobile and particle-laden immobilized macrophages. The model assumes a constant maximum volume capacity of the macrophages for particle uptake and a material-dependent critical macrophage load that results in total loss of macrophage mobility. Sequestration of those macrophages heavily loaded with a particle burden close to a volume load capacity is treated in a sophisticated manner by approximating the particle load distribution in the macrophages. The macrophage pool is compartmentalized in terms of numbers of macrophages that are subject to discrete particle load intervals. Upon macrophage death, the phagocytized particle is released back to the alveolar surface; thus phagocytic particle collection competes to some extent with this release back to the alveolar surface. This recycled particle load is also divided into particle clusters of size intervals defining a cluster size distribution on the alveolar surface. The model yields a time-dependent frequency distribution of loaded macrophages that is sensitive to both exposure and recovery periods in inhalation studies.

The POCK model also emphasizes the importance of interstitial burden in the particle overload phenomenon and indicates that particle overload (Section 3.4) is a function of a massive increase in particle burden of the interstitial space rather than total burden of the macrophage pool. The relevance of the increased particle burden in the interstitial space lies with the fact that this compartmental burden is not available for macrophage-mediated clearance and, therefore, persists even after cessation of exposure.

Although the POCK model is the most sophisticated in the physiological complexity it introduces, it suffers from a major disadvantage. Experimental retention studies provide data only on total alveolar and lymph node mass burdens of the particles as a function of time. The relative fraction of the deposition between the alveolar subcompartments in the Stöber model therefore cannot be obtained experimentally; the model thus uses a large number of parameters that are simultaneously fit to experimental data. Although the model predictions are tenable, experimental data are not currently available to substantiate the proposed compartmental burdens or the transfer rates associated with these compartments. Thus, overparameterization in the model leads to the possibility that the model may not provide a unique solution that may be used for a variety of exposure scenarios, and for the same reason, cannot be used for extrapolation to humans. Stöber et al. have not developed an equivalent model for humans; therefore the use of their model in our risk assessment for diesel is not attempted.

3.6.2.4. *Combined Models (for interspecies extrapolation)*

Currently available data for long-term inhalation exposures to poorly soluble particles (e.g., TiO_2, carbon black, and DPM) show that pulmonary retention and clearance of these particles are not adequately described by simple first-order kinetics and a single compartment

representing the alveolar macrophage particle burden. A two-compartment lung model that could be applied to both humans and animals was developed by Smith (1985) and includes alveolar and interstitial compartments. For uptake and clearance of particles by alveolar surface macrophages and interstitial encapsulation of particles (i.e., quartz dust), available experimental data show that the rate-controlling functions followed Michaelis-Menton type kinetics, whereas other processes affecting particle transfer are assumed to be linear. The model was used in an attempt to estimate interstitial dust and fibrosis levels among a group of 171 silicon carbide workers; the levels were then compared with evidence of fibrosis from chest radiographs. A significant correlation was found between estimated fibrosis and profusion of opacities on the radiographs. This model provides as many as seven different rate constants derived by various estimations and under various conditions from both animal and human sources. The model was intended for estimation of generalized dust described only as respirable without any other regard to sizing for establishing the various particle-related rate constants. As most of the described functions could not be validated with experimental data, the applicability of this model, especially for particulates in the size range of DPM, was unclear.

Yu et al. (1991; also reported as Yu and Yoon, 1990) have developed a three-compartment lung model that consists of tracheobronchial (T), alveolar (A), and lymph node (L) compartments (Appendix A, Figure A-1) and, in addition, considered filtration by a nasopharyngeal or head (H) compartment. The tracheobronchial compartment is important for short-term considerations, whereas long-term clearance takes place via the alveolar compartment. In contrast to the Stöber and Strom approaches, the macrophage compartment in the Yu model contains all of the phagocytized particles; that is, there is no separate (and hypothetical) sequestered macrophage subcompartment. Absorption by the blood (B) and gastrointestinal (G) compartments was also considered. Although the treatment of alveolar clearance is physiologically less sophisticated than that of the Stöber et al. model, the Yu model provides a more comprehensive treatment of clearance by including systemic compartments and the head, and including the clearance of the organic components of DPM in addition to the relatively insoluble carbon core.

In order to progress beyond the classical human ICRP66 retention model, Yu has addressed the impairment of long-term clearance (the overload effect) by using a set of variable transport rates for clearance from the alveolar region as a function of the mass of DPM in the alveolar compartment. A functional relationship for this was derived mathematically (Yu et al., 1989) based upon Morrow's hypothesis for the macrophage overload effect discussed earlier in the section on pulmonary overload. The extent of the impairment depends on the initial particle burden, with greater particulate concentration leading to slower clearance.

Within this model, DPM is treated as being composed of three material components: a relatively insoluble carbonaceous core, slowly cleared organics (10% particle mass), and fast-cleared organics (10% particle mass). Such a partitioning of organics was based on observations that the retention of particle-associated organics in lungs shows a biphasic decay curve (Sun et al., 1984; Bond et al., 1986). For any compartment, each of these components has a different transport rate. The total alveolar clearance rate of each material component is the sum of clearance rates of that material from the alveolar to the tracheobronchial, lymph, and blood compartments. In the Strom and Stöber models discussed above, the clearance kinetics of DPM were assumed to be entirely dictated by those of the relatively insoluble carbonaceous core. For those organic compounds that become dissociated from the carbon core, clearance rates are likely to be very different, and some of these compounds may be metabolized in the pulmonary tissue or be absorbed by blood.

The transport rates for the three components were derived from experimental data for rats using several approximations. The transport rates for the carbonaceous core and the two organic components were derived by fitting to data from separate experiments. Lung and lymph node burdens from the experiment of Strom et al. (1988) were used to determine the transport rate of the carbonaceous core. The Yu model incorporates the impairment of clearance by including a mass dependency in the transport rate. This mass dependency is easily extracted because the animals in the experiment were sacrificed over varying periods following the end of exposure.

It was assumed that the transport rates from the alveolar and lymph compartments to the blood were equal and independent of the particulate mass in the alveolar region. The clearance rates of particle-associated organics for rats were derived from the retention data of Sun et al. (1984) for B[a]P and the data of Bond et al. (1986) for nitropyrene adsorbed on diesel particles.

In their model Yu et al. (1991) make two important assumptions to carry out the extrapolation in consideration of inadequate human data. First, the transport rates of organics in the DPM do not change across species. This is based upon lung clearance data of inhaled lipophilic compounds (Schanker et al., 1986), where the clearance was seen to be dependent on the lipid/water partition coefficient. In contrast, the transport rate of the carbonaceous core is considered to be significantly species dependent (Bailey et al., 1982). DPM clearance rate is determined by two terms in the model (see Equation A-82 in Appendix A). The first, corresponding to macrophage-mediated clearance, is a function of the lung burden and is assumed to vary significantly across species. The second term, a constant, corresponding to clearance by dissolution, is assumed to be species independent. The mass-dependent term for humans is assumed to vary in the same proportion as in rats under the same unit surface particulate dose. The extrapolation is then achieved by using the data of Bailey et al. (1982) for the low lung burden limit of the clearance rate. This value of 0.0017/day was lower (i.e., slower)

than the rat value by a factor of 7.6. This is elaborated further in Appendix A. Other transport rates that have lung burden dependence are extrapolated in the same manner.

It should be noted that the Bailey et al. (1982) experiment in humans used fused monodisperse aluminosilicate particles of 1.9 and 6.1 μm aerodynamic diameters. Yu and co-workers have used the longer of the half-times observed in this experiment to obtain an alveolar human clearance rate (λ), of 0.00169/day. In using such data for DPM 0.2 μm in diameter, they have assumed the clearance of relatively insoluble particles to be independent of size over the range in diameter from 6.1 down to 0.2 μm. This assumption is consistent with observations and views currently in the literature indicating that clearance mechanisms are not particularly particle-size dependent (Morrow et al., 1967a,b; Snipes et al., 1983). That the linear dimensions of an alveolar macrophage, considered to be the principal means of clearance in the A region, are significantly larger, roughly 10 μm (Yu et al., 1996), and could therefore accommodate engulfment of a range of particle sizes also makes this assumption reasonable. Snipes (1979), however, has reported in rats a λ (converted here from half-time values) of 0.0022/day for 1 and 2 μm particles but a higher value of 0.0039/day for 0.4 μm particles indicating that clearance rates may indeed depend on size. In the absence of reliable data for 0.2 μm particles, the slower clearance rate pertaining to this larger particle size, i.e., 0.00169/day, is being used. Such a choice may underestimate the actual DPM clearance rate in humans. The resulting model output (i.e., lung DPM burden) from this slower rate would predict more DPM in the alveolar space than may actually be present at any given time. Therefore, use of this slower λ may be considered to be more protective of human health. Long-term clearance rates for particle sizes more comparable to DPM are available, e.g., iron oxide and polystyrene spheres (Waite and Ramsden, 1971; Jammet et al., 1978), but these data show a large range in the values obtained for half-lives or are based upon a very small number of trials, and therefore compare unfavorably with the quality of data from the Bailey experiment.

The deposition fractions of particulate matter in the pulmonary and tracheobronchial regions of the human lung remain relatively unchanged over the particle size range between 0.2 and 1.0 μm, on the basis of analysis done with the ICRP model (ICRP66, 1994). As the clearance of relatively insoluble particles is also likely to remain the same over this range, the dosimetry results in this report for the carbonaceous core component of DPM could also be extended to other particles in this size range within the $PM_{2.5}$. For respirable particles with diameters larger than this range, e.g., between 1.0 and 3.5 μm, the extent of the fraction deposited in the pulmonary region is unclear. Results from the ICRP66 (1994) model predict little change in human deposition for this diameter range, whereas the earlier model of Yu and Diu (1983) predicts a significant increase as reported in ICRP66 (1994). It is therefore unclear if either model would be applicable for particles in this larger-sized range without changing the value for

the deposition fractions. As will be presented and discussed below, regional deposition fractions of DPM-sized particles from the MPPDep, the ICRP66 (1994) and draft NCRP models compare favorably with the human alveolar deposition in humans specific for DPM, which has been estimated with the Yu model to be 7% to 13% (Yu and Xu, 1986).

Although there was good agreement between experimental and modeled results, this agreement follows a circular logic (as adequately pointed out by Yu and Yoon [1990]) because the same experimental data that figured into the derivation of transport rates were used in the model. Nevertheless, even though this agreement is not a validation, it provides an important consistency check on the model. Further experimental data and policy definitions on what constitutes validation would be necessary for a more formal validation.

The model showed that at low lung burdens, alveolar clearance is dominated by mucociliary transport to the tracheobronchial region, and at high lung burdens, clearance is dominated by transport to the lymphatic system. The head and tracheobronchial compartments showed quick clearance of DPM by mucociliary transport and dissolution. Lung burdens of both the carbonaceous core and organics were found to be greater in humans than in rats for similar periods of exposure.

The Yu and Yoon (1990) version of the model provides a parametric study of the dosimetry model, examining variation over a range of exposure concentrations, breathing scenarios, and ventilation parameters; particle mass median aerodynamic diameters; and geometric standard deviations of the aerosol size distribution. It examines how lung burden varies with age for exposure over a lifespan, provides dosimetry extrapolations to children, and examines changes in lung burden with lung volume. The results showed that children would exhibit more diminished alveolar clearance of DPM at high lung burden than adults when exposed to equal concentrations of DPM. These features make the model easy to use in risk assessment studies. The reader is referred to Appendix A for further details on the model and for analyses of the sensitivity of the model to change in parameter values.

The Yu model presents some uncertainties in addition to those discussed earlier in the context of particle size dependence of clearance rate. The reports of Yu and Yoon (1990) as well as Yu et al. (1991) underwent extensive peer review; we list below the most important among the model uncertainties discussed by the review panel. The experimental data used by the Yu model for adsorbed organics used passively adsorbed radiolabeled compounds as surrogates for combustion-derived organics. These compounds may adhere differently to the carbon core than do those formed during combustion. Yu has estimated that slowly cleared organics represent 10% of the total particle mass; the actual figure could be substantially less; the reviewers estimate that the amount of tightly bound organics is probably only 0.1% to 0.25% of the particle mass.

The model was based upon the experimental data of Strom et al. (1988), where Fischer-344 rats were exposed to DPM at a concentration of 6.0 mg/m^3 for 20 h/day and 7 days/week for periods ranging from 3 to 84 days. Such exposures lead to particle overload effects in rats, whereas human exposure patterns are usually to much lower levels at which overload will not occur. Parameters obtained by fitting to data under the conditions of the experimental scenario for rats may not be optimal for the human exposure and concentration of interest.

The extrapolation of retained dose from rats to humans assumed that the macrophage-mediated mechanical clearance of the DPM varies with the specific particulate dose to the alveolar surface in the same proportion in humans and in rats, whereas clearance rates by dissolution were assumed to be invariant across species. These assumptions have not been validated.

It should also be noted that the Yu et al. (1991) model does not possess a formal interstitial compartment although the lymph nodes, which would be the repository of particles from the interstitium, are represented. The work of Nikula et al. (1997a,b) and of Kuempel (2000) provide compelling information on the significance of an extensive interstitilization process in primates and in humans. Kuempel (2000) developed a lung dosimetry model to describe the kinetics of particle clearance and retention in coal miners' lungs. Models with overloading of lung clearance, as observed in rodent studies, were found to be inadequate to describe the end-of-life lung dust burdens in those miners. The model that provided the best fit to the human data included a sequestration process representing the transfer of particles to the interstitium. These findings are consistent with a study showing reduced lung clearance of particles in retired coal miners (Freedman and Robinson, 1988) and with studies showing increased retention of particles in the lung interstitium of humans and nonhuman primates compared to rodents exposed to coal dust and/or DE (Nikula et al., 1997a,b). These findings are also consistent with the established observation that humans and primates clear particles slowly from the alveolar interstitium compared with rates in rodent species such as rats and mice (Hsieh and Yu, 1998). Because several aspects of the Yu model have not been validated on human data and because it does not include a formal interstitial compartment, it is acknowledged that this model may therefore have some uncertainty concerning the lung burdens in humans exposed to occupational levels of dust. However, it is also not known whether the model based on coal miner data (Kuempel, 2000) would also describe the clearance and retention processes in the lungs of humans with exposures to particles at lower environmental concentrations, or to submicrometer particles such as DE particulate. Further investigation of these issues is needed.

3.6.2.5. *Use of the Yu et al. (1991) Model for Interspecies Extrapolation*

In addressing the objectives of this chapter, i.e., consideration of what is known and applicable to DPM concerning particle disposition and the bioavailability of adsorbed organics on DPM, it is apparent that the database is considerable for both the processes involved in particle dosimetry and for DPM. This information makes the goal of predicting a human internal dose from animal data through a model utilizing this database both feasible and appropriate.

In their charge to EPA through "Science and Judgment in Risk Assessment" (NRC, 1995), the National Research Council opines that EPA should have principles for judging when and how to depart from default options. The extensive data presented in this chapter their scientific validity, and the limitations of the current default procedures provide a basis for departing from the default options currently identified by the Agency for extrapolating from animals to humans. The default option of assuming external concentrations of DPM in animal studies as being representative of a human concentration (and an equivalent internal dose) is clearly not adequate given the differences in the basic processes of deposition and clearance between animals and humans documented by these data. Use of an alternate default option, the Agency's dosimetric adjustment procedures for inhaled particles in animal-to-human scenarios (described in U.S. EPA, 1994), is also inadequate as only deposition is predicted and then only down to an MMAD of 0.5 μm, whereas the MMAD of DPM is typically 0.2 μm or smaller. Models have been described in this section that consider both deposition and retention specifically for DPM in both laboratory animals and in humans. These points provide justification for moving away from default options and utilizing the best scientific information available (i.e., that integrated into deposition/clearance models) in performing the animal-to-human extrapolation.

Evaluation of the various models discussed in this chapter should be considered from the aspect of both the rat and the human. For rats it is fairly clear that the rat portion of the model of Yu et al. (1991) is the most appropriate because it is based on data, especially extensive information on lung burdens, from actual DPM exposures. The model provides for both deposition and integrated clearance for DPM as well as for two classes of adsorbed organics. The transport rates in the Yu model are derived directly from experiments with DPM exposed rats.

For humans, however, several models are available and discussed above, none of which is based on DPM-specific data. Deposition, but not clearance, modules are available for all models, and Table 3-3 is an attempt to compare deposition projections of the various models to the extent possible for particles in the range of characteristics of size, distribution, and density of DPM. Intake parameters such as breathing rates and minute volumes were also matched among the various models. As alluded to above and shown in Table 3-3, DPM deposition is predicted to

Table 3-3. Model comparison for deposition of DPM under equivalent conditions

Compartment	Yu[a]	ICRP66[b]	MPPDep1.11[c]	NCRP[d]
A (model designation)	13% (A)	14.1% (AI)	16.6% (P)	17.3% (P)
ET (model designation)	8% (H)	6% ($ET_1 + ET_2$)	8.7% (H)	6.6% (NOPL)
TB (model designation)	8% (TB)	4% (BB + bb)	7.2% (TB)	6.2% (TB)
Total	29%	24.1%	32.5%	30.1%

[a]Yu and Xu, 1987 (estimated from Figures 1 and 3).
[b]Jarvis et al., 1996.
[c] Freijer et al., 1999 (The Yeh-Schum 5-lobe and URT volume of 50 mL options were used.)
[d]NCRP, 1997.
Note: Particle characteristics were set at 0.2 MMAD, 2.4 sigma g, 1.5 shape factor (equivalent to 0.3 packing factor), density 1.5 and a concentration of 5 $\mu g/m^3$. Lung parameters were set at 15 breaths per minute, a tidal volume of 0.926 L/hr, and a functional residual capacity (FRC) of 3300 mL.

occur in all regions of the respiratory tract but, because diffusion would be the most likely mechanism of deposition, is most prominent in the alveolar region. When run under equivalent conditions, all models show that higher deposition in the alveolar region is higher, generally by a factor of about 2, than the other regions of the respiratory tract. The percentages projected by the different models to be deposited in the alveolar regions were all similar to one another with a range of only 13% for the Yu model to 17.3 % for the NCRP model. The total deposition of DPM-like particles predicted by the models was also very similar at around 30%. Only the ICRP model differed appreciably from the others in total deposition by a factor of about 1.3 less at 22.9%. Due to its verity and completeness in representation of the lung, the MPPDep model could be considered the most theoretically advanced of these deposition models and, presumably, the most accurate. It can be seen that, at least at the concentration tested, the Yu results and those of the MPPDep model could be judged very similar if not the same in the ET and TB regions, albeit with the MPPDep predicting slightly more deposition in the A region. Based on this limited analysis, total and regional DPM deposition in the human respiratory tract predicted by the Yu model appear similar to other available human models.

Further model comparison may be undertaken for those human models that have clearance as well as deposition modules available; from Table 3-3, these include the Yu et al. (1991) and ICRP66 models. Therefore, the human lung burden outputs of these two models were compared under equivalent physiological parameters, particle characteristics, and duration (70 years) and concentrations of exposure (Figure 3-9).

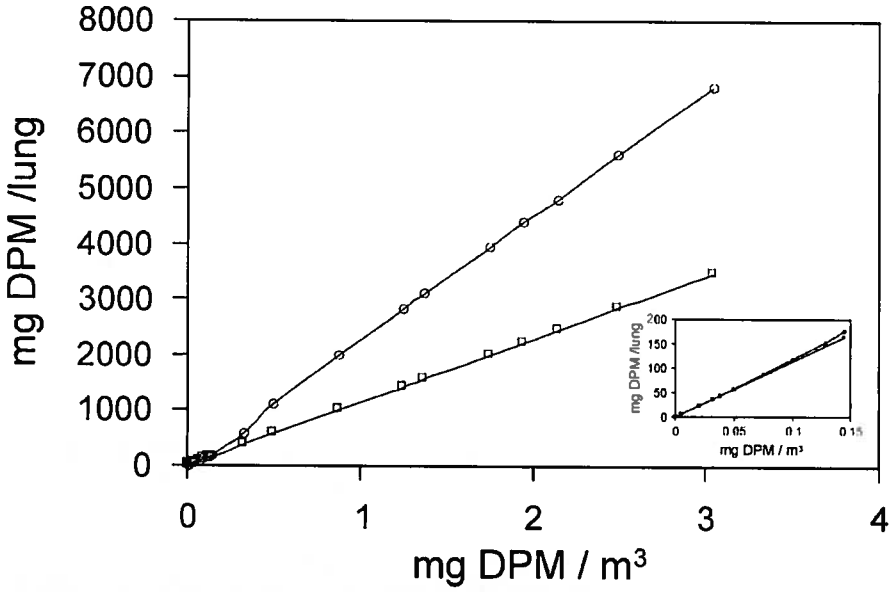

Figure 3-9. Modeled estimates of lung burden in humans after a simulated lifetime exposure to DPM using the Yu et al. (1991;[o]) and ICRP66 (□) models. Simulations include both deposition and clearance. Simulations were run for 70 years using a respiratory frequency of 15 min^{-1} and a tidal volume of 0.926 L/breath for a total daily air intake of 20 m^3/day for the various concentrations shown. Particle characteristics in the ICRP66 model, including MMAD, σ_g, density, and packing/shape factor were all matched to those used in the Yu model.

At DPM concentrations up to about 0.2 mg/m^3, the outputs (lung burden) from these two models are essentially identical (see insert) indicating little if any difference between them in this concentration range. This observation is consonant with the minor differences noted in deposition (Table 3-3).

Above 0.2 mg/m^3 DPM, both models continue to demonstrate a monotonic increase in lung burden with increasing concentration. However, the output of the Yu et al. (1991) model begins to diverge markedly from the burdens predicted by the ICRP model such that the Yu model predicts a greater burden for a given concentration of DPM than does the ICRP66 model. This situation would be predicted based on the assumption in the human portion of the Yu model of a concentration-dependent macrophage inhibition and particle overload occurring in humans; such an inhibition would result in impaired clearance processes, thereby allowing for a greater accumulation of material in the lung with increasing concentrations of DPM. This assumption is not made in the ICRP model, and materials are therefore not predicted to accumulate in the lung to the extent predicted by the Yu model.

Based on this limited analysis of models and the predictions from them for both deposition and clearance of DPM in humans, the model of Yu et al. (1991) can be seen to perform similarly to other available state-of-the-art models. The Yu model(s) are chosen for further analysis for the purposes of this document primarily because the animal portion of the model is based on DPM-specific data and the human components of the model have both deposition and clearance capacities that do not appear different from other available human respiratory tract models.

3.6.2.6. *Model Variability*

As demonstrated in Table 3-3 and Figure 3-9, there appears to be little variability among state-of-the-art models available for predicting disposition (both for deposition and for clearance integrated with deposition) of low levels of DPM (i.e., up to about 200 $\mu g/m^3$) in the respiratory tracts of humans.

Intersubject variability and its relationship to model output, however, is acknowledged in the ICRP model for deposition efficiencies (ICRP, 1994). This variability, recognized as substantial by ICRP, is addressed through use of scaling constants derived from estimates of the upper and lower confidence bounds for regional deposition efficiencies, with the scaling constants representing the variability in the population. It should be noted that the same philosophy is inherent in dose-response methodologies such as the RfC, where variability in the population is accommodated by a 10-fold uncertainty factor rather than by scaling constants. Inspection of data in ICRP66 (e.g., Figures D-4 through D-7 in the ICRP reference) on nasal and extrathoracic deposition in adult males shows that these upper and lower boundaries on output due to intersubject variability are considerably less than 10-fold different from one another. Thus, dividing model outputs by a factor of 10 such as is done in RfC derivation may well be inclusive of not only intersubject variability but also of any model-to-model variability as they exist currently.

3.6.2.7. *Model Comparison — Estimations of Deposition of Adsorbed Organics*

The data presented in Table 3-3 may be viewed as single-breath estimates of DPM deposition patterns in the various regions of the human lung under the breathing patterns and conditions described in the table for the different models considered in this report. From these data it is possible to estimate the total mass of DPM deposited in the pulmonary region under a given set of conditions. Furthermore, if the fraction of organics present on DPM and their ability to be desorbed or eluted from the DPM are assumed also to be the same, then these deposition data could be used to estimate the dose of organics to pulmonary tissues. Such a comparison would not only yield an estimate of the amount of organics but also lend a further comparison

between the different human models. This exercise was performed for humans breathing 5 μg DPM/m^3 continuously, and the results are presented in Table 3-4 below.

Table 3-4. Comparative model estimates of DPM deposition in human lungs from exposure to 5 μg/m^3 continuously for one year

	A	B	C	D
Human deposition model	Alveolar Dep[a]	μg DPM deposited/year[b]	μg organics deposited/year[c]	μg carcinogenic PAH deposited/year[d]
Yu et al. (1991)	13%	4745	598	1.82
ICRP66	14.1%	5147	649	1.98
MPPDep	16.6%	6059	763	2.33
NCRP	17.3%	6315	796	2.43

[a]Alveolar deposition fractions predicted for DPM (Yu et al., 1991) and for particles with DPM characteristics (from Table 3-3). No clearance is included in this calculation.

[b]A total air intake of 20 m^3/day is assumed. These numbers were obtained by factoring 20 m^3 × 5 μg DPM/m^3 × Alveolar deposition % (column A) × 365 days/year.

[c]In three samples of DPM extract, DPM-associated organics were noted as being 11.1%, 14.7%, and 12.1% wt. organics/wt. DPM (Tong and Karasek, 1984) with the average being 12.6%; column B is factored by this average to generate column C.

[d]Those seven PAHs identified as being carcinogenic either to humans or to animals (U.S. EPA, 1993) were summed from the data of Tong and Karasek (1984), where they are reported as a concentration in extract from DPM-associated organics. In three different samples, the content of these 7 PAHs was noted as 4739, 2054, and 2360 ng/mg of organic extract, with the average being 3051 ng/mg (3.051 μg/mg) organic extract. This average value was factored with Column C (in mg) to generate column D.

Note: Estimates from different human deposition models of the total amount of DPM-associated organics deposited in the pulmonary regions in humans breathing DPM at 5 μg/m^3 continuously for 1 year.

As may be expected, the relatively minor differences (17.3 % / 13% = 1.3) in the deposition of DPM among the different human models leads to similarly minor differences in projections of dose of carcinogenic PAHs to the lung at a relatively low concentration of 5 μg/m^3 DPM. Somewhat unexpected is the small absolute quantity of carcinogenic PAH that may be delivered to the lung tissues under the conditions of exposure to DPM in this exercise. It should be noted that exercises similar to this have been carried out by others, e.g., Valberg and Watson (1999). However, the possibility that high concentrations of DPM may result in localized areas of deposition (such as the conducting airways), the fact that human exposures may be

considerably greater than those presupposed in the exercise (e.g., 5 μg/m^3), the nature of the assays (i.e., in vitro in Chapter 4 vs. actual inhalation exposures), and the findings that DNA adducts may result from other known noncarcinogens such as carbon black (Bond et al., 1990) make the interpretation of such exercises problematic and their meaning unclear.

3.7. SUMMARY AND DISCUSSION

The most consistent historical measure of exposure for DE is DPM in units of μg or mg particles/m^3, with the underlying assumption that all components of diesel emissions (e.g., organics in the form of volatilized liquids or gases) are present in proportion to the DPM mass. DPM is used as the basic dosimeter for effects from various scenarios such as chronic and acute exposures as well as for different endpoints such as irritation, fibrosis, or even cancer. There is, however, little evidence currently available to prove or refute DPM as being the most appropriate dosimeter.

DPM dose to the tissue is related to the extent of the deposition and clearance of DPM. DPM may deposit throughout the respiratory tract via sedimentation or diffusion, with the latter being prevalent in the alveolar region. Particles that deposit upon airway surfaces may be cleared from the respiratory tract completely or may be translocated to other sites by regionally distinct processes that can be categorized as either absorptive (i.e., dissolution) or nonabsorptive (i.e., transport of intact particles via mucociliary transport). Other mechanisms that can affect retention of DPM include endocytosis by alveolar lining cells and interstitialization, which lead to the accumulation of DPM in the interstitial compartment of the lung and subsequent translocation of DPM to lymph nodes; interstitialization of poorly soluble particles may be prominent in primates and humans compared with rodents, although different rates for this path could also explain observed results. For poorly soluble particles such as DPM, species-dependent rate constants exist for the various clearance pathways that can be modified by factors such as respiratory tract disease.

In rats, prolonged exposure to high concentrations of particles will result in particle overload, a condition that is defined as the overwhelming of macrophage-mediated clearance by the deposition of particles at a rate exceeding the capacity of that clearance pathway. This condition seems to begin to occur in rats when the pulmonary dust burden exceeds about 1 mg particles/g lung tissue. On the other hand, there is no clear evidence for particle overload in humans. Macrophage-mediated clearance is slower in humans than in rats, and kinetics relating to interstitialization of poorly soluble particulate matter may have a greater consequence in humans than in rats.

The degree of bioavailability of the organic fraction of DPM is still somewhat uncertain. However, reports of DNA alterations in occupationally exposed workers, as well as results of

animal studies using radiolabeled organics deposited on DPM, indicate that at least a fraction of the organics present are eluted prior to particle clearance. Carcinogenic organics eluted in regions where diffusion may be a relatively long process, such as in the conducting airways vs the alveolar region, may remain in the lung long enough to be metabolized to an active form or to interact directly with vital cellular components. The current information suggests that DPM-associated organics could be involved in a carcinogenic process, although the quantitative data are far from adequate to make any firm conclusions.

Use of laboratory animal data in an assessment meant to be applied to humans obligates some form of interspecies extrapolation. Review and evaluation of the considerable, specific database in humans and animals on disposition of DPM, its adsorbed organics, and other poorly soluble particles led to the judgment that default options available for interspecies dosimetry adjustment could be set aside for more scientifically valid, DPM-specific processes. Refinement of this process led to the evaluation of several applicable dosimetry models that in turn led to the identification and choice of the Yu et al. (1991) model to conduct interspecies extrapolation. This model has a three-compartment lung consisting of tracheobronchial, alveolar, and lymph node compartments. It treats DPM as being composed of the insoluble carbonaceous core, slowly cleared organics, and fast-cleared organics, and considers in an integrative manner the simultaneous processes of both deposition and clearance through empirical data derived from both laboratory animals and humans. Also, the model has some limited consideration of model variability in its outputs describing dose to the lung. Major assumptions made in this model include that transport rates of organics in DPM do not change across species and that the transport rate of the carbonaceous core is species dependent, with the clearance rate varying with the dose to the alveolar surface in the same proportion in humans as in rats. Limitations of the model include the lack of definitive information on variability and, quite possibly, the lack of a formal interstitial compartment that may be of consequence in humans. The basis of this model is to derive an internal dose from an external DPM concentration by utilizing species-specific physiological and pharmacokinetic parameters and, as such, is considered to have addressed the pharmacokinetic aspects of interspecies dosimetry. This aspect of the model addresses some of the critical data needs for the quantitative analysis of noncancer effects from DPM, the subject of Chapter 6.

As parallels have been drawn between DPM and $PM_{2.5}$ in other chapters, it is perhaps appropriate to compare them also from the aspect of dosimetry. Obvious comparisons include the nature of the particle distribution, defined artificially for $PM_{2.5}$ as compared with the thorough characterization of DPM for both MMAD (which, at around 0.2 μm, is typically more than an order of magnitude less than the $PM_{2.5}$ cutoff and which, more properly, should be termed a mass median thermodynamic diameter, an MMTD) and geometric standard deviation. It is clear that a

larger portion of $PM_{2.5}$ particles than DPM would be above the aerodynamic equivalent diameter (d_{ae}) of 0.5 μm, which is often considered as a boundary between diffusion and aerodynamic mechanisms of deposition. This would imply that a somewhat larger portion of DPM may pass on to the lower respiratory tract than would $PM_{2.5}$. Alveolar deposition in humans specific for DPM has been estimated with the Yu model to be 7%-13% (Yu and Xu, 1986), a figure that is consistent with deposition predictions of other human models (see Table 3-3). This fractional deposition may be compared to one calculated for $PM_{2.5}$ and reported in U.S. EPA (1996a); assuming a MMAD of 2.25 μm and a geometric standard deviation of 2.4, a fractional alveolar deposition of 10.2% was reported. This value is within the range and quite comparable to that obtained by Yu and Xu (1986), indicating that little difference may exist in alveolar deposition between DPM and $PM_{2.5}$, at least for this assumed geometric standard deviation.

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4. MUTAGENICITY

The application of mutagenicity data to the question of the potential carcinogenicity of diesel emissions is based on the premise that genetic alterations are found in all cancers and that several of the chemicals found in diesel emissions possess mutagenic activity in a variety of genetic assays. These genetic alterations can be produced by gene mutations, deletions, translocations, aneuploidy, or amplification of genes; hence no single genotoxicity assay should be expected to predict rodent carcinogenicity. Additionally, because of the inherent biological differences of measured endpoints, both within genotoxicity assays and between genotoxicity assays and cancer bioassays, a direct extrapolation should not be expected (see Brusick [1987] for a more detailed discussion). Indeed, most genotoxicity data are generated with in vitro assays that frequently employ concentrations of test agent that may be orders of magnitude greater than encountered in environmental situations. With diesel emissions or other mixtures, additional complications arise because of the complexity of the material being tested.

Since 1978, more than 100 publications have appeared in which genotoxicity assays were used with diesel emissions, the volatile and particulate fractions (including extracts), or individual chemicals found in diesel emissions. The Huisingh et al. (1978) report not only identified mutagenic activity in salmonella in several fractions of diesel particular mater (DPM) extracts, but also indicated that the mutagenic activity, especially quantitatively, was affected by the extraction solvent as well as method and length of storage. Much of the ensuing research employed bioassays (most commonly salmonella TA98 without S9) to evaluate (1) extraction procedures, (2) fuel modifications, (3) bioavailability of chemicals from DPM, and (4) exhaust filters or other modifications and other variables associated with diesel emissions. The interest in the contribution of mutagens to carcinogenicity was high in the early 1980s and the lack of long- term rodent carcinogenicity information on diesel emissions led to the use of semiquantitative mutagenicity (and in vitro cell transformation) data from diesel emissions and epidemiology based cancer potency estimations to derive a comparative potency estimate for diesel emissions first published by Albert et al. (1983) and more fully discussed in Appendix C of this report.

As indicated in Chapter 2, the number of chemicals in diesel emissions is very large. Many of these have been determined to exhibit mutagenic activity in a variety of assay systems (see Table II. in Claxton, 1983). Although a detailed discussion of those data is beyond the scope of this document, some of the mutagenically active compounds found in the gas phase are ethylene, benzene, 1,3-butadiene, acrolein and several PAHs (see Table 2-21). Of the particle-associated chemicals, several PAHs and nitro-PAHs have been the focus of mutagenic investigations both in bacteria and in mammalian cell systems (see Table 2-22). Several review

articles, some containing more detailed descriptions of the available studies, are available (Claxton, 1983; Pepelko and Peirano, 1983; International Agency for Research on Cancer, 1989; Shirnamé-Moré, 1995). Discussions of genotoxicity in the proceedings of several symposia on the health effects of diesel emissions (U.S. EPA, 1980; Lewtas, 1982; Ishinishi et al., 1986) are also available.

4.1. GENE MUTATIONS

Huisingh et al. (1978) demonstrated that dichloromethane extracts from DPM were mutagenic in strains TA1537, TA1538, TA98, and TA100 of *S. typhimurium*, both with and without rat liver S9 activation. This report contained data from several fractions as well as DPM from different vehicles and fuels. Similar results with diesel extracts from various engines and fuels have been reported by a number of investigators using the salmonella frameshift-sensitive strains TA1537, TA1538, and TA98 (Siak et al., 1981; Claxton, 1981; Dukovich et al., 1981; Brooks et al., 1984). Similarly, mutagenic activity was observed in salmonella forward mutation assays measuring 8-azaguanine resistance (Claxton and Kohan, 1981) and in *E. coli* mutation assays (Lewtas, 1983).

One approach to identifying significant mutagens in chemically complex environmental samples such as diesel exhaust or ambient particulate extracts is the combination of short-term bioassays with chemical fractionation (Scheutzle and Lewtas, 1986). The analysis is most frequently carried out by sequential extraction with increasingly polar or binary solvents. Fractionation by silica-column chromatography separates compounds by polarity or into acidic, basic, and neutral fractions. The resulting fractions are too complex to characterize by chemical methods, but the bioassay analysis can be used to determine fractions for further analysis. In most applications of this concept, salmonella strain TA98 without the addition of S9 has been used as the indicator for mutagenic activity. Generally, a variety of nitrated polynuclear aromatic compounds have been found that account for a substantial portion of the mutagenicity (Liberti et al., 1984; Schuetzle and Frazer, 1986; Schuetzle and Perez, 1983). However, not all bacterial mutagenicity has been identified in this way, and the identity of the remaining mutagenic compounds remains unknown. The nitrated aromatics thus far identified in diesel engine exhaust (DE) were the subject of review in the IARC monograph on DE (International Agency for Research on Cancer, 1989). In addition to the simple qualitative identification of mutagenic chemicals, several investigators have used numerical data to express mutagenic activity as activity per distance driven or mass of fuel consumed. These types of calculations have been the basis for estimates that the nitroarenes (both mono- and dinitropyrenes) contribute a significant amount of the total mutagenic activity of the whole extract (Nishioka et al., 1982; Salmeen et al., 1982; Nakagawa et al., 1983). In a 1983 review, Claxton discussed a number of

factors that affected the mutagenic response in salmonella assays. Citing the data from the Huisingh et al. (1978) study, the author noted that the mutagenic response could vary by a factor of 100 using different fuels in a single diesel engine. More recently, Crebelli et al. (1995) used salmonella to examine the effects of different fuel components. They reported that although mutagenicity was highly dependent on aromatic content, especially di- or triaromatics, there was no clear effect of sulfur content of the fuel. Later, Sjögren et al. (1996) using multivariate statistical methods with ten diesel fuels concluded that the most influential chemical factors in salmonella mutagenicity were sulfur contents, certain PAHs (1-nitropyrene) and naphthenes.

Matsushita et al. (1986) tested particle-free DE gas and a number of benzene nitro-derivatives and polycyclic aromatic hydrocarbons (PAHs) (many of which have been identified as components of DE gas). The particle-free exhaust gas was positive in both TA100 and TA98, but only without S9 activation. Of the 94 nitrobenzene derivatives tested, 61 were mutagenic, and the majority showed greatest activity in TA100 without S9. Twenty-eight of 50 PAHs tested were mutagenic, all required the addition of S9 for detection, and most appeared to show a stronger response in TA100. When 1,6-dinitropyrene was mixed with various PAHs or an extract of heavy-duty (HD) DE, the mutagenic activity in TA98 was greatly reduced when S9 was absent but was increased significantly when S9 was present. These latter results suggested that caution should be used in estimating mutagenicity (or other toxic effects) of complex mixtures from the specific activity of individual components.

Mitchell et al. (1981) reported mutagenic activity of DPM extracts of diesel emissions in the mouse lymphoma L5178Y mutation assay. Positive results were seen both with and without S9 activation in extracts from several different vehicles, with mutagenic activity only slightly lower in the presence of S9. These findings have been confirmed in a number of other mammalian cell systems using several different genetic markers. Casto et al. (1981), Chescheir et al. (1981), Li and Royer (1982), and Brooks et al. (1984) all reported positive responses at the HPRT locus in Chinese hamster ovary (CHO) cells. Morimoto et al. (1986) used the APRT and Oua^r loci in CHO cells; Curren et al. (1981) used Oua^r in BALB/c 3T3 cells. In all of these studies, mutagenic activity was observed without S9 activation. Liber et al. (1981) used the thymidine kinase (TK) locus in the TK6 human lymphoblast cell line and observed induced mutagenesis only in the presence of rat liver S9 when testing a methylene chloride extract of DE. Barfknecht et al. (1982) also used the TK6 assay to identify some of the chemicals responsible for this activation-dependent mutagenicity. They suggested that fluoranthene, 1-methylphenanthrene, and 9-methylphenanthrene could account for over 40% of the observed activity.

Morimoto et al. (1986) injected DPM extracts (250 to 4,000 mg/kg) into pregnant Syrian hamsters and measured mutations at the APRT locus in embryo cells cultivated 11 days after i.p.

injection. Although neutral fractions from both light-duty (LD) and HD particle extracts resulted in increased mutation frequency at 2,000 and 4,000 mg/kg, the response at 1,000 mg/kg was not different from controls. Also, because the authors did not present data on toxicity or cloning efficiency, the value of the apparent positive findings at extremely high concentrations is uncertain at best. Belisario et al. (1984) applied the Ames test to urine from Sprague-Dawley rats exposed to single applications of DPM administered by gastric intubation, i.p. injection, or s.c. gelatin capsules. In all cases, dose-related increases were seen in TA98 (without and with S9) from urine concentrates taken 24 h after particle administration. Urine from Swiss mice exposed by inhalation to filtered exhaust (particle concentration 6 to 7 mg/m^3) for 7 weeks (Pereira et al., 1981a) or Fischer 344 rats exposed to DPM at a concentration of 1.9 mg/m^3 for 3 months to 2 years (Ong et al., 1985) was negative in salmonella strains.

Schuler and Niemeier (1981) exposed drosophila males in a stainless steel chamber connected to the 3 m^3 chamber used for the chronic animal studies at EPA (see Hinners et al., 1980 for details). Flies were exposed for 8 h and mated to untreated females 2 days later. Although the frequency of sex-linked recessive lethals from treated males was not different from that of controls, the limited sample size precluded detecting less than a threefold increase over controls. The authors noted that, because there were no signs of toxicity, the flies might tolerate exposures to higher concentrations for longer time periods.

Driscoll et al. (1996) exposed Fischer 344 male rats to aerosols of carbon black (1.1, 7.1, and 52.8 mg/m^3) or air for 13 weeks (6 hr/day, 5 days/week) and measured *hprt* mutations in alveolar type II cells in animals immediately after exposure and at 12 and 32 weeks after the end of exposure. Both of the two higher concentrations resulted in significant increases in mutant frequency. Whereas the mutant frequency from the 7.1 mg/m^3 group returned to control levels by 12 weeks, the mutant frequency of the high-exposure group was still higher than controls even after 32 weeks. Carbon black particles have very little adsorbed PAHs, hence a direct chemically induced mechanism is highly unlikely. Induction of *hprt* mutations were also observed in rat alveolar epithelial cells after intratracheal instillation with carbon black, α-quartz, and titanium dioxide (Driscoll et al., 1997). All three types of particles elicited an inflammatory response as shown by significant increases of neutrophils in bronchoalveolar lavage (BAL) fluid. Culturing the BAL from exposed rats with a rat lung epithelial cell line also resulted in elevation of *hprt* mutational response. This response was effectively eliminated when catalase was included in the incubation mixture, providing evidence for cell-derived oxidative damage. Recently, Sato et al. (2000) exposed male Big Blue transgenic F344 rats to diluted DE (1 and 6 mg/m^3 suspended particle concentration) for 4 weeks. Mutant frequency in lung DNA was significantly elevated (4.8x control) at 6 mg/m^3 but not at 1 mg/m^3. Lung DNA adduct levels measured by ^{32}P-postlabeling and 8-hydroxydeoxyguanosine measured by HPLC

were elevated at both particle concentrations, but to a lesser extent than mutant frequencies. Sequence analysis of mutants indicated that some, but not all, of the mutations could be explained by an oxidative damage mechanism.

Specific-locus mutations were not induced in (C3H × 101)F_1 male mice exposed to DE 8 h/day, 7 days/week for either 5 or 10 weeks (Russell et al., 1980). The exhaust was a 1:18 dilution and the average particle concentration was 6 mg/m^3. After exposure, males were mated to T-stock females and matings continued for the reproductive life of the males. The results were unequivocally negative; no mutants were detected in 10,635 progeny derived from postspermatogonial cells or in 27,917 progeny derived from spermatogonial cells.

Hou et al. (1995) measured DNA adducts and *hprt* mutations in peripheral lymphocytes of 47 bus maintenance workers and 22 control individuals. All were nonsmoking men from garages in the Stockholm area and the exposed group consisted of 16 garage workers, 25 mechanics, and 6 other garage workers. There were no exposure data, but the three groups were considered to be of higher to lower exposure to diesel engine exhaust. Levels of DNA adducts determined by ^{32}P-postlabeling were significantly higher in workers than controls (3.2 versus 2.3 × 10^{-8}), but *hprt* mutant frequencies were not different 8.6 versus 8.4 × 10^{-6}). Although group mean mutant frequencies were not different, both adduct level and mutagenicity were highest among the 16 most exposed and mutant frequency was significantly correlated with adduct level. All individuals were genotyped for glutathione transferase GSTM1 and aromatic amino transferase NAT2 polymorphism. Neither GSTM1 nulls nor NAT2 slow acetylators exhibited effects on either DNA adducts or *hprt* mutant frequencies.

4.2. CHROMOSOME EFFECTS

Mitchell et al. (1981) and Brooks et al. (1984) reported increases in sister chromatid exchanges (SCE) in CHO cells exposed to DPM extracts of emissions from both LD and HD diesel engines. Morimoto et al. (1986) observed increased SCE from both LD and HD DPM extracts in PAH-stimulated human lymphocyte cultures. Tucker et al. (1986) exposed human peripheral lymphocyte cultures from four donors to direct DE for up to 3 h. Exhaust was cooled by pumping through a plastic tube about 20 feet long; airflow was 1.5 L/min. Samples were taken at 16, 48, and 160 min of exposure. Cell cycle delay was observed in all cultures; significantly increased SCE levels were reported for two of the four cultures. Structural chromosome aberrations were induced in CHO cells by DPM extracts from a Nissan diesel engine (Lewtas, 1983) but not by similar extracts from an Oldsmobile diesel engine (Brooks et al., 1984).

DPM dispersed in an aqueous mixture containing dipalmitoyl lecithin (DPL), a component of pulmonary surfactant or extracted with dichloromethane (DCM) induced similar

responses in SCE assays in Chinese hamster V79 cells (Keane et al., 1991), micronucleus tests in V79 and CHO cells (Gu et al., 1992), and unscheduled DNA synthesis (UDS) in V79 cells (Gu et al., 1994). After separating the samples into supernatant and sediment fractions, mutagenic activity was confined to the sediment fraction of the DPL sample and the supernatant of the DCM sample. These findings suggest that the mutagenic activity of DPM inhaled into the lungs could be made bioavailable through solubilization and dispersion of pulmonary surfactants. In a later study in the same laboratory, Liu et al. (1996) found increased micronuclei in V79 cells treated with crystalline quartz and a noncrystalline silica, but response was reduced after pretreatment of the particles with the simulated pulmonary surfactant.

Pereira et al. (1981a) exposed female Swiss mice to DE 8 h/day, 5 days/week for 1, 3, and 7 weeks. The incidence of micronuclei and structural aberrations was similar in bone marrow cells of both control and exposed mice. Increased incidences of micronuclei, but not SCE, were observed in bone marrow cells of male Chinese hamsters after 6 months of exposure to DE (Pereira et al., 1981b).

Guerrero et al. (1981) observed a linear concentration-related increase in SCE in lung cells cultured after intratracheal instillation of DPM at doses up to 20 mg/hamster. However, they did not observe any increase in SCE after 3 months of inhalation exposure to DE particles (6 mg/m^3).

Pereira et al. (1982) measured SCE in embryonic liver cells of Syrian hamsters. Pregnant females were exposed to DE diluted with air 1:9 to contain about 12 mg/m^3 particles from days 5 to 13 of gestation or injected intraperitoneally with diesel particles or particle extracts on gestational day 13 (18 h before sacrifice). Neither the incidence of SCE nor mitotic index was affected by exposure to DE. The injection of DPM extracts but not DPM resulted in a dose-related increase in SCE; however, the toxicity of the DPM was about twofold greater than the DPM extract.

In the only studies with mammalian germ cells, Russell et al. (1980) reported no increase in either dominant lethals or heritable translocations in males of T-stock mice exposed by inhalation to diesel emissions. In the dominant lethal test, T-stock males were exposed for 7.5 weeks and immediately mated to females of different genetic backgrounds (T-stock; [C3H × 101]; [C3H × C57BL/6]; [SEC × C57BL/6]). There were no differences from controls in any of the parameters measured in this assay. For heritable translocation analysis, T-stock males were exposed for 4.5 weeks and mated to (SEC × C57BL/6) females, and the F_1 males were tested for the presence of heritable translocations. Although no translocations were detected among 358 progeny tested, the historical control incidence is less than 1/1,000.

4.3. OTHER GENOTOXIC EFFECTS

Pereira et al. (1981b) exposed male strain A mice to DE emissions for 31 or 39 weeks using the same exposure regimen noted in the previous section. Analyses of caudal sperm for sperm-head abnormalities were conducted independently in three separate laboratories. Although the incidence of sperm abnormalities was not significantly above controls in any of the three laboratories, there were extremely large differences in scoring among the three (control values were 9.2%, 14.9%, and 27.8% in the three laboratories). Conversely, male Chinese hamsters exposed for 6 mo (Pereira et al., 1981c) exhibited almost a threefold increase in sperm-head abnormalities. It is noted that the control incidence in the Chinese hamsters was less than 0.5%. Hence, it is not clear whether the differing responses reflect true species differences or experimental artifacts.

A number of studies measuring DNA adducts in animals exposed to DPM, carbon black or other particles have been reported and are reviewed by Shirnamé-Moré (1995). Although modest increases in DNA adducts have been observed in lung tissue of rats after inhalation of DPM (Wong et al., 1986; Bond et al., 1990), the magnitude of the increases is small in comparison with those induced by chemical carcinogens present in DE (Smith et al., 1993). While Gallagher et al. (1994) found no increases in total DNA adducts in lung tissue of rats exposed to DE, carbon black, or titanium dioxide they did observe an increase in an adduct with migration properties similar to nitrochrysene and nitro-benzo(a)pyrene adducts from diesel but not carbon black or titanium dioxide exposures. The majority of the studies used the ^{32}P-postlabeling assay to detect adducts. Although this method is sensitive, chemical identity of adducts can only be inferred if an adduct spot migrates to the same location as a known prepared adduct.

DNA adducts have also been measured in humans occupationally exposed to DE. Distinct adduct patterns were found among garage workers occupationally exposed to DE when compared to nonexposed controls (Nielsen and Autrup, 1994). Furthermore, the findings were concordant with the adduct patterns observed in groups exposed to low concentrations of PAHs from combustion processes. Hemminki et al. (1994) also reported significantly elevated levels of DNA adducts in lymphocytes from garage workers with known DE exposure compared with unexposed mechanics. Hou et al. (1995) found elevated adduct levels in bus maintenance workers exposed to DE. Although no difference in mutant frequency was observed between the groups, the adduct levels were significantly different (3.2 vs. 2.3×10^{-8}). Nielsen et al. (1996) reported significantly increased levels of three biomarkers (lymphocyte DNA adducts, hydroxyethylvaline adducts in hemoglobin, and 1-hydroxypyrene in urine) in DE-exposed bus garage workers.

The role of oxidative damage in causing mutations has received increasing focus recently. More than 50 different chemicals have been studied in rodents usually measuring the formation of 8-hydroxydeoxyguanosine (8-OH-dG), a highly mutagenic adduct (Loft et al., 1998). Increases in the mutagenic DNA adduct 8-hydroxydeoxyguanosine were found in mouse lung DNA after intratracheal instillation of diesel particles (Nagashima et al., 1995). The response was dose dependent. Mice fed on a high-fat diet showed an increased response whereas the responses were partially reduced when the antioxidant, β-carotene, was included in the diet (Ichinose et al., 1997). Oxidative damage also has been measured in rat lung tissue after intratracheal instillation of quartz (Nehls et al., 1997) and in rat alveolar macrophages after in vitro treatment with silica dust (Zhang et al., 2000). Arimoto et al. (1999) demonstrated that redissolved methanol extracts of DPM also induced the formation of 8-OH-dG adducts in L120 mouse cells. The response was dependent on both DPM concentration and P450 reductase. A detailed discussion of the potential role of oxidative damage in DE carcinogenesis is presented in Chapter 7, Section 7.4.

4.4. SUMMARY AND DISCUSSION

Extensive studies with salmonella have unequivocally demonstrated mutagenic activity in both particulate and gaseous fractions of DE. In most of the studies using salmonella, DPM extracts and individual nitropyrenes exhibited the strongest responses in strain TA98 when no exogenous activation was provided. Gaseous fractions reportedly showed greater response in TA100, whereas benzo[*a*]pyrene and other unsubstituted PAHs are mutagenic only in the presence of S9 fractions. The induction of gene mutations has been reported in several in vitro mammalian cell lines after exposure to extracts of DPM. Note that only the TK6 human cell line did not give a positive response to DPM extracts in the absence of S9 activation. Mutagenic activity was recovered in urine from animals treated with DPM by gastric intubation and i.p. and s.c. implants, but not by inhalation of DPM or diluted diesel exhaust. Dilutions of whole diesel exhaust did not induce sex-linked recessive lethals in drosophila or specific-locus mutations in male mouse germ cells.

Structural chromosome aberrations and SCE in mammalian cells have been induced by particles and extracts. Whole exhaust induced micronuclei but not SCE or structural aberrations in bone marrow of male Chinese hamsters exposed to whole diesel emissions for 6 mo. In a shorter exposure (7 weeks), neither micronuclei nor structural aberrations were increased in bone marrow of female Swiss mice. Likewise, whole DE did not induce dominant lethals or heritable translocations in male mice exposed for 7.5 and 4.5 weeks, respectively.

The application of mutagenicity data to the question of the potential carcinogenicity of diesel emissions is based on the premise that genetic alterations are found in all cancers and that

several of the chemicals found in diesel emissions possess mutagenic activity in a variety of genetic assays. These genetic alterations can be produce by gene mutations, deletions, translocations, aneuploidy, or amplification of genes, hence no single genotoxicity assay should be expected to either qualitatively or quantitatively predict rodent carcinogenicity. With diesel emissions or other mixtures, additional complications arise because of the complexity of the material being tested. Exercises that combined the salmonella mutagenic potency with the total concentration of mutagenic chemicals deposited in the lungs could not account for the observed tumor incidence in exposed rats (Rosenkranz, 1993; Goldstein et al., 1998). However, such calculations ignored the contribution of gaseous phase chemicals which have been estimated to contribute from less than 50% (Rannug et al., 1983) to over 90% (Matsushita et al., 1986) of the total mutagenicity. This wide range is partly reflective of the differences in material tested, semivolatile extracts in the former and whole gaseous emission in the latter. Of greater importance is that these calculations are based on a reverse mutation assay in bacteria with metabolic processes strikingly different from mammals. This is at least partly reflected in the observations that different nitro-PAHs give different responses in bacteria and in CHO cells (Li and Dutcher, 1983) or in human hepatoma-derived cells (Eddy et al., 1986).

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5. NONCANCER HEALTH EFFECTS OF DIESEL EXHAUST

The objective of this chapter is to review and evaluate potential health effects other than cancer associated with inhalation exposure to diesel engine exhaust (DE). Data have been obtained from diverse human, laboratory animal, and in vitro test systems. The human studies comprise both occupational and human experimental exposures, the former consisting of exposure to DE in the occupational environment, and the latter consisting of exposure to diluted DE or diesel particulate matter (DPM) under controlled conditions. The laboratory animal studies consist of both acute and chronic exposures of laboratory animals to DE or DPM. Diverse in vitro test systems composed of human and laboratory animal cells treated with DPM or components of DPM have also been used to investigate the effects of DPM at the cellular and molecular levels. DPM mass (mg/m^3) has been used almost exclusively as a measure of DE exposure in human and experimental studies. The noncancer health effects of DPM have been reviewed previously by the Health Effects Institute (HEI, 1995) and in the Air Quality for Particulate Matter Criteria Document, the PM CD (U.S. EPA, 1996). The noncancer health effects attributable to ambient particulate matter (PM), which is composed in part of DPM, as well as the potential mechanisms underlying these effects have also been previously reviewed in the PM CD (U.S. EPA, 1996) and have been summarized in this document in Chapter 6, Section 6.4.

This chapter begins with descriptions of studies that have shown various health effects occurring as a result of exposure to DE/DPM (Section 5.1). The human studies portion of this section (5.1.1) discusses results from both short-term and long-term studies as well as specialized studies such as those of populations contiguous to major highways (5.1.2). Studies using laboratory animals are ordered into various subsections under Section 5.1.3. Investigations devoted to elucidating the possible modes of action of DE/DPM are covered in Section 5.2; the mode-of-action issue of particle overload in animals is discussed elsewhere in the document (Chapter 3, Section 3.4). Section 5.3 describes evidence for the various interactions of DPM with other conditions such as disease. Other sections address issues such as species-comparative responses to DE/DPM (Section 5.4) and influence of dose rate (Section 5.5). The summary/conclusion of this chapter, relating the totality of this information to possible human effects of DE/DPM, is in Section 5.6.

5.1. HEALTH EFFECTS OF WHOLE DIESEL EXHAUST

5.1.1. Human Studies

5.1.1.1. *Short-Term Exposures*

In a controlled human study, Rudell et al. (1990, 1994) exposed eight healthy subjects in an exposure chamber to diluted exhaust from a diesel engine for 1 h, with intermittent exercise. Dilution of the DE was controlled to provide a median NO_2 level of approximately 1.6 ppm. Median particle number was $4.3 \times 10^6/cm^3$, and median levels of NO and CO were 3.7 and 27 ppm, respectively (particle size and mass concentration were not provided). There were no effects on spirometry or on closing volume using nitrogen washout. Five of eight subjects experienced unpleasant smell, eye irritation, and nasal irritation during exposure. Bronchoalveolar lavage (BAL) was performed 18 hours after exposure and was compared with a control BAL performed 3 weeks prior to exposure; there was no control air exposure. Small but statistically significant reductions were seen in numbers of BAL mast cells, extent of AM phagocytosis of opsonized yeast particles, and lymphocyte CD4/CD8 ratios. A small increase in recovery of polymorphonuclear cells (PMNs) was also observed. These findings suggest that DE may induce mild airway inflammation in the absence of spirometric changes. This study provides an intriguing glimpse of the effect of DE exposure in humans, but only one exposure level was used, the number of subjects was low, and a limited range of endpoints was reported, so the data are inadequate to generalize about the human response.

Rudell et al. (1996) exposed volunteers to DE for 1 h in an exposure chamber. Light work on a bicycle ergometer was performed during exposure. Exposures included either DE or exhaust with particle numbers reduced 46% by a particle trap. The engine used was a new Volvo model 1990, a six-cylinder direct-injection turbocharged diesel with an intercooler, which was run at a steady speed of 900 rpm during the exposures. Comparison of this study with others was difficult because neither exhaust dilution ratios nor particle concentrations were reported. Carbon monoxide concentrations of 27-30 ppm and NO of 2.6-2.7 ppm, however, suggested DPM concentrations may have equaled several mg/m^3. The most prominent symptoms during exposure were irritation of the eyes and nose and an unpleasant smell. Both airway resistance and specific airway resistance increased significantly during the exposures. Despite the 46% reduction in particle numbers by the trap, effects on symptoms and lung function were not significantly attenuated.

Nordenhall et al. (2000) had 15 healthy human subjects (13 males, 2 females) breathe in an exposure chamber diluted DE from an idling diesel engine to give a PM_{10} concentration of 300 $\mu g/m^3$, which was also associated with a median steady-state NO_2 concentration of 1.6 ppm.

Exposures were for 1 h, with each individual serving as their own control by being exposed to filtered air, also for 1 h but at a different time. Sputum production was then induced and sputum examined at 6 and 24 hr postexposure (for both air and DPM) with differential cell counts and soluble protein counts performed. In comparing the same individual's results after exposure to air and after exposure to DE, increases were found in the percentage of sputum neutrophiles (37.7% vs. 26.2%) after 6 hr, along with increases in concentrations of the soluble proteins interleukin-6 (12.0 vs. 6.3 pg/mL) and methylhistamine (0.11 vs. 0.12 ug/L). These differences between air and DPM were not present at 24 hr. Thus, breath exposure to DE produces early induction of an inflammatory response in healthy humans that can be detected using sputum analysis.

Wade and Newman (1993) describe the situation of three railroad workers who developed persistent asthma associated with overexposure to DE from locomotives. The overexposure was a consequence of multiple hours of high levels of diesel exposure from riding in locomotive units trailing immediately behind the lead locomotive. Lines of evidence supporting railroad locomotive DE inducing asthma in these individuals include, (1) all three exhibited clear signs of asthma leading (in two of the three cases) to immediate first-time hospitalization and treatment for asthma, (2) all three developed symptoms within a few hours of the overexposure, and (3) all three experienced exacerbation of symptoms upon reexposure to locomotive DE. Although this report and that of Kahn et al. (1988) described below both provide supporting evidence for DE being able to cause asthma in humans under extreme but uncharacterized conditions, both suffer from the same limitations, including no reliable data on the concentration of diesel emissions and associated gaseous components, the duration of the exposures, or information on others that were exposed under these conditions but who did not develop asthma symptoms.

Kahn et al. (1988) reported the occurrence of 13 cases of acute overexposure to DE among Utah and Colorado coal miners. Twelve miners had symptoms of mucous membrane irritation, headache, and lightheadedness. Eight individuals reported nausea; four reported a sensation of unreality; four reported heartburn; three reported weakness, numbness, and tingling in their extremities; three reported vomiting; two reported chest tightness; and two others reported wheezing. Each miner lost time from work because of these symptoms, which resolved within 24 to 48 h. No air monitoring data were presented; poor work practices were described as the predisposing conditions for overexposure. No follow-up was available for these exposed individuals.

El Batawi and Noweir (1966) reported that among 161 workers from two garages where diesel-powered buses were serviced and repaired, 42% complained of eye irritation, 37% of headaches, 30% of dizziness, 19% of throat irritation, and 11% of cough and phlegm. Ranges of

mean concentrations of DE components in the two diesel bus garages were as follows: 0.4 to 1.4 ppm NO_2, 0.13 to 0.81 ppm SO_2, 0.6 to 44.1 ppm aldehydes, and 1.34 to 4.51 mg/m^3 of DPM; the highest concentrations were obtained close to the exhaust systems of the buses.

Eye irritation was reported by Battigelli (1965) in six subjects after 40 s of chamber exposure to diluted DE containing 4.2 ppm NO_2, 1 ppm SO_2, 55 ppm CO, 3.2 ppm total hydrocarbons, and 1 to 2 ppm total aldehydes; after 3 min and 20 s of exposure to diluted DE containing 2.8 ppm NO_2, 0.5 ppm SO_2, 30 ppm CO, 2.5 ppm total hydrocarbons, and <1 to 2 ppm total aldehydes; and after 6 min of exposure to diluted DE containing 1.3 ppm NO_2, 0.2 ppm SO_2, <20 ppm CO, <2.0 ppm total hydrocarbons, and <1.0 ppm total aldehydes. The concentration of DPM was not reported.

Katz et al. (1960) described the experience of 14 chemists and their assistants monitoring the environment of a train tunnel used by diesel-powered locomotives. Although workers complained on three occasions of minor eye and throat irritation, no correlation was established with concentrations of any particular component of DE.

The role of radicals generated from particulate matter, including DPM, in producing toxicity has been discussed in the literature (Valavanidis et al., 2000), as has the role of antioxidant defenses in protecting against species such as radicals that may arise from acute DE exposure. Blomberg et al. (1998) investigated changes in the antioxidant defense network within the respiratory tract lining fluids of human subjects following DE exposure. Fifteen healthy, nonsmoking, asymptomatic subjects were exposed to filtered air or DE (DPM 300 μg/m^3) for 1 h on two separate occasions at least 3 weeks apart. Nasal lavage fluid and blood samples were collected prior to, immediately after, and 5 ½ h post exposure. Bronchoscopy was performed 6 h after the end of DE exposure. Nasal lavage ascorbic acid concentration increased tenfold during DE exposure, but returned to basal levels 5.5 h postexposure. DE had no significant effects on nasal lavage uric acid or GSH concentrations, and did not affect plasma, bronchial wash, or bronchoalveolar lavage antioxidant concentrations, nor malondialdehyde or protein carbonyl concentrations. The authors concluded that the physiological response to acute DE exposure is an acute increase in the level of the antioxidant ascorbic acid in the nasal cavity.

5.1.1.1.1. ***Diesel exhaust odor.*** The odor of DE is considered by most people to be objectionable; at high intensities, it may produce sufficient physiological and psychological effects to warrant concern for public health. The intensity of the odor of DE is an exponential function of its concentration such that a tenfold change in the concentration will alter the intensity of the odor by one unit. Two human panel rating scales have been used to measure DE odor intensity. In the first (Turk, 1967), combinations of odorous materials were selected to simulate DE odor; a set of 12 mixtures, each having twice the concentration of that of the

previous mixture, is the basis of the diesel odor intensity scale (D-scale). The second method is the TIA (total intensity of aroma) scale based on seven steps, ranging from 0 to 3, with 0 being undetectable, ½ very slight, and 1 slight and increasing in one-half units up to 3, strong (Odor Panel of the CRC-APRAC Program Group on Composition of Diesel Exhaust, 1979; Levins, 1981).

Surveys, utilizing volunteer panelists, have been taken to evaluate the general public's response to the odor of DE. Hare and Springer (1971) and Hare et al. (1974) found that at a D rating of about 2 (TIA = 0.9, slight odor intensity), about 90% of the participants perceived the odor, and almost 60% found it objectionable. At a D rating of 3.2 (TIA = 1.2, slight to moderate odor intensity), about 95% perceived the odor, and 75% objected to it, and, at a D rating of 5 (TIA = 1.8, almost moderate), about 95% objected to it.

Linnell and Scott (1962) reported odor threshold measurement in six subjects and found that the dilution factor needed to reach the threshold ranged from 140 to 475 for this small sample of people. At these dilutions, the concentrations of formaldehyde ranged from 0.012 to 0.088 ppm.

5.1.1.1.2. ***Pulmonary and respiratory effects.*** Battigelli (1965) exposed 13 volunteers to three dilutions of DE obtained from a one-cylinder, four-cycle, 7-hp diesel engine (fuel type unspecified) and found that 15-min to 1-h exposures had no significant effects on pulmonary resistance. Pulmonary resistance was measured by plethysmography utilizing the simultaneous recording of esophageal pressure and airflow determined by electrical differentiation of the volume signal from a spirometer. The concentrations of the constituents in the three diluted exhausts were 1.3, 2.8, and 6.2 ppm NO_2; 0.2, 0.5, and 1 ppm SO_2; <20, 30, and 55 ppm CO; and <1.0, <1 to 2, and 1 to 2 ppm total aldehydes, respectively. DPM concentrations were not reported.

A number of studies have evaluated changes in pulmonary function occurring over a workshift in workers occupationally exposed to DE (specific time period not always reported but assumed to be 8 h). In a study of coal miners, Reger (1979) found that both forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) decreased by 0.05 L in 60 diesel-exposed miners, an amount not substantially different from reductions seen in non-diesel-exposed miners (0.02 and 0.04 L, respectively). Decrements in peak expiratory flow rates were similar between diesel and non-DE-exposed miners. Although the monitoring data were not reported, the authors stated that there was no relationship between the low concentrations of measured respirable dust or NO_2 (personal samplers) when compared with shift changes for any lung function parameter measured for the diesel-exposed miners. In summary, this study (available as an abstract only) states that no evidence was found for additional lung function effect over a shift for miners

exposed to diesel emissions as compared with controls, i.e., nonexposed office workers and coal miners not exposed to diesel emissions.

Ames et al. (1982) compared the pulmonary function of 60 coal miners exposed to DE with that of a control group of 90 coal miners not exposed to DE for evidence of acute respiratory effects associated with exposure to DE. Changes over the workshift in FVC, FEV_1, and forced expiratory flow rate at 50% FVC (FEF_{50}) were the indices for acute respiratory effects. The environmental concentrations of the primary pollutants were 2.0 mg/m^3 respirable dust (<10 μm MMAD), 0.2 ppm NO_2, 12 ppm CO, and 0.3 ppm formaldehyde. The investigators reported a statistically significant decline in FVC and FEV_1 over the workshift in both the diesel-exposed and comparison groups. Current smokers had greater decrements in FVC, FEV_1, and FEF_{50} than did ex-smokers and nonsmokers. There was a marked disparity between the ages and the time spent underground for the two study groups. Diesel-exposed miners were about 15 years younger and had worked underground for 15 fewer years (4.8 versus 20.7 years) than miners not exposed to DE. The significance to the results of these differences between the populations is difficult to ascertain.

Except for the expected differences related to age, 120 underground iron ore miners exposed to DE had no workshift changes in FVC and FEV_1 when compared with 120 matched surface miners (Jörgensen and Svensson, 1970). Both groups had equal numbers (30) of smokers and nonsmokers. The frequency of bronchitis was higher among underground workers, much higher among smokers than nonsmokers, and also higher among older than younger workers. The authors reported that the underground miners had exposures of 0.5 to 1.5 ppm NO_2 and between 3 and 9 mg/m^3 particulate matter, with 20% to 30% of the particles <5 μm MMAD. The majority of the particles were iron ore; quartz was 6% to 7% of the fraction <5 μm MMAD.

Gamble et al. (1979) measured preshift FEV_1 and FVC in 187 salt miners and obtained peak flow forced expiratory flow rates at 25%, 50%, and 75% of FVC (FEF_{25}, FEF_{50}, or FEF_{75}). Postshift pulmonary function values were determined from total lung capacity and flows at preshift percentages of FVC. The miners were exposed to mean NO_2 levels of 1.5 ppm and mean respirable particulate levels of 0.7 mg/m^3. No statistically significant changes were found between changes in pulmonary function and in NO_2 and respirable particles combined. Slopes of the regression of NO_2 and changes in FEV_1, FEF_{25}, FEF_{50}, and FEF_{75} were significantly different from zero. The authors concluded that these small reductions in pulmonary function were attributable to variations in NO_2 within each of the five salt mines that contributed to the cohort.

Gamble et al. (1987a) investigated the acute effects of DE in 232 workers in four diesel bus garages using an acute respiratory questionnaire and before and after workshift spirometry.

The prevalence of burning eyes, headaches, difficult or labored breathing, nausea, and wheeze experienced at work was higher in the diesel bus garage workers than in a comparison population of lead/acid battery workers who had not previously shown a statistically significant association of acute symptoms with acid exposure. Comparisons between the two groups were made without adjustment for age and smoking. There was no detectable association of exposure to NO_2 (0.23 ppm ± 0.24 S.D.) or inhalable (less than 10 μm MMAD) particles (0.24 mg/m^3 ± 0.26 S.D.) and acute reductions in FVC, FEV_1, peak flows, FEF_{50}, and FEF_{75}. Workers who had respiratory symptoms had slightly greater but statistically insignificant reductions in FEV_1 and FEF_{50}.

Ulfvarson et al. (1987) evaluated workshift changes in the pulmonary function of 17 bus garage workers, 25 crew members of two types of car ferries, and 37 workers on roll-on/roll-off ships. The latter group was exposed primarily to DE; the first two groups were exposed to both gasoline and DE. The diesel-only exposures that averaged 8 h consisted of 0.13 to 1.0 mg/m^3 particulate matter, 0.02 to 0.8 mg/m^3 (0.016 to 0.65 ppm) NO, 0.06 to 2.3 mg/m^3 (0.03 to 1.2 ppm) NO_2, 1.1 to 5.1 mg/m^3 (0.96 to 4.45 ppm) CO, and up to 0.5 mg/m^3 (0.4 ppm) formaldehyde. The largest decrement in pulmonary function was observed during a workshift following no exposure to DE for 10 days. Forced vital capacity and FEV_1 were significantly reduced over the workshift (0.44 L and 0.30 L, $p<0.01$ and $p<0.001$, respectively). There was no difference between smokers and nonsmokers. Maximal midexpiratory flow, closing volume expressed as the percentage of expiratory vital capacity, and alveolar plateau gradient (phase 3) were not affected. Similar but less pronounced effects on FVC (−0.16 L) were found in a second, subsequent study of stevedores (n = 24) only following 5 days of no exposure to diesel truck exhaust. Pulmonary function returned to normal after 3 days without occupational exposure to DE. No exposure-related correlation was found between the observed pulmonary effects and concentrations of NO, NO_2, CO, or formaldehyde; however, it was suggested that NO_2 adsorbed onto the DE particles may have contributed to the overall dose of NO_2 to the lungs. In a related study, six workers (job category not defined) were placed in an exposure chamber and exposed to diluted DE containing 0.6 mg/m^3 DPM and 3.9 mg/m^3 (2.1 ppm) NO_2. The exhaust was generated by a 6-cylinder, 2.38-L diesel engine, operated for 3 h and 40 min at constant speed, equivalent to 60 km/h, and at about one-half full engine load. No effect on pulmonary function was observed.

In a hypothesis-generating study, Kilburn (2000) examined neurobehavioral and pulmonary function of a small group of workers exposed to DE either as railroad workers (n=10) over a range of 15 to 50 years or as electricians (n=6) over a range of 0.6 to 1.5 years. Neurobehavioral and visual functions batteries showed nearly all of these individuals to be neurobehaviorally impaired in relation to a referent population in one or more areas, including

reaction time, balance, blink reflex latency, verbal recall, and color vision confusion indices. Pulmonary function tests also showed that 10 of the 16 had airway obstruction and another group of 10 of the 16 had chronic bronchitis, chest pain, tightness, and hyperreactive airways. This work implies that with sufficiently sensitive methods, noncancer effects from DPM/DE exposure may be detectable in sufficiently exposed human populations.

5.1.1.1.3. ***Immunological effects.*** Salvi et al. (1999) exposed healthy human subjects to diluted DE (DPM 300 μg/m^3) for 1 h with intermittent exercise. Although there were no changes in pulmonary function, there were significant increases in neutrophils and B lymphocytes as well as histamine and fibronectin in airway lavage fluid. Bronchial biopsies obtained 6 h after DE exposure showed a significant increase in neutrophils, mast cells, and CD4+ and CD8+ T lymphocytes, along with upregulation of the endothelial adhesion molecules ICAM-1 and VCAM-1 and increases in the number of LFA-1+ in the bronchial tissue. Significant increases in neutrophils and platelets were observed in peripheral blood following exposure to DE.

In a follow-up investigation of potential mechanisms underlying the DE-induced airway leukocyte infiltration, Salvi et al. (2000) exposed healthy human volunteers to diluted DE, on two separate occasions for 1 h each, in an exposure chamber. Fiber-optic bronchoscopy was performed 6 h after each exposure to obtain endobronchial biopsies and bronchial wash (BW) cells. These workers observed that DE exposure enhanced gene transcription of IL-8 in the bronchial tissue and BW cells and increased growth-regulated oncogene-a protein expression and IL-8 in the bronchial epithelium; there was also a trend toward an increase in IL-5 mRNA gene transcripts in the bronchial tissue.

In an attempt to evaluate the potential allergenic effects of DPM in humans, Diaz-Sanchez and associates carried out a series of clinical investigations. In the first of these (Diaz-Sanchez et al., 1994), healthy human volunteers were challenged by spraying either saline or 0.30 mg (300 μg) DPM into their nostrils. The authors considered this dose to be equivalent to breathing the outdoor air in Los Angeles for a 24-h period on an average day. Enhanced IgE levels were noted in nasal lavage cells in as little as 24 h, with peak production observed 4 days after DPM challenge. The effects seemed to be somewhat isotype-specific, because in contrast to IgE results, DPM challenge had no effect on the levels of IgG, IgA, IgM, or albumin. The selective enhancement of local IgE production was demonstrated by a dramatic increase in IgE-secreting cells.

Although direct effects of DPM on B-cells have been demonstrated by in vitro studies, it was considered likely that other cells regulating the IgE response may also be affected. Cytokine production was therefore measured in nasal lavage cells from healthy human volunteers challenged with DPM (0 or 0.15 mg in 200 μL saline) sprayed into each nostril (Diaz-

Sanchez et al., 1996). Before challenge with DPM, most subjects' nasal lavage cells had detectable levels of only interferon-γ, IL-2, and IL-13 *m*RNA. After challenge with DPM, the cells produced readily detectable levels of *m*RNA for IL-2, IL-4, IL-5, IL-6, IL-10, IL-13, and interferon-γ. Although the cells in the nasal lavage before and after challenge do not necessarily represent the same ones either in number or type, the broad increase in cytokine production was considered by the authors not to be simply the result of an increase in T cells recovered in the lavage fluid. On the basis of these findings, the authors concluded that the increase in nasal cytokine expression after exposure to DPM can be predicted to contribute to enhanced local IgE production and thus play a role in pollutant-induced airway disease.

The ability of DPM to act as an adjuvant to the ragweed allergen Amb a I was also examined by nasal provocation in ragweed-allergic subjects using 0.3 mg (300 μg) DPM, Amb a I, or both (Diaz-Sanchez et al., 1997). Although allergen and DPM each enhanced ragweed-specific IgE, DPM plus allergen promoted a 16-times greater antigen-specific IgE production. Nasal challenge with DPM also influenced cytokine production. Ragweed challenge resulted in a weak response, DPM challenge caused a strong but nonspecific response, and allergen plus DPM caused a significant increase in the expression of mRNA for TH0 and TH2-type cytokines (IL-4, IL-5, IL-6, IL-10, IL-13), with a pronounced inhibitory effect on IFN-γ gene expression. The author concluded that DPM can enhance B-cell differentiation and, by initiating and elevating IgE production, may be a factor in the increased incidence of allergic airway disease.

In a further extension of these studies, Diaz-Sanchez et al. (1999) examined the potential for DPM to lead to primary sensitization of humans by driving a de novo mucosal IgE response to a neoantigen, keyhole limpet hemocyanin (KLH). Ten atopic subjects were given an initial nasal immunization of KLH followed by two biweekly nasal challenges with KLH. Fifteen different atopic subjects were treated identically, except that DPM was administered 24 h before each KLH exposure. Intranasal administration of KLH alone led to the generation of an anti-KLH IgG and IgA humoral response, which was detected in nasal fluid samples. No anti-KLH IgE was observed in any of these subjects. In contrast, when challenged with KLH preceded by DPM, 9 of the 15 subjects produced anti-KLH-specific IgE. KLH-specific IgG and IgA at levels similar to those seen with KLH alone were also detected. Subjects who received DPM and KLH had significantly increased IL-4, but not IFN-gamma, levels in nasal lavage fluid, whereas these levels were unchanged in subjects receiving KLH alone. These investigators concluded that DPM can function as a mucosal adjuvant to a de novo IgE response and may increase allergic sensitization among atopic individuals.

5.1.1.1.4. ***Human cell culture studies.*** The potential mechanisms by which DPM may act to cause allergenic effects has been examined in human cell culture studies. Takenaka et al. (1995)

reported that DPM extracts enhanced IgE production from purified human B cells. IgE production in these cells (stimulated by exogenous addition of interleukin-4 plus monoclonal antibody) was enhanced (i.e., further stimulated) 20% to 360% by the addition of DPM extracts (1-50 ng/mL) over a period of 10-14 days. DPM extracts in the absence of exogenously added IL-4 and/or monoclonal antibodies did not themselves induce IgE production or synergize with interleukin-4 alone to induce IgE from purified B cells, suggesting that the extracts were enhancing ongoing IgE production rather than inducing germline transcription or isotype switching. The authors concluded that enhancement of IgE production in the human airway resulting from the organic fraction of DPM may be an important factor in the increasing incidence of allergic airway disease.

Terada et al. (1997) examined the effects of DPM and DPM extract on eosinophil adhesion, survival rate, and degranulation. Eosinophils, human mucosal microvascular endothelial cells (HMMECs), and human nasal epithelial cells (HNECs) were preincubated in the presence of DPM and DPM extract. 35S-labeled eosinophils were allowed to adhere to monolayers of HMMECs and HNECs. Although neither DPM nor DPM extract affected the adhesiveness of HMMECs and HNECs to eosinophils, DPM and DPM extract each significantly increased eosinophil adhesiveness to HNECs; neither affected eosinophil adhesiveness to HMMECs. DPM extract also induced eosinophil degranulation without changing the eosinophil survival rate. These results indicate that DPM may play an important role in promoting the nasal hypersensitivity induced by enhanced eosinophil infiltration of epithelium and eosinophil degranulation. It should also be noted that eosinophils are major components of allergic inflammatory disorders, including asthma and nasal allergy.

Terada et al. (1999) examined the effects of DPM extract on the expression of histamine H1 receptor (H1R) mRNA in HNECs and HMMECs, and on the production of IL-8 and GM-CSF induced by histamine. HNECs and HMMECs, isolated from human nasal mucosa specimens, were cultured with DPM extract. DPM extract increased the expression of H1R mRNA in both HNECs and HMMECs. The amount of IL-8 and GM-CSF induced by histamine was also significantly higher in HNECs and HMMECs treated with DPM extract. These results strongly suggest that DPM accelerates the inflammatory change by not only directly upregulating H1R expression but also by increasing histamine-induced IL-8 and GM-CSF production. Histamine is the most important chemical mediator in the pathogenesis of nasal allergy.

Steerenberg et al. (1998) studied the effects of exposure to DPM on airway epithelial cells, the first line of defense against inhaled pollutants. Cells from a human bronchial cell line (BEAS-2B) were cultured in vitro and exposed to DPM (0.04-0.33 mg/mL) and the effects on IL-6 and IL-8 production were observed. Increases in IL-6 and IL-8 production compared to the

nonexposed cells (11- and 4-fold, respectively) were found after 24 or 48 h exposure to DPM. This increase was lower (17- and 3.3-fold) compared to silica and higher compared to titanium dioxide, which showed no increase for either IL-6 or IL-8. The study was extended to observe the effects of DPM on inflammation-primed cells. BEAS-2B cells were exposed to TNF-α followed by DPM. Additive effects on IL-6 and IL-8 production by BEAS-2B cells were found after TNF-α priming and subsequent exposure to DPM only at a low dose of DPM and TNF-α (0.05-0.2 ng/mL). The investigators concluded that BEAS-2B phagocytized DPM and produced an increased amount of IL-6 and IL-8, and that in TNF-α-primed BEAS-2B cells DPM increased interleukin production only at low concentrations of DPM and TNF-α.

Ohtoshi et al. (1998) studied the effect of suspended particulate matter (SPM), obtained from high-volume air samplers, and DPM obtained from exhaust of a stationary diesel engine on the production of IL-8 and granulocyte-colony stimulating factor (GM-CSF) by human airway epithelial cells in vitro. Nontoxic doses of DPMs stimulated production of IL-8 and GM-CSF by three kinds of human epithelial cells (nasal polyp-derived upper airway, normal bronchial, and transformed bronchial epithelial cells) in a dose- and time-dependent fashion at a DPM concentration as low as 10 μg/mL. SPM applied at 250 and 2,500 μg/mL had a stimulatory effect on GM-CSF, but not on IL-8 production. The effects could be blocked with a protein synthesis inhibitor, suggesting that the process required de novo protein synthesis, and appeared to be due to an extractable component because neither charcoal nor graphite showed such stimulatory effects. The authors concluded that SPM and DPM, a component of SPM, may be important air pollutants in the activation of airway cells for the release of cytokines relevant to allergic airway inflammation.

The mechanisms underlying DPM-induced injury to airway cells were investigated in human bronchial epithelial cells (HBECs) in culture (Bayram et al., 1998a). HBECs from bronchial explants obtained at surgery were cultured and exposed to DPM (10-100 μg/mL) suspended in a serum-free supplemented medium (SF-medium) or to a SF-medium filtrate of DPM. The filtrate was obtained by incubating DPM (50 μg/mL) in SF-medium for 24 h. The effects of DPM and DPM filtrate on permeability, ciliary beat frequency (CBF), and release of inflammatory mediators were observed. DPM and filtered solution of DPM significantly increased the electrical resistance of the cultures but did not affect movement of bovine serum albumin across cell cultures. DPM and filtered DPM solution significantly attenuated the CBF of these cultures and significantly increased the release of IL-8. DPM also increased the release by these cultures of GM-CSF and soluble intercellular adhesion molecule-1 (sICAM-1). These authors also observed that activated charcoal was not able to induce changes in electrical resistance, attenuate CBF, and increase the release of inflammatory mediators from HBEC, and proposed that these effects were due most likely to the compounds adsorbed onto the DPM

rather than the size of DPM. The authors concluded that exposure of airway cells to DPM may lead to functional changes and release of proinflammatory mediators and that these effects may influence the development of airway disease.

Bayram et al. (1998b) investigated the sensitivity of cultured airway cells from asthmatic patients to DPM. Incubation with DPM (10-100 μg/mL) significantly attenuated the CBF in both the asthmatic and nonasthmatic bronchial epithelial cell cultures. Cultured airway cells from asthmatic patients constitutively released significantly greater amounts of IL-8, GM-CSF, and sICAM-1 than cell cultures from nonasthmatic subjects. Only cultures from asthmatic patients additionally released RANTES. The authors concluded that cultured airway cells from asthmatic subjects differ with regard to the amounts and types of proinflammatory mediators they can release and that the increased sensitivity of bronchial epithelial cells of asthmatic subjects to DPM may result in exacerbation of their disease symptoms.

Devalia et al. (1999) investigated the potential sensitivity of HBECs biopsied from atopic mild asthmatic patients and non-atopic nonasthmatic subjects to DPM. HBECs from asthmatic patients constitutively released significantly greater amounts of IL-8, GM-CSF, and sICAM-1 than HBECs from nonasthmatic subjects. RANTES was only released by HBECs of asthmatic patients. Incubation of the asthmatic cultures with 10 μg/mL DPM significantly increased the release of IL-8, GM-CSF, and sICAM-1 after 24 h. In contrast, only higher concentrations (50-100 μg/mL DPM) significantly increased the release of IL-8 and GM-CSF from HBECs of nonasthmatics. The authors conclude that the increased sensitivity of the airways of asthmatics to DPM may be, at least in part, a consequence of greater constitutive and DPM-induced release of specific pro-inflammatory mediators from bronchial epithelial cells.

Abe and co-workers have demonstrated formation of increased cytokine levels in cultured human bronchial epithelial cells exposed to freshly generated DE, but not to filtered DE, i.e., particle-free DE (Abe et al., 2000). Cytokine IL-8 protein as well as transforming growth factor (TGF)-β1 mRNAs were induced in a time-dependent manner (from 0.5 to 14 h of exposure) in BET-1A human bronchial epithelial cells in response to exposure to freshly generated, cooled, humidified DE that was diluted to 2.9 mg DPM/m^3. The gas obtained by filtration of DE alone did not show any sustained increase in these indicators, suggesting that DE particles play a more important role in eliciting these responses than do the accompanying gases (10.6 ppm CO, 7.3 ppm NO_2, and 3.3 ppm SO_2).

To elucidate the intracellular signal transduction pathway regulating IL-8 and RANTES production, Hashimoto et al. (2000) examined the role of p38 mitogen-activated protein (MAP) kinase in DPM-induced (DPM = 10, 50, or 100 μg/mL) IL-8 and RANTES production by HBECs. They also examined the effect of a thiol-reducing agent, N-acetylcysteine (NAC), on DPM-induced p38 MAP kinase activation and cytokine production. The authors conclude that

p38 MAP kinase plays an important role in the DPM-activated signaling pathway that regulates IL-8 and RANTES production by HBECs and that the cellular redox state is critical for DPM-induced p38 MAP kinase activation leading to IL-8 and RANTES production.

Boland et al. (1999) compared the biological effects of carbon black and DPM (2.5 $\mu g/cm^2$ culture surface) collected from catalyst- and noncatalyst-equipped diesel vehicles in cultures of both human bronchial epithelial cells and human nasal epithelial cells. Transmission electron microscopy indicated that DPM was phagocytosed by epithelial cells and translocated through the epithelial cell sheet. The time and dose dependency of phagocytosis and its nonspecificity for different particles (DPM, carbon black, and latex particles) were established by flow cytometry. DPM also induced a time-dependent increase in interleukin-8, GM-CSF, and interleukin-1β release. The inflammatory response occurred later than phagocytosis and, because carbon black had no effect on cytokine release, its extent appeared to depend on the content of adsorbed organic compounds. Furthermore, treatment of the exhaust gas to decrease the adsorbed organic fraction reduced the DPM-induced increase in GM-CSF factor release. These results indicate that DPM can be phagocytosed by and induce a specific inflammatory response in airway epithelial cells.

5.1.1.1.5. ***Summary.*** In the available exposure studies, considerable variability is reported in DE detection threshold. The odor scales described in some of these studies have no general use at present because they are not objectively defined; however, the studies do clearly indicate substantial interindividual variability in the ability to detect odor and the level at which it becomes objectionable. Much of what is known about the acute effects of DE comes from case reports that lack clear measurements of exposure concentrations. The studies of pulmonary function changes in exposed humans have looked for changes occurring over a workshift or after a short-term exposure. The overall conclusion of these studies is that reversible changes in pulmonary function in humans can occur in relation to DE exposure, although it is not possible to relate these changes to specific exposure levels. Numerous studies described in this section, conducted in humans and in isolated cell systems derived from humans exposed to DPM, revealed various biochemical and pathophysiological alterations, such as IgE changes, altered levels of cytokines/chemokines, and goblet-cell hyperplasia, with nearly all these responses being key changes and markers of allergic inflammatory disorders of the airways such as asthma and nasal allergies (Nel et al., 1998). Thus, a major point of significance about these findings is that they indicate that DPM could be viewed as having the potential to elicit inflammatory and immunological responses and responses typical of asthma, and that DPM may be a likely factor in the increasing incidence of allergic hypersensitivity. These studies have also shown that effects are due primarily to the organic fraction and that DPM enhances the allergic response to

known allergens. Results from these studies, including those wih laboratory animals, indicate that DPM could be viewed as having the potential to influence the development of airway inflammation and disease through its adjuvant properties and by causing the release of proinflammatory mediators.

5.1.1.2. *Long-Term Exposures*

Several epidemiologic studies have evaluated the effects of chronic exposure to DE on occupationally exposed workers.

Battigelli et al. (1964) measured several indices of pulmonary function, including vital capacity, FEV_1, peak flow, nitrogen washout, and diffusion capacity in 210 locomotive repairmen exposed to DE in 3 engine houses. The average exposure of these locomotive repairmen to DE was 9.6 years. When compared with a control group matched for age, body size, "past extrapulmonary medical history" (no explanation given), and job status (154 railroad yard workers), no significant clinical differences were found in pulmonary function or in the prevalence of dyspnea, cough, or sputum between the DE-exposed and nonexposed groups. Exposure to DE showed marked seasonal variations because the doors of the engine house were open in the summer and closed in the winter. For the exposed group, the maximum daily workplace concentrations of air pollutants measured were 1.8 ppm NO_2, 1.7 ppm total aldehydes, 0.15 ppm acrolein, 4.0 ppm SO_2, and 5.0 ppm total hydrocarbons. The concentration of airborne particles was not reported.

Gamble et al. (1987b) examined 283 diesel bus garage workers from four garages in two cities to determine if there was excess chronic respiratory morbidity associated with exposure to DE. Tenure of employment was used as a surrogate of exposure; mean tenure of the study population was 9 years ± 10 years S.D. Exposure-effect relationships within the study population showed no detectable associations of symptoms with tenure. Reductions in FVC, FEV_1, peak flow, and FEF_{50} (but not FEF_{75}) were associated with increasing tenure. Compared with a control population (716 nonexposed blue-collar workers) and after indirect adjustment for age, race, and smoking, the exposed workers had a higher incidence of cough, phlegm, and wheezing; however, there was no correlation between symptoms and length of employment. Dyspnea showed an exposure-response trend but no apparent increase in prevalence. Mean FEV_1, FVC, FEF_{50}, and peak flow were not reduced in the total cohort compared with the reference population, but were reduced in workers with 10 years or more tenure.

Purdham et al. (1987) evaluated respiratory symptoms and pulmonary function in 17 stevedores employed in car ferry operations who were exposed to both diesel and gasoline exhausts and in a control group of 11 on-site office workers. Twenty-four percent of the exposed group and 36% of the controls were smokers. If a particular symptom was considered

to be influenced by smoking, smoking status was used as a covariate in the logistic regression analysis; pack-years smoked was a covariate for lung function indices. The frequency of respiratory symptoms was not significantly different between the two groups; however, baseline pulmonary function measurements were significantly different. The latter comparisons were measured by multiple regression analysis using the actual (not percentage predicted) results and correcting for age, height, and pack-years smoked. The stevedores had significantly lower FEV_1, FEV_1/FVC, FEF_{50}, and FEF_{75} ($p<0.021$, $p<0.023$, $p<0.001$, and $p<0.008$, respectively), but not FVC. The results from the stevedores were also compared with those obtained from a study of the respiratory health status of Sydney, Nova Scotia, residents. These comparisons showed that the dock workers had higher FVC, similar FEV_1, but lower FEV_1/FVC and flow rates than the residents of Sydney. Based on these consistent findings, the authors concluded that the lower baseline function measurements in the stevedores provided evidence of an obstructive ventilatory defect, but caution in interpretation was warranted because of the small sample size. There were no significant changes in lung function over the workshift, nor was there a difference between the two groups. The stevedores were exposed to significantly ($p<0.04$) higher concentrations of particulate matter (0.06 to 1.72 mg/m^3, mean 0.50 mg/m^3) than the controls (0.13 to 0.58 mg/m^3, mean not reported). Exposures of stevedores to SO_2, NO_2, aldehydes, and PAHs were very low; occasional CO concentrations in the 20 to 100 ppm range could be detected for periods up to 1 h in areas where blockers were chaining gasoline-powered vehicles.

Additional epidemiologic studies on the health hazards posed by exposure to DE have been conducted for mining operations. Reger et al. (1982) evaluated the respiratory health status of 823 male coal miners from six diesel-equipped mines compared with 823 matched coal miners not exposed to DE. The average tenure of underground work for the underground miners and their controls was only about 5 years; on average, the underground workers in diesel mines spent only 3 of those 5 years underground in diesel-use mines. Underground miners exposed to DE reported a higher incidence of symptoms of cough and phlegm but proportionally fewer symptoms of moderate to severe dyspnea than their matched counterparts. These differences in prevalence of symptoms were not statistically significant. The diesel-exposed underground miners, on the average, had lower FVC, FEV_1, FEF_{50}, FEF_{75}, and FEF_{90} but higher peak flow and FEF_{25} than their matched controls. These differences, however, were not statistically significant. Health indicators for surface workers and their matched controls were directionally the same as for matched underground workers. There were no consistent relationships between the findings of increased respiratory symptoms, decreased pulmonary function, smoking history, years of exposure, or monitored atmosphere pollutants (NO_x, CO, particles, and aldehydes). Mean concentrations of NO_x at the six mines ranged from 0 to 0.6 ppm for short-term area

samples, 0.13 to 0.28 ppm for full-shift personal samples, and 0.03 to 0.80 for full-shift area samples. Inhalable particles (less than 10 μm MMAD) averaged 0.93 to 2.73 mg/m^3 for personal samples and 0 to 16.1 mg/m^3 for full-shift area samples. Ames et al. (1984), using a portion of the miners studied by Reger, examined 280 diesel-exposed underground miners in 1977 and again in 1982. Each miner in this group had at least 1 year of underground mining work history in 1977. The control group was 838 miners with no exposure to DE. The miners were evaluated for prevalence of respiratory symptoms, chronic cough, phlegm, dyspnea, and changes in FVC, FEV_1, and FEF_{50}. No air monitoring data were reported; exposure to DE gases and mine dust particles were described as very low. These authors found no decrements in pulmonary function or increased prevalence of respiratory symptoms attributable to exposure to DE. In fact, the 5-year incidences of cough, phlegm, and dyspnea were greater in miners without exposure to DE.

Attfield (1978) studied 2,659 miners from 21 mines (8 metal, 6 potash, 5 salt, and 2 trona). Diesels were employed in only 18 of the mines, but the 3 mines not using diesels were not identified. The years of diesel usage, ranging from 8 in trona mines to 16 in potash mines, were used as a surrogate for exposure to DE. Based on a questionnaire, an increased prevalence of persistent cough was associated with exposure to aldehydes; this finding, however, was not supported by the pulmonary function data. No adverse respiratory symptoms or pulmonary function impairments were related to CO_2, CO, NO_2, inhalable dust, or inhalable quartz. The author failed to comment on whether the prevalence of cough was related to the high incidence (70%) of smokers in the cohort.

Questionnaire, chest radiograph, and spirometric data were collected by Attfield et al. (1982) on 630 potash miners from six potash mines. These miners were exposed for an average of 10 years (range 5 to 14 years) to 0.1 to 3.3 ppm NO_2, 0.1 to 4.0 ppm aldehyde, 5 to 9 ppm CO, and total dust concentrations of 9 to 23 mg/m^3. No attempt was made to measure diesel-derived particles separately from other dusts. The ratio of total to inhalable (<10 μm MMAD) dust ranged from 2 to 11. An increased prevalence of respiratory symptoms was related solely to smoking. No association was found between symptoms and tenure of employment, dust exposure, NO_2, CO, or aldehydes. A higher prevalence of symptoms of cough and phlegm was found, but no differences in pulmonary function (FVC and FEV_1) were found in these diesel-exposed potash miners when compared with the predicted values derived from a logistics model based on blue-collar workers working in nondusty jobs.

Gamble et al. (1983) investigated respiratory morbidity in 259 miners from 5 salt mines in terms of increased respiratory symptoms, radiographic findings, and reduced pulmonary function associated with exposure to NO_2, inhalable particles (<10 μm MMAD), or years worked underground. Two of the mines used diesel extensively; no diesels were used in one salt

mine. Diesels were introduced into each mine in 1956, 1957, 1963, or 1963 through 1967. Several working populations were compared with the salt miner cohort. After adjustment for age and smoking, the salt miners showed no increased prevalence of cough, phlegm, dyspnea, or airway obstruction (FEV_1/FVC) compared with aboveground coal miners, potash miners, or blue-collar workers. The underground coal miners consistently had an elevated level of symptoms. Forced expiratory volume at 1 s, FVC, FEF_{50}, and FEF_{75} were uniformly lower for salt miners in relation to all the comparison populations. There was, however, no association between changes in pulmonary function and years worked, estimated cumulative inhalable particles, or estimated NO_2 exposure. The highest average exposure to particulate matter was 1.4 mg/m^3 (particle size not reported, measurement includes NaCl). Mean NO_2 exposure was 1.3 ppm, with a range of 0.17 ppm to 2.5 ppm. In a continuation of these studies, Gamble and Jones (1983) grouped the salt miners into low-, intermediate-, and high-exposure categories based on tenure in jobs with DE exposure. Average concentrations of inhalable particles and NO_2 were 0.40, 0.60, and 0.82 mg/m^3 and 0.64, 1.77, and 2.21 ppm for the three diesel exposure categories, respectively. A statistically significant concentration-response association was found between the prevalence of phlegm in the salt miners and exposure to DE ($p<0.0001$) and a similar, but nonsignificant, trend for cough and dyspnea. Changes in pulmonary function showed no association with diesel tenure. In a comparison with the control group of nonexposed, blue-collar workers, adjusted for age and smoking, the overall prevalence of cough and phlegm (but not dyspnea) was elevated in the diesel-exposed workers. Forced expiratory volumes at 1 s and FVC were within 4% of expected, which was considered to be within the normal range of variation for a nonexposed population.

In a preliminary study of three subcohorts from bus company personnel (clerks [lowest exposure], bus drivers [intermediate exposure], and bus garage workers [highest exposure]) representing different levels of exposure to DE, Edling and Axelson (1984) found a fourfold higher risk ratio for cardiovascular mortality in bus garage workers, even after adjusting for smoking history and allowing for at least 10 years of exposure and 15 years or more of induction latency. Carbon monoxide was hypothesized as the etiologic agent for the increased cardiovascular disease but was not measured. However, in a more comprehensive epidemiologic study, Edling et al. (1987) evaluated mortality data covering a 32-year period for a cohort of 694 bus garage employees and found no significant differences between the observed and expected number of deaths from cardiovascular disease. Information on exposure components and their concentrations was not reported.

The absence of reported noncancerous human health effects, other than infrequently occurring effects related to respiratory symptoms and pulmonary function changes, is notable. Unlike studies in laboratory animals, to be described later in this chapter, studies of the impact

of DE on the defense mechanisms of the human lung have not been performed. No direct evidence is available in humans regarding doses of DE, gas phase, particulate phase, or total exhaust that lead to impaired particle clearance or enhanced susceptibility to infection. A summary of epidemiologic studies is presented in Table 5-1.

Table 5-1. Human studies of exposure to diesel exhaust

Study	Description	Findings
	Acute exposures	
Kahn et al. (1988)	13 cases of acute exposure, Utah and Colorado coal miners.	Acute reversible sensory irritation, headache, nervous system effects, bronchoconstriction were reported at unknown exposures.
El Batawi and Noweir (1966)	161 workers, two diesel bus garages.	Eye irritation (42%), headache (37%), dizziness (30%), throat irritation (19%), and cough and phlegm (11%) were reported in this order of incidence by workers exposed in the service and repair of diesel-powered buses.
Battigelli (1965)	Six subjects, eye exposure chamber, three dilutions.	Time to onset was inversely related and severity of eye irritation was associated with the level of exposure to DE.
Katz et al. (1960)	14 persons monitoring DE in a train tunnel.	Three occasions of minor eye and throat irritation; no correlation established with concentrations of DE components.
Hare and Springer (1971) Hare et al. (1974)	Volunteer panelists who evaluated general public's response to odor of DE.	Slight odor intensity, 90% perceived, 60% objected; slight to moderate odor intensity, 95% perceived, 75% objected; moderate odor intensity, 100% perceived, almost 95% objected.
Linnell and Scott (1962)	Odor panel under highly controlled conditions determined odor threshold for DE.	In six panelists, the volume of air required to dilute raw DE to an odor threshold ranged from a factor of 140 to 475.
Rudell et al. (1990, 1994)	Eight healthy nonsmoking subjects exposed for 60 min in chamber to DE (3.7 ppm NO, 1.5 ppm NO_2, 27 ppm CO, 0.5 mg/m^3 formaldehyde, particles (4.3×10^6/cm^3). Exercise, 10 of each 20 min (75 W).	Odor, eye and nasal irritation in 5/8 subjects. BAL findings: small decrease in mast cells, lymphocyte subsets and macrophage phagocytosis; small increase in PMNs.
Rudell et al. (1996)	Volunteers exposed to DE for 1 h while doing light work. Exposure concentrations uncertain.	Unpleasant smell along with irritation of eyes and nose reported. Airway resistance increased. Reduction of particle concentration by trapping did not affect results.
Battigelli (1965)	13 volunteers exposed to three dilutions of DE for 15 min to 1 h.	No significant effects on pulmonary resistance were observed as measured by plethysmography.
Wade and Newman (1993)	Three railroad workers acutely exposed to DE.	The workers developed symptoms of asthma.
Diaz-Sanchez et al. (1994)	Volunteers challenged by a nasal spray of 0.30 mg DPM.	Enhancement of IgE production reported due to a dramatic increase in IgE-secreting cells.

Table 5-1. Human studies of exposure to diesel exhaust (continued)

Study	Description	Findings
Takenaka et al. (1995)	Volunteers challenged by a nasal spray of 0.30 mg DPM.	DPM extracts enhanced interleukin-4 plus monoclonal antibody-stimulated IgE production as much as 360%, suggesting an enhancement of ongoing IgE production rather than inducing germline transcription or isotype switching.
Diaz-Sanchez et al. (1996)	Volunteers challenged by a nasal spray of 0.30 mg DPM.	A broad increase in cytokine expression predicted to contribute to enhanced local IgE production.
Diaz-Sanchez et al. (1997)	Ragweed-sensitive volunteers challenged by a nasal spray of 0.30 mg DPM alone or in combination with ragweed allergen.	Ragweed allergen plus DPM-stimulated ragweed-specific IgE to a much greater degree than ragweed alone, suggesting DPM may be a key feature in stimulating allergen-induced respiratory allergic disease.
Salvi et al. (1999)	Volunteers exposed to diluted DE (DPM 300 $\mu g/m^3$) for 1 h with intermittent exercise.	• No changes in pulmonary function, but significant increases in neutrophils, B lymphocytes, histamine, and fibronectin in airway lavage fluid. • Bronchial biopsies 6 h after exposure showed significant increase in neutrophils, mast cells, CD4+ and CD8+ T lymphocytes; upregulation of ICAM-1 and VCAM-1; increases in the number of LFA-1+ in bronchial tissue. • Significant increases in neutrophils and platelets observed in peripheral blood.
Salvi et al. (2000)	Volunteers exposed to diluted DE (DPM 300 $\mu g/m^3$) for 1 h.	• DPM enhanced gene transcription of IL-8 in bronchial tissue and bronchial wash cells • Increased expression of growth-regulated oncogene-α and IL-8 in bronchial epithelium; trend towards increased IL-5 mRNA gene transcripts.
Nightingale et al. (2000)	Volunteers exposed to resuspended DPM (200 ug/m^3) for 2 h at rest	• DPM increased exhaled levels of CO • DPM increased sputum neutrophils and myeloperoxidase
	Studies of cross-shift changes	
Reger (1979)	Five or more VC maneuvers by each of 60 coal miners exposed to DE at the beginning and end of a workshift.	FEV_1, FVC, and PEFR were similar between diesel and non-diesel-exposed miners. Smokers had an increased number of decrements over shift than nonsmokers.

Table 5-1. Human studies of exposure to diesel exhaust (continued)

Study	Description	Findings
Ames et al. (1982)	Pulmonary function of 60 diesel-exposed compared with 90 non-diesel-exposed coal miners over workshift.	Significant workshift decrements occurred in miners in both groups who smoked; no significant differences in ventilatory function changes between miners exposed to DE and those not exposed.
Jörgensen and Svensson (1970)	240 iron ore miners matched for diesel exposure, smoking, and age were given bronchitis questionnaires and spirometry pre- and postworkshift.	Among underground (surrogate for diesel exposure) miners, smokers, and older age groups, frequency of bronchitis was higher. Pulmonary function was similar between groups and subgroups except for differences accountable to age.
Gamble et al. (1979)	200 salt miners performed before- and after-workshift spirometry. Personal environmental NO_2 and inhalable particle samples were collected.	Smokers had greater but not significant reductions in spirometry than ex- or nonsmokers. NO_2 but not particulate levels significantly decreased FEV1, FEF_{25}, FEF_{50}, and FEF_{75} over the workshift.
Gamble et al. (1987a)	232 workers in 4 diesel bus garages administered acute respiratory questionnaire and before and after workshift spirometry. Compared to lead/acid battery workers previously found to be unaffected by their exposures.	Prevalence of burning eyes, headache, difficult or labored breathing, nausea, and wheeze were higher in diesel bus workers than in comparison population.
Ulfvarson et al. (1987)	Workshift changes in pulmonary function were evaluated in crews of roll-on/ roll-off ships and car ferries and bus garage staff. Pulmonary function was evaluated in six volunteers exposed to diluted DE, 2.1 ppm NO_2, and 0.6 mg/m^3 particulate matter.	Pulmonary function was affected during a workshift exposure to DE, but it normalized after a few days with no exposure. Decrements were greater with increasing intervals between exposures. No effect on pulmonary function was observed in the experimental exposure study.
	Cross-sectional and longitudinal studies	
Battigelli et al. (1964)	210 locomotive repairmen exposed to DE for an average of 9.6 years in railroad engine houses were compared with 154 railroad yard workers of comparable job status but no exposure to DE.	No significant differences in VC, FEV_1, peak flow, nitrogen washout, or diffusion capacity or in the prevalence of dyspnea, cough, or sputum were found between the DE-exposed and nonexposed groups.

Table 5-1. Human studies of exposure to diesel exhaust (continued)

Study	Description	Findings
Gamble et al. (1987b)	283 male diesel bus garage workers from four garages in two cities were examined for impaired pulmonary function (FVC, FEV_1, and flow rates). Study population with a mean tenure of 9 ± 10 years S.D. was compared to a nonexposed blue-collar population.	Analyses within the study population showed no association of respiratory symptoms with tenure. Reduced FEV_1 and FEF_{50} (but not FEF_{75}) were associated with increasing tenure. The study population had a higher incidence of cough, phlegm, and wheezing unrelated to tenure. Pulmonary function was not affected in the total cohort of diesel-exposed but was reduced with 10 or more years of tenure.
Purdham et al. (1987)	Respiratory symptoms and pulmonary function were evaluated in 17 stevedores exposed to both diesel and gasoline exhausts in car ferry operations; control group was 11 on-site office workers.	No differences between the two groups for respiratory symptoms. Stevedores had lower baseline lung function consistent with an obstructive ventilatory defect compared with controls and those of Sydney, Nova Scotia, residents. Caution in interpretation is warranted because of small sample size. No significant changes in lung function over workshift or difference between two groups.
Reger et al. (1982)	Differences in respiratory symptoms and pulmonary function were assessed in 823 coal miners from 6 diesel-equipped mines compared to 823 matched coal miners not exposed to DE.	Underground miners in diesel-use mines reported more symptoms of cough and phlegm and had lower pulmonary function. Similar trends were noted for surface workers at diesel-use mines. Pattern was consistent with small airway disease but factors other than exposure to DE thought to be responsible.
Ames et al. (1984)	Changes in respiratory symptoms and function were measured during a 5-year period in 280 diesel-exposed and 838 nonexposed U.S. underground coal miners.	No decrements in pulmonary function or increased prevalence of respiratory symptoms were found attributable to DE. In fact, 5-year incidences of cough, phlegm, and dyspnea were greater in miners without exposure to DE than in miners exposed to DE.
Attfield (1978)	Respiratory symptoms and function were assessed in 2,659 miners from 21 underground metal mines (1,709 miners) and nonmetal mines (950 miners). Years of diesel usage in the mines were surrogate for exposure to DE.	Questionnaire found an association between an increased prevalence of cough and aldehyde exposure; this finding was not substantiated by spirometry data. No adverse symptoms or pulmonary function decrements were related to exposure to NO_2, CO, CO_2, dust, or quartz.

Table 5-1. Human studies of exposure to diesel exhaust (continued)

Study	Description	Findings
Attfield et al. (1982)	Respiratory symptoms and function were assessed in 630 potash miners from 6 potash mines through a questionnaire, chest radiographs, and spirometry. A thorough assessment of the environment of each mine was made concurrently.	No obvious association indicative of diesel exposure was found between health indices, dust exposure, and pollutants. Higher prevalences of cough and phlegm but no differences in FVC and FEV_1 were found in these diesel-exposed potash workers when compared with predicted values from a logistic model based on blue-collar staff working in nondusty jobs.
Gamble et al. (1983)	Respiratory morbidity was assessed in 259 miners in 5 salt mines by respiratory symptoms, radiographic findings, and spirometry. Two mines used diesels extensively, two had limited use, and one used no diesels in 1956, 1957, 1963, or 1963 through 1967. Several working populations were compared with the salt-mine cohort.	After adjustment for age and smoking, salt miners showed no symptoms or increased prevalence of cough, phlegm, dyspnea, or air obstruction (FEV_1/FVC) compared with aboveground coal miners, potash workers, or blue-collar workers. FEV_1, FVC, FEF_{50}, and FEF_{75} were uniformly lower for salt miners in comparison with all the comparison populations. No changes in pulmonary function were associated with years of exposure or cumulative exposure to inhalable particles or NO_2.
Gamble and Jones (1983)	Same as above. Salt miners were grouped into low-, intermediate-, and high-exposure categories based on tenure in jobs with diesel exposure.	A statistically significant dose-related association of phlegm and diesel exposure was noted. Changes in pulmonary function showed no association with diesel tenure. Age- and smoking-adjusted rates of cough, phlegm, and dyspnea were 145%, 169%, and 93% of an external comparison population. Predicted pulmonary function indices showed small but significant reductions; there was no dose-response relationship.
Edling and Axelson (1984)	Pilot study of 129 bus company employees classified into 3 diesel-exhaust exposure categories: clerks (0), bus drivers (1), and bus garage workers.	The most heavily exposed group (bus garage workers) had a fourfold increase in risk of dying from cardiovascular disease, even after correction for smoking and allowing for 10 years of exposure and 14 years or more of induction latency time.
Edling et al. (1987)	Cohort of 694 male bus garage employees followed from 1951 through 1983 was evaluated for mortality from cardiovascular disease. Subcohorts categorized by levels of exposure were clerks (0), bus drivers (1), and bus garage employees (2).	No increased mortality from cardiovascular disease was found among the members of these five bus companies when compared with the general population or grouped as subcohorts with different levels of exposure.

To date, no large-scale epidemiologic study has looked for effects of chronic exposure to DE on pulmonary function. In the long-term longitudinal and cross-sectional studies, a relationship was generally observed between work in a job with diesel exposure and respiratory symptoms (such as cough and phlegm), but there was no consistent effect on pulmonary function. The interpretation of these results is hampered by lack of measured DE exposure levels and the short duration of exposure in these cohorts. The studies are further limited in that only active workers were included, and it is possible that workers who have developed symptoms or severe respiratory disease are likely to have moved away from these jobs. The relationship between work in a job with diesel exposure and respiratory symptoms may be due to short-term exposure.

5.1.2. Traffic Studies

The relationship between traffic density and respiratory health in children has been examined in a series of studies in Holland in children attending schools located near major freeways. Cough, wheeze, runny nose, and doctor-diagnosed asthma were reported more often for children living within 100 m of freeways carrying between 80,000 and 150,000 vehicles per day (van Vliet et al., 1997). Separate counts for truck traffic indicated a range from 8,000 to 17,500 trucks per day. Truck traffic intensity and concentration of "black smoke," considered by the authors to be a proxy for DPM, measured in schools were found to be significantly associated with chronic respiratory symptoms, with the relationships being more pronounced in girls than in boys.

Brunekreef et al. (1997) measured lung function in children in six areas located near major motorways and assessed their exposure to traffic-related air pollution using separate traffic counts for automobiles and trucks. They also measured air pollution in the children's schools. Although lung function was associated with truck traffic density, there was a lesser association with automobile traffic density. The association was stronger in those children living closest (300 m) to the roadways. Lung function was also associated with concentration of "black smoke" (source and constitution unclear from the study) measured inside the schools. The associations were stronger in girls than in boys. The authors conclude that exposure to vehicular pollution, in particular DPM, may lead to reduced lung function in children living near major motorways.

In a follow-up study of traffic-related air pollution and its effect on the respiratory health of children living near roadways, Brunekreef et al. (2000) showed that the intensity of truck traffic was significantly associated with the prevalence of wheeze, phlegm, bronchitis, eye symptoms, and allergy to dust and pets. Associations with yearly averaged $PM_{2.5}$ and "soot" concentrations measured inside and outside the schools showed similar patterns. Truck traffic

intensity was also significantly associated with a positive skin prick test or elevated IgE for outdoor allergens. There were no associations between traffic intensity or $PM_{2.5}$ and "soot" concentrations and lung function, bronchial responsiveness, and allergic reactions to indoor allergens. Further analysis of the data showed that the associations between traffic-related air pollution and symptoms were almost entirely related to children with bronchial hyperreactivity or sensitization to common allergens.

5.1.3. Laboratory Animal Studies

Because humans and laboratory animals show similar nonneoplastic responses to inhaled particles (ILSI, 2000), animal studies have been conducted to assess the pathophysiologic effects of DPM. Because of the large number of statistical comparisons made in the laboratory animal studies, and to permit uniform, objective evaluations within and among studies, data will be reported as significantly different (i.e., $p<0.05$) unless otherwise specified. The exposure regimens used and the resultant exposure conditions employed in the laboratory animal inhalation studies are summarized in Tables 5-2 through 5-16. Other than the pulmonary function studies performed by Wiester et al. (1980) on guinea pigs during their exposure in inhalation chambers, the pulmonary function studies performed by other investigators, although sometimes unreported, were interpreted as being conducted on the following day or thereafter and not immediately following exposure.

5.1.3.1. *Acute Exposures*

The acute toxicity of undiluted DE to rabbits, guinea pigs, and mice was assessed by Pattle et al. (1957). Four engine operating conditions were used, and 4 rabbits, 10 guinea pigs, and 40 mice were tested under each exposure condition for 5 h (no controls were used). Mortality was assessed up to 7 days after exposure. With the engine operating under light load, the exhaust was highly irritating but not lethal to the test species, and only mild tracheal and lung damage was observed in the exposed animals. The exhaust contained 74 mg/m^3 DPM (particle size not reported), 560 ppm CO, 23 ppm NO_2, and 16 ppm aldehydes. Exhaust containing 5 mg/m^3 DPM, 380 ppm CO, 43 ppm NO_2, and 6.4 ppm aldehydes resulted in low mortality rates (mostly below 10%) and moderate lung damage. Exhaust containing 122 mg/m^3 DPM, 418 ppm CO, 51 ppm NO_2, and 6.0 ppm aldehydes produced high mortality rates (mostly above 50%) and severe lung damage. Exhaust containing 1,070 mg/m^3 DPM, 1,700 ppm CO, 12 ppm NO_2, and 154 ppm aldehydes resulted in 100% mortality in all three species. High CO levels, which resulted in a carboxyhemoglobin value of 60% in mice and 50% in rabbits and guinea pigs, were considered to be the main cause of death in the latter case. High NO_2 levels

were considered to be the main cause of lung damage and mortality seen in the other three tests. Aldehydes and NO_2 were considered to be the main irritants in the light load test.

Kobayashi and Ito (1995) administered 1, 10, or 20 mg/kg DPM in phosphate-buffered saline to the nasal mucosa of guinea pigs. The administration increased nasal airway resistance, augmented increased airway resistance and nasal secretion induced by a histamine aerosol, increased vascular permeability in dorsal skin, and augmented vascular permeability induced by histamine. The increases in nasal airway resistance and secretion are considered typical responses of nasal mucosa against allergic stimulation. Similar results were reported for guinea pigs exposed via inhalation for 3 h to DE diluted to DPM concentrations of either 1 or 3.2 mg/m^3 (Kobayashi et al., 1997). These studies show that short-term exposure to DPM augments nasal mucosal hyperresponsiveness induced by histamine in guinea pigs.

5.1.3.2. *Short-Term and Subchronic Exposures*

A number of inhalation studies have employed a regimen of 20 h/day, 7 days/week for varying exposure periods up to 20 weeks to differing concentrations of airborne particulate matter, vapor, and gas concentrations of diluted DE. Exposure regimens and characterization of gas-phase components for these studies are summarized in Table 5-2.

Pepelko et al. (1980a) evaluated the pulmonary function of cats exposed under these conditions for 28 days to 6.4 mg/m^3 DPM. The only significant functional change observed was a decrease in maximum expiratory flow rate at 10% vital capacity. The excised lungs of the exposed cats appeared charcoal gray, with focal black spots visible on the pleural surface. Pathologic changes included a predominantly peribronchial localization of black-pigmented macrophages within the alveoli characteristic of focal pneumonitis or alveolitis.

The effects of a short-term DE exposure on arterial blood gases, pH, blood buffering, body weight changes, lung volumes, and deflation pressure-volume (PV) curves of young adult rats were evaluated by Pepelko (1982a). Exposures were 20 h/day, 7 days/week for 8 days to a concentration of 6.4 mg/m^3 DPM in the nonirradiated exhaust (RE) and 6.75 mg/m^3 in the irradiated exhaust (IE). In spite of the irradiation, levels of gaseous compounds were not substantially different between the two groups (Table 5-2). Body weight gains were significantly reduced in the RE-exposed rats and to an even greater degree in rats exposed to IE. Arterial blood gases and standard bicarbonate were unaffected, but arterial blood pH was significantly reduced in rats exposed to IE. Residual volume and wet lung weight were not affected by either exposure, but vital capacity and total lung capacity were increased significantly following exposure to RE. The shape of the deflation PV curves were nearly identical for the control, RE, and IE groups.

Table 5-2. Short-term effects of diesel exhaust on laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, F344, M; Mouse, A/J, M; Hamster, Syrian, M	20 h/day 7 days/week 10-13 weeks	1.5 0.19 µm MMD	2,100 to 2,730	6.9	0.49	—	Increase in lung wt; increase in thickness of alveolar walls; minimal species difference	Kaplan et al. (1982)
Rat, F344, M, F; Mouse, CD-1, M, F	7 h/day 5 days/week 19 weeks	0.21 1.0 4.4	140 665 2,926	— — —	— — —	— — —	No effects on lung function in rats (not done in mice); increase in PMNs and proteases and AM aggregation in both species	Mauderly et al. (1981)
Cat, Inbred, M	20 h/day 7 days/week 4 weeks	6.4	3,584	14.6	2.1	2.1	Few effects on lung function; focal pneumonitis or alveolitis	Pepelko et al. (1980a)
Rat, Sprague-Dawley, M	20 h/day 7 days/week 4 weeks	6.4 6.8[a]	3,584 3,808	16.9 16.1[a]	2.49 2.76[a] (<0.01 ppm O_3)[a]	2.10 1.86[a]	Decreased body wt; arterial blood pH reduced; vital capacity, total lung capacities increased	Pepelko (1982a)
Guinea Pig, Hartley, M, F	20 h/day 7 days/week 4 weeks	6.8[a]	3,808	16.7	2.9 (<0.01 ppm O_3)[a]	1.9	Exposure started when animals were 4 days old; increase in pulmonary flow; bardycardia	Wiester et al. (1980)
Rat, F344, M	20 h/day 5.5 days/week 4 weeks	6.0 6.8 µm MMD	2,640	—	—	—	Macrophage aggregation; increase in PMNs; Type II cell proliferation; thickened alveolar walls	White and Garg (1981)
Guinea Pig, Hartley, M	30 min	1-2 mg DPM Intranasally	—	—	—	—	Augmented increases in nasal airway resistance and vascular permeability induced by a histamine aerosol	Kobayashi and Ito (1995)
Guinea Pig, Hartley, M	3 h	1 3.2	0.5 1.6	5.9 12.9	1.4 4.4	0.13 0.34	Similar results to those reported in the previous study using intranasal challenge	Kobayashi et al. (1997)

Table 5-2. Short-term effects of diesel exhaust on laboratory animals (continued)

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Guinea Pig, Hartley, M, F	20 h/day 7 days/week 8 weeks	6.3	7,056	17.4	2.3	2.1	Increase in relative lung wt. AM aggregation; hypertrophy of goblet cells; focal hyperplasia of alveolar epithelium	Wiester et al. (1980)
Mouse ICR, M	6 weeks	100 μg DPM intranasally	—	—	—	—	DPM aggravated ovalbumin-induced airway inflammation and provided evidence that DPM can enhance manifestations of allergic asthma	Takano et al. (1997)
Rat, Sprague-Dawley, M	24 h	5-100 $\mu g/10^6$ AM/mL of DPM	—	—	—	—	Unchanged, but not organic-free DPM enhanced production of proinflammatory cytokines	Yang et al. (1997)

[a]Irradiated exhaust.
PMN = Polymorphonuclear leukocyte.
AM = Alveolar macrophage.

In related studies, Wiester et al. (1980) evaluated pulmonary function in 4-day-old guinea pigs exposed for 20 h/day, 7 days/week for 28 days to IE having a concentration of 6.3 mg/m^3 DPM. When housed in the exposure chamber, pulmonary flow resistance increased 35%, and a small but significant sinus bradycardia occurred as compared with controls housed and measured in control air chambers (p<0.002). Respiratory rate, tidal volume, minute volume, and dynamic compliance were unaffected, as were lead-1 electrocardiograms.

A separate group of adult guinea pigs was necropsied after 56 days of exposure to IE, to diluted RE, or to clean air (Wiester et al., 1980). Exposure resulted in a significant increase in the ratio of lung weight to body weight (0.68% for controls, 0.78% for IE, and 0.82% for RE). Heart/body weight ratios were not affected by exposure. Microscopically, there was a marked accumulation of black pigment-laden AMs throughout the lung, with a slight to moderate accumulation in bronchial and carinal lymph nodes. Hypertrophy of goblet cells in the tracheobronchial tree was frequently observed, and focal hyperplasia of alveolar lining cells was occasionally observed. No evidence of squamous metaplasia of the tracheobronchial tree, emphysema, peribronchitis, or peribronchiolitis was noted.

White and Garg (1981) studied pathologic alterations in the lungs of rats (16 exposed and 8 controls) after exposure to DE containing 6 mg/m^3 DPM. Two rats from the exposed group and one rat from the control group (filtered room air) were sacrificed after each exposure interval of 6 h and 1, 3, 7, 14, 28, 42, and 63 days; daily exposures were for 20 h and were 5.5 days/week. Evidence of AM recruitment and phagocytosis of diesel particles was found at the 6-h sacrifice; after 24 h of exposure there was a focal, scattered increase in the number of Type II cells. After 4 weeks of exposure, there were morphologic changes in size, content, and shape of AM, septal thickening adjacent to clusters of AMs, and an appearance of inflammatory cells, primarily within the septa. At 9 weeks of exposure, focal aggregations of particle-laden macrophages developed near the terminal bronchi, along with an influx of PMNs, Type II cell proliferation, and thickening of alveolar walls. The affected alveoli occurred in clusters that, for the most part, were located near the terminal bronchioles, but occasionally were focally located in the lung parenchyma. Hypertrophy of goblet cells in the tracheobronchial tree was frequently observed, and focal hyperplasia of alveolar lining cells was occasionally observed. No evidence of squamous metaplasia of the tracheobronchial tree, emphysema, peribronchitis, or peribronchiolitis was noted.

Mauderly et al. (1981) exposed rats and mice by inhalation to diluted DE for 545 h over a 19-week period on a regimen of 7 h/day, 5 days/week at concentrations of 0, 0.21, 1.02, or 4.38 mg/m^3 DPM. Indices of health effects were minimal following 19 weeks of exposure. There were no significant exposure-related differences in mortality or body weights of the rats or mice. There also were no significant differences in respiratory function (breathing patterns,

dynamic lung mechanics, lung volumes, quasi-static PV relationships, forced expirograms, and CO-diffusing capacity) in rats; pulmonary function was not measured in mice. No effect on tracheal mucociliary or deep lung clearances were observed in the exposed groups. Rats, but not mice, had elevated immune responses in lung-associated lymph nodes at the two higher exposure levels. Inflammation in the lungs of rats exposed to 4.38 mg/m^3 DPM was indicated by increases in PMNs and lung tissue proteases. Histopathologic findings included AMs that contained DPM, an increase in Type II cells, and the presence of particles in the interstitium and tracheobronchial lymph nodes.

Kaplan et al. (1982) evaluated the effects of subchronic exposure to DE on rats, hamsters, and mice. The exhaust was diluted to a concentration of 1.5 mg/m^3 DPM; exposures were 20 h/day, 7 days/week. Hamsters were exposed for 86 days, rats and mice for 90 days. There were no significant differences in mortality or growth rates between exposed and control animals. Lung weight relative to body weight of rats exposed for 90 days was significantly higher than the mean for the control group. Histological examination of tissues of all three species indicated particle accumulation in the lungs and mediastinal lymph nodes. Associated with the larger accumulations, there was a minimal increase in the thickness of the alveolar walls, but the vast majority of the particles elicited no response. After 6 mo of recovery, considerable clearance of the DPM from the lungs occurred in all three species, as evaluated by gross pathology and histopathology. However, no quantitative estimate of clearance was provided.

Toxic effects in animals from acute exposure to DE appear to be primarily attributable to the gaseous components (i.e., mortality from CO intoxication and lung injury caused by cellular damage resulting from NO_2 exposure). The results from short-term exposures indicate that rats experience minimal lung function impairment even at DE levels sufficiently high to cause histological and cytological changes in the lung. In subchronic studies of durations of 4 weeks or more, frank adverse health effects are not readily apparent and, when found, are mild and result from exposure to concentrations of about 6 mg/m^3 DPM and durations of exposures of 20 h/day. There is ample evidence that subchronic exposure to lower levels of DE affects the lung, as indicated by accumulation of particles, evidence of inflammatory response, AM aggregation and accumulation near the terminal bronchioles, Type II cell proliferation, and thickening of alveolar walls adjacent to AM aggregates. Little evidence exists, however, that subchronic exposure to DE impairs lung function.

5.1.3.3. *Chronic Exposures*

5.1.3.3.1. ***Effects on growth and longevity.*** Changes in growth, body weight, absolute or relative organ weights, and longevity can be measurable indicators of chronic toxic effects.

Such effects have been observed in some, but not all, of the long-term studies conducted on laboratory animals exposed to DE. There was limited evidence for an effect on survival in the published chronic animal studies; deaths occurred intermittently early in one study in female rats exposed to 3.7 mg/m^3 DPM; however, the death rate began to decrease after 15 mo, and the survival rate after 30 mo was slightly higher than that of the control group (Ishinishi et al., 1988). Studies of the effects of chronic exposure to DE on survival and body weight or growth are detailed in Table 5-3.

Increased lung weights and lung-to-body weight ratios have been reported in rats, mice, and hamsters. These data are summarized in Table 5-4. In rats exposed for up to 36 weeks to 0.25 or 1.5 mg/m^3 DPM, lung wet weights (normalized to body weight) were significantly higher in the 1.5 mg/m^3 exposure group than control values after 12 weeks of exposure (Misiorowski et al., 1980). Rats and Syrian hamsters were exposed for 2 years (five 16-h periods per week) to DE diluted to achieve concentrations of 0.7, 2.2, and 6.6 mg/m^3 DPM (Brightwell et al., 1986). At necropsy, a significant increase in lung weight was seen in both rats and hamsters exposed to DE compared with controls. This finding was more pronounced in the rats in which the increase was progressive with both duration of exposure and particulate matter level. The increase was greatest at 30 mo (after the end of a 6-mo observation period in the high-concentration male group where the lung weight was 2.7 times the control and at 24 mo in the high-concentration female group [3.9 times control]). Heinrich et al. (1986a,b; see also Stöber, 1986) found a significant increase in wet and dry weights of the lungs of rats and mice exposed at 4.24 mg/m^3 DPM for 1 year in comparison with controls. After 2 years, the difference was a factor of 2 (mice) or 3 (rats). After the same exposure periods, the hamsters showed increases of 50% to 75%, respectively. Exposure to equivalent filtered DE (i.e., without DPM) caused no significant effects in any of the species. Vinegar et al. (1980, 1981a,b) exposed hamsters to two levels of DE with resultant concentrations of about 6 and 12 mg/m^3 DPM for 8 h/day, 7 days/week for 6 mo. Both exposures significantly increased lung weight and lung-weight to body-weight ratios. The difference between lung weights of exposed and control hamsters exposed to 12 mg/m^3 DPM was approximately twice that of those exposed to 6 mg/m^3.

Heinrich et al. (1995) reported that rats exposed to 2.5 and 7 mg/m^3 DPM for 18 h/day, 5 days/week for 24 mo showed significantly lower body weights than controls starting at day 200 in the high-concentration group and at day 440 in the low-concentration group. Body weight in the low-concentration group was unaffected, as was mortality in any group. Lung weight was increased in the 7 mg/m^3 group starting at 3 mo and persisting throughout the study, while the 2.5 mg/m^3 group showed increased lung weight only at 22 and 24 mo of exposure. Mice (NMRI strain) exposed to 7 mg/m^3 in this study for 13.5 mo had no increase in mortality and insignificant decreases in body weight. Lung weights were dramatically affected, with

Table 5-3. Effects of chronic exposures to diesel exhaust on survival and growth of laboratory animals

Species/sex	Exposure period	Particles (mg/m³)	C × T (mg·h/m³)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, F344, M, F; Monkey, Cynomolgus, M	7 h/day 5 days/week 104 weeks	2.0 0.23–0.36μ m MMD	7,280	11.5	1.5	0.8	No effects on growth or survival	Lewis et al. (1989)
Rat, F344, M; Guinea Pig, Hartley, M	20 h/day 5 days/week 106 weeks	0.25 0.75 1.5 0.19 μm MMD	2,650 7,950 15,900	2.7[a] 4.4[a] 7.1[a]	0.1[b] 0.27[b] 0.5[b]	— — —	Reduced body weight in rats at 1.5 mg/m³	Schreck et al. (1981)
Hamster, Chinese, M	8 h/day 7 days/week 26 weeks	6.0 12.0	8,736 17,472	— —	— —	— —	No effect on growth	Vinegar et al. (1981a,b)
Rat, Wistar, M	6 h/day 5 days/week 87 weeks	8.3 0.71 μm MMD	21,663	50.0	4.0–6.0	—	No effect on growth or mortality rates	Karagianes et al. (1981)
Rat, F344, M, F; Mouse, CD-1, M, F	7 h/day 5 days/week 130 weeks	0.35 3.5 7.1 0.25 μm MMD	1,592 15,925 31,850	2.9 16.5 29.7	0.05 0.34 0.68	— — —	No effect on growth or mortality rates	Mauderly et al. (1984, 1987a)
Rat, Wistar, F; Mouse, MMRI, F	19 h/day 5 days/week 104 weeks	4.24 0.35 μm MMD	41,891	12.5	1.5	1.1	Reduced body wts; increased mortality in mice	Heinrich et al. (1986a)
Rat, F344 M, F	16 h/day 5 days/week 104 weeks	0.7 2.2 6.6	5,824 18,304 54,912	— — 32.0	— — —	— — —	Growth reduced at 2.2 and 6.6 mg/m³	Brightwell et al. (1986)
Rat[c] F344/Jcl.	16 h/day 6 days/week 130 weeks	0.11[d] 0.41[d] 1.08[d] 2.31[d] 3.72[e] 0.2–0.3 μm MMD	1,373 5,117 13,478 28,829 46,426	1.23 2.12 3.96 7.10 12.9	0.08 0.26 0.70 1.41 3.00	0.38 1.06 2.42 4.70 4.57	Concentration-dependent decrease in body weight; earlier deaths in females exposed to 3.72 mg/m³, stabilized by 15 mo	Research Committee for HERP Studies (1988)
Rat, Wistar, F; Mouse, NMRI, F (7 mg/m³ only)	18 h/day 5 days/week 24 mo	0.84 2.5 6.98	7,400 21,800 61,700	2.6 8.3 21.2	0.3 1.2 3.8	0.3 1.1 3.4	Reduced body weight in rats at 2.5 and 6.98 mg/m³ and no effect in mice	Heinrich et al. (1995)

Table 5-3. Effects of chronic exposures to diesel exhaust on survival and growth of laboratory animals (continued)

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Mice, NMRI, F; C57BL/6N, F	18 h/day 5 days/week 13.5 mo (NMRI) 24 mo (C57BL/N)	6.98	35,500 - NMRI 38,300 - C57	14.2	2.3	2.8	Reduced body weight in NMRI mice but not in C57BL/6N mice	Heinrich et al. (1995)
Rats, F344, M	16 h/day 5 days/week 23 mo	2.44 6.33	19,520 50,640	— —	— —	— —	Reduced survival in 6.33 mg/m^3 after 300 days. Body weight significantly lower at 6.33 mg/m^3	Nikula et al. (1995)
Mouse, CD-1, M,F	7 h/day 5 days/week 104 weeks	0.35 3.5 7.1 0.25 μm MDD	1,274 12,740 25,844	3 17 30	0.1 0.3 0.7	— — —	No effect on growth or mortality rates	Mauderly et al. (1996)

[a]Estimated from graphically depicted mass concentration data.
[b]Estimated from graphically presented mass concentration data for NO_2 (assuming 90% NO and 10% NO_2).
[c]Data for tests with light-duty engine; similar results with heavy-duty engine.
[d]Light-duty engine.
[e]Heavy-duty engine.

Table 5-4. Effects of chronic exposures to diesel exhaust on organ weights and organ-to-body-weight ratios

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, F344, M; Mouse, A/J, M; Hamster, Syrian, M	20 h/day 7 days/week 12-13 weeks	1.5 0.19 µm MMD	2,520-2,730	—	—	—	No effect on liver, kidney, spleen, or heart weights	Kaplan et al. (1982)
Rat, F344, M, F	7 h/day 5 days/week 52 weeks	2.0 0.23–0.36 µm MMD	3,640	12.7	1.6	0.83	No effects on weights of lungs, liver, heart, spleen, kidneys, and testes	Green et al. (1983)
Rat, F344, M	20 h/day 5.5 days/ week 36 weeks	0.25 1.5 0.19 µm MMD	990 5,940	— —	— —	— —	Increase in relative lung weight at 1.5 mg/m^3 only initially seen at 12 weeks	Misiorowski et al. (1980)
Rat, F344, F	7 h/day 5 days/week 104 weeks	2.0 0.23–0.36 µm MMD	7,280	11.5	1.5	0.81	No effects on heart weights	Vallyathan et al. (1986)
Rat, F344; M Guinea Pig, Hartley, M	20 h/day 5.5 days/ week 78 weeks	0.25 0.75 1.5 0.19 µm MMD	2,145 6,435 12,870	— — —	— — —	— — —	No effects on heart mass	Penney et al. (1981)
Hamster, Chinese, M	8 h/day 7 days/week 26 weeks	6.0 12.0	8,736 17,472	— —	— —	— —	Increase in lung weight and lung/body weight ratio	Vinegar et al. (1981a,b)
Rat, Wistar, F; Hamster, Syrian, M, F Mouse, NMRI, F	19 h/day 5 days/week 120-140 weeks	4.24 0.35 µm MMD	48,336-56,392	12.5	1.5	1.1	Increase in rat, mouse, and hamster lung weight and dry weights	Heinrich et al. (1986a,b) Stöber (1986)
Rat, F344, M, F; Hamster, Syrian, M, F	16 h/day 5 days/week 104 weeks	0.7[a] 2.2[b] 6.6	5,824 18,304 54,912	— — 32.0	— — —	— — —	Increase in lung weight concentration related in rats; heart weight/body weight ratio greater at 6.6 mg/m^3	Brightwell et al. (1986)
Cat, inbred, M	8 h/day 7 days/week 124 weeks	6.0[a] 12.0[b]	41,664 83,328	20.2 33.2	2.7 4.4	2.7 5.0	Decrease in lung and kidney weights	Pepelko et al. (1980b, 1981) Moorman et al. (1985)
Mouse, NMRI, F (7 mg/m^3 only)	18 h/day 5 days/week 24 mo	0.84 2.5 6.98	7,400 21,800 61,700	2.6 8.3 21.2	0.3 1.2 3.8	0.3 1.1 3.4	Increased rat and mouse lung weight at 7 mg/m^3 from 6 mo and at 2.5 mg/m^3 at 22 and 24 mo	Heinrich et al. (1995)

Table 5-4. Effects of chronic exposures to diesel exhaust on organ weights and organ-to-body-weight ratios (continued)

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Mouse, NMRI, F; C57BL/6N, F	18 h/day 5 days/week 13.5 mo (NMRI) 24 mo (C57BL/N)	6.98	35,500 - NMRI 38,300 - C57	14.2	2.3	2.8	Increased lung weight	Heinrich et al. (1995)
Rats, F344, M	16 h/day 5 days/week 23 mo	2.44 6.33	19,520 50,640	— —	— —	— —	Increase in lung weight was significant at 2 and 6 mg/m^3	Nikula et al. (1995)
Rat		0.8 2.5 6.98					Increased lung weight in rats and mice at 3.5 and 7.1 mg/m^3	Henderson et al. (1988a)
Mouse		6.98 4.5						

[a]1 to 61 weeks of exposure.
[b]62 to 124 weeks of exposure.

increases progressing throughout the study from 1.5-fold at 3 mo to 3-fold at 12 mo. Mice (NMRI and C57BL/6N strains) were also exposed to 4.5 mg/m^3 for 23 mo. In NMRI mice, the body weights were reported to be significantly lower than controls, but the magnitude of the change is not reported, so biological significance cannot be assessed. Mortality was slightly increased, but statistical significance is not reported. The C57BL/6N mice showed minimal effects on body weight and mortality, which were not statistically significant. Lung weights were dramatically affected in both strains.

Nikula et al. (1995) exposed male and female F344 rats to DPM concentrations of 2.4 and 6.3 mg/m^3 for 16 h/day, 5 days/week for 23 mo in a study designed to compare the effects of DPM with those of carbon black. Significantly reduced survival was observed in males exposed to 6.3 mg/m^3 but not in females or at the lower concentration. Body weights were decreased by exposure to 6.3 mg/m^3 DPM in both male and female rats throughout the exposure period. Significant increases in lung weight were first seen at 6 mo in the high-exposure group and at 12 to 18 mo in the low-exposure group.

No evidence was found in the published literature that chronic exposure to DE affected the weight of body organs other than the lung and heart (e.g., liver, kidney, spleen, or testes) (Table 5-4). Morphometric analysis of hearts from rats and guinea pigs exposed to 0.25, 0.75, or 1.5 mg/m^3 DPM 20 h/day, 5.5 days/week for 78 weeks revealed no significant alteration in mass at any exposure level or duration of exposure (Penney et al., 1981). The analysis included relative wet weights of the right ventricle, left ventricle, combined atria, and ratio of right to left ventricle. Vallyathan et al. (1986) found no significant differences in heart weights and the ratio of heart weight to body weight between rats exposed to 2 mg/m^3 DPM for 7 h/day, 5 days/week for 24 mo and their respective clean-air chamber controls. No significant differences were found in the lungs, heart, liver, spleen, kidney, and testes of rats exposed for 52 weeks, 7 h/day, 5 days/week to diluted DE containing 2 mg/m^3 DPM compared with their respective controls (Green et al., 1983).

5.1.3.3.2. ***Effects on pulmonary function.*** The effect of long-term exposure to DE on pulmonary function has been evaluated in laboratory studies of rats, hamsters, cats, and monkeys. These studies are summarized in Table 5-5, along with more details on the exposure characteristics, in general order of increasing dose (C × T) of DPM. The text will be presented using the same approach.

Lewis et al. (1989) evaluated functional residual capacity and airway resistance and conductance in 10 control and 10 diesel-exposed rats (2 mg/m^3 DPM, 7 h/day, 5 days/week for 52 or 104 weeks). At the 104-week evaluation, the rats were also examined for maximum flow volume impairments. No evidence of impaired pulmonary function as a result of the exposure to

Table 5-5. Effects of diesel exhaust on pulmonary function of laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, F344, M, F	7 h/day 5 days/week 104 weeks	2.0 0.23–0.36 µm MMD	7,280	11.5	1.5	0.8	No effect on pulmonary function	Lewis et al. (1989)
Monkey, Cynomolgus, M	7 h/day 5 days/week 104 weeks	2.0 0.23-0.36 µm MMD	7,280	11.5	1.5	0.8	Decreased expiratory flow; no effect on vital or diffusing capacities	Lewis et al. (1989)
Rat, F344, M	20 h/day 5.5 days/week 87 weeks	1.5 0.19 µm MMD	14,355	7.0	0.5	—	Increased functional residual capacity, expiratory volume, and flow	Gross (1981)
Rat, Wistar, F	7-8 h/day 5 days/week 104 weeks	3.9 0.1 µm MMD	14,196-16,224	18.5	1.2	3.1	No effect on minute volume, compliance, or resistance	Heinrich et al. (1982)
Hamster, Chinese, M	8 h/day 7 days/week 26 weeks	6.0 12.0	8,736 17,472	— —	— —	— —	Decrease in vital capacity, residual volume, and diffusing capacity; increase in static deflation lung volume	Vinegar et al. (1980, 1981a,b)
Rat, F344, M, F	7 h/day 5 days/week 130 weeks	0.35 3.5 7.1 0.23–0.26 µm MMD	1,593 15,925 31,850	2.9 16.5 29.7	0.05 0.34 0.68	— — —	Diffusing capacity, lung compliance reduced at 3.5 and 7.1 mg/m^3	Mauderly et al. (1988) McClellan et al. (1986)
Rat, F344, M, F; Hamster, Syrian, M, F	16 h/day 5 days/week 104 weeks	0.7 2.2 6.6	5,824 18,304 54,912	— — —	— — —	— — —	Large number of pulmonary function changes consistent with obstructive and restrictive airway diseases at 6.6 mg/m^3 (no specific data provided)	Brightwell et al. (1986)
Hamster, Syrian, M, F	19 h/day 5 days/week 120 weeks	4.24 0.35 µm MMD	48,336	12.5	1.5	1.1	Significant increase in airway resistance	Heinrich et al. (1986a)
Rat, Wistar, F	19 h/day 5 days/week 140 weeks	4.24 0.35 µm MMD	56,392	12.5	1.5	1.1	Decrease in dynamic lung compliance; increase in airway resistance	Heinrich et al. (1986a)
Cat, inbred, M	8 h/day 7 days/week 124 weeks	6.0[a] 12.0[b]	41,664 83,328	20.2 33.3	2.7 4.4	2.1 5.0	Decrease in vital capacity, total lung capacity, and diffusing capacity after 2 years; no effect on expiratory flow	Pepelko et al. (1980b, 1981) Moorman et al. (1985)

[a]1 to 61 weeks exposure.
[b]62 to 124 weeks of exposure.

DE was found in rats. Lewis et al. (1989) exposed male cynomolgus monkeys to DE for 7 h/day, 5 days/week for 24 mo. Groups of 15 monkeys were exposed to air, DE (2 mg/m^3), coal dust, or combined coal dust and DE. Pulmonary function was evaluated prior to exposure and at 6-mo intervals during the 2-year exposure, including compliance and resistance, static and dynamic lung volumes, distribution of ventilation, diffusing capacity, and maximum ventilatory performance. There were no effects on lung volumes, diffusing capacity, or ventilation distribution, so there was no evidence of restrictive disease. There was, however, evidence of obstructive airway disease as measured by low maximal flow rates in diesel-exposed monkeys. At 18 mo of exposure, forced expiratory flow at 25% of vital capacity and forced expiratory flow normalized to FVC were decreased. The measurement of forced expiratory flow at 40% of total lung capacity was significantly decreased at 12, 18, and 24 mo of exposure. The finding of an obstructive effect in monkeys contrasts with the finding of restrictive type effects in other laboratory animal species (Vinegar et al., 1980, 1981a; Mauderly et al., 1988; Pepelko et al., 1980b, 1981) and suggests a possible difference in effect between primate and small animal respiratory tracts. In these monkeys there were no specific histopathological effects reported (see next section), although particle aggregates were reported in the distal airways, suggesting more small airway deposition.

Gross (1981) exposed rats for 20 h/day, 5.5 days/week for 87 weeks to DE containing 1.5 mg/m^3 DPM. When the data were normalized (e.g., indices expressed in units of airflow or volume for each animal by its own forced expiratory volume), there were no apparent functionally significant changes occurring in the lungs at 38 weeks of exposure that might be attributable to the inhalation of DE. After 87 weeks of exposure, functional residual capacity (FRC) and its component volumes (expiratory reserve [ER] and residual volume [RV]), maximum expiratory flow (MEF) at 40% FVC, MEF at 20% FVC, and $FEV_{0.1}$ were significantly greater in the diesel-exposed rats. An observed increase in airflow at the end of the forced expiratory maneuver when a decreased airflow would be expected from the increased FRC, ER, and RV data (the typical scenario of human pulmonary disease) showed these data to be inconsistent with known clinically significant health effects. Furthermore, although the lung volume changes in the diesel-exposed rats could have been indicative of emphysema or chronic obstructive lung disease, this interpretation was contradicted by the airflow data, which suggest simultaneous lowering of the resistance of the distal airways.

Heinrich et al. (1982) evaluated the pulmonary function of rats exposed to a concentration of 3.9 mg/m^3 DPM for 7 to 8 h/day, 5 days/week for 2 years. When compared with a control group, no significant changes in respiratory rate, minute volume, compliance, or resistance occurred in the exposed group (number of rats per group was not stated).

Chinese hamsters (eight or nine per group) were exposed 8 h/day, 7 days/week, for 6 mo to concentrations of either about 6 mg/m^3 or about 12 mg/m^3 DPM (Vinegar et al., 1980,

1981a,b). Vital capacity, vital capacity/lung weight ratio, residual lung volume by water displacement, and CO_2 diffusing capacity decreased significantly in hamsters exposed to 6 mg/m^3 DPM. Static deflation volume-pressure curves showed depressed deflation volumes for diesel-exposed hamsters when volumes were corrected for body weight and even greater depressed volumes when volumes were corrected for lung weight. However, when volumes were expressed as percentage of vital capacity, the diesel-exposed hamsters had higher lung volumes at 0 and 5 cm H_2O. In the absence of confirmatory histopathology, the authors tentatively concluded that these elevated lung volumes and the significantly reduced diffusing capacity in the same hamsters were indicative of possible emphysematous changes in the lung. Similar lung function changes were reported in hamsters exposed at 12 mg/m^3 DPM, but detailed information was not reported. It was stated, however, that the decrease in vital capacity was 176% greater in the second experiment than in the first.

Mauderly et al. (1988; see also McClellan et al., 1986) examined the impairment of respiratory function in rats exposed for 7 h/day, 5 days/week for 24 mo to diluted DE with 0.35, 3.5, or 7.1 mg/m^3 DPM. After 12 mo of exposure to the highest concentration of DE, the exposed rats (n = 22) had lower total lung capacity (TLC), dynamic lung compliance (C_{dyn}), FVC, and CO diffusing capacity than controls (n = 23). After 24 mo of exposure to 7.1 mg/m^3 DPM, mean TLC, C_{dyn}, quasi-static chord compliance, and CO diffusing capacity were significantly lower than control values. Nitrogen washout and percentage of FVC expired in 0.1 s were significantly greater than control values. There was no evidence of airflow obstruction. The functional alterations were attributed to focal fibrotic and emphysematous lesions and thickened alveolar membranes observed by histological examination. Similar functional alterations and histopathologic lesions were observed in the rats exposed to 3.5 mg/m^3 DPM, but such changes usually occurred later in the exposure period and were generally less pronounced. There were no significant decrements in pulmonary function for the 0.35 mg/m^3 group at any time during the study nor were there reported histopathologic changes in this group.

Mauderly et al. (1989) examined the effects of DE on normal rats and on rats with experimentally induced pulmonary emphysema to see if emphysematous rats have increased susceptibility to DPM. The results from parallel lifetime exposures of these 2 groups of rats at 3.5 mg/m^3 DPM showed that only possibly 1 of 65 measured parameters gave results suggesting that rats with emphysematous lungs might be more susceptible than rats with normal lungs to the effects of DE exposure.

Additional studies were conducted by Heinrich et al. (1986a,b; see also Stöber, 1986) on the effects of long-term exposure to DE on the pulmonary function of hamsters and rats. The exhaust was diluted to achieve a concentration of 4.24 mg/m^3 DPM; exposures were for 19 h/day, 5 days/week for a maximum of 120 weeks (hamsters) or 140 weeks (rats). After 1 year of exposure to the DE, the hamsters exhibited a significant increase in airway resistance and a

nonsignificant reduction in lung compliance. For the same time period, rats showed increased lung weights, a significant decrease in C_{dyn}, and a significant increase in airway resistance. These indices did not change during the second year of exposure.

Syrian hamsters and rats were exposed to 0.7, 2.2, or 6.6 mg/m^3 DPM for five 16-h periods per week for 2 years (Brightwell et al., 1986). There were no treatment-related changes in pulmonary function in the hamster. Rats exposed to the highest concentration of DE exhibited changes in pulmonary function (data not presented) that were reported to be consistent with a concentration-related obstructive and restrictive disease.

Pepelko et al. (1980b; 1981; see also Pepelko, 1982b) and Moorman et al. (1985) measured the lung function of adult cats chronically exposed to DE. The cats were exposed for 8 h/day and 7 days/week for 124 weeks. Exposures were at 6 mg/m^3 for the first 61 weeks and 12 mg/m^3 from weeks 62 to 124. No definitive pattern of pulmonary function changes was observed following 61 weeks of exposure; however, a classic pattern of restrictive lung disease was found at 124 weeks. The significantly reduced lung volumes (TLC, FVC, FRC, and inspiratory capacity [IC]) and the significantly lower single-breath diffusing capacity, coupled with normal values for dynamic ventilatory function (mechanics of breathing), indicate the presence of a lesion that restricts inspiration but does not cause airway obstruction or loss of elasticity. This pulmonary physiological syndrome is consistent with an interstitial fibrotic response that was later verified by histopathology (Plopper et al., 1983).

Pulmonary function impairment has been reported in rats, hamsters, cats, and monkeys chronically exposed to DE. In all species but the monkey, the pulmonary function testing results have been consistent with restrictive lung disease. The monkeys demonstrated evidence of small airway obstructive responses. The disparity between the findings in monkeys and those in rats, hamsters, and cats could be in part the result of increased particle retention in the smaller species resulting from (1) exposure to DE that has higher airborne concentrations of gases, vapors, and particles and/or (2) longer duration of exposure. The nature of the pulmonary impairment is also dependent on the site of deposition and routes of clearance, which are determined by the anatomy and physiology of the test laboratory species and the exposure regimen. The data on pulmonary function effects raise the possibility that DE produces small airway disease in primates compared with primarily alveolar effects in small animals and that similar changes might be expected in humans and monkeys. The findings of Nikula et al. (1997a,b) suggest that a larger fraction of particles are translocated to the interstitium of the respiratory tract in primates that are heavily exposed than in rats that are heavily exposed, including the interstitium of the respiratory bronchioles, an anatomical site absent in rats. Nikula and co-workers' pulmonary histopathological findings may have a relationship to these functional findings (see Chapter 3 for a complete discussion). Unfortunately, the available data in primates are too limited to draw clear conclusions.

5.1.3.3.3. ***Lung morphology, biochemistry, and lung lavage analysis.*** Several studies have examined the morphological, histological, and histochemical changes occurring in the lungs of laboratory animals chronically exposed to DE. The histopathological effects of diesel exposure in the lungs of laboratory animals are summarized in Table 5-6, ranked in order of C × T. Table 5-6 also contains an expanded description of exposures.

Kaplan et al. (1982) performed macroscopic and microscopic examinations of the lungs of rats, mice, and hamsters exposed for 20 h/day, 7 days/week for 3 mo to DE containing 1.5 mg/m^3 DPM. Gross examination revealed diffuse and focal deposition of the diesel particles that produced a grayish overall appearance of the lungs with scattered, denser black areas. There was clearance of particles via the lymphatics to regional lymph nodes. Microscopic examination revealed no anatomic changes in the upper respiratory tract; the mucociliary border was normal in appearance. Most of the particles were in macrophages, but some were free as small aggregates on alveolar and bronchiolar surfaces. The particle-laden macrophages were often in masses near the entrances of the lymphatic drainage and respiratory ducts. Associated with these masses was a minimal increase in the thickness of the alveolar walls; however, the vast majority of the particles elicited no response. After 6 mo of recovery, the lungs of all three species contained considerably less pigment, as assessed by gross pathological and histopathological examinations.

Lewis et al. (1989; see also Green et al., 1983) performed serial histological examinations of rat lung tissue exposed to DE containing 2 mg/m^3 DPM for 7 h/day, 7 days/week for 2 years. Accumulations of black-pigmented AMs were seen in the alveolar ducts adjacent to terminal bronchioles as early as 3 mo of exposure, and particles were seen within the interstitium of the alveolar ducts. These macular lesions increased in size up to 12 mo of exposure. Collagen or reticulum fibers were seen only rarely in association with deposited particles; the vast majority of lesions showed no evidence of fibrosis. There was no evidence of focal emphysema with the macules. Multifocal histiocytosis (24% of exposed rats) was observed only after 24 mo of exposure. These lesions were most commonly observed subpleurally and were composed of collections of degenerating macrophages and amorphous granular material within alveoli, together with fibrosis and chronic inflammatory cells in the interstitium. Epithelial lining cells

Table 5-6. Histopathological effects of diesel exhaust in the lungs of laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, F344, M; Mouse, A/J, M; Hamster, Syrian, M	20 h/day 7 days/week 12-13 weeks	1.5 0.19 µm MDD	2,520-2,730	—	—	—	Inflammatory changes, increase in lung weight, increase in thickness of alveolar walls	Kaplan et al. (1982)
Monkey, Cynomolgus, M	7 h/day 5 days/week 104 weeks	2.0 0.23–0.36 µm MDD	7,280	11.5	1.5	0.8	AM aggregation; no fibrosis, inflammation, or emphysema	Lewis et al. (1989)
Rat, F344, M, F	7 h/day 5 days/week 104 weeks	2.0 0.23–0.36 µm MDD	3,640	11.5	1.5	0.8	Multifocal histiocytosis, inflammatory changes, Type II cell proliferation, fibrosis	Bhatnagar et al. (1980) Pepelko (1982a)
Rat, Sprague-Dawley, M; Mouse, A/HEJ, M	8 h/day 7 days/week 39 weeks	6.0	13,104	—	—	—	Increase in lung protein content and collagen synthesis but a decrease in overall lung protein synthesis in both species; prolylhydroxylase activity increased in rats in utero	Bhatnagar et al. (1980) Pepelko (1982a)
Hamster, Chinese, M	8 h/day 5 days/week 26 weeks	6.0 12.0	6,240 12,480	— —	— —	— —	Inflammatory changes, AM accumulation, thickened alveolar lining, Type II cell hyperplasia,edema, increase in collagen	Pepelko (1982b)
Hamster, Syrian, M, F	7-8 h/day 5 days/week 120 weeks	3.9 0.1 µm MDD	16,380-18,720	18.5	1.2	3.1	Inflammatory changes, 60% adenomatous cell proliferation	Heinrich et al. (1982)
Rat, Wistar, M	6 h/day 5 days/week 87 weeks	8.3 0.71 µm MDD	21,663	50.0	4.0-6.0	—	Inflammatory changes, AM aggregation, alveolar cell hypertrophy, interstitial fibrosis, emphysema (diagnostic methodology not described)	Karagianes et al. (1981)
Rat, F344, F	8 h/day 7 days/week 104 weeks	4.9	28,538	7.0	1.8	13.1	Type II cell proliferation, inflammatory changes, bronchial hyperplasia, fibrosis	Iwai et al. (1986)
Rat, F344, M, F; Mouse, CD-1, M, F	7 h/day 5 days/week 130 weeks	0.35 3.5 7.1 0.23 µm MDD	1,592 15,925 31,850	2.9 16.5 29.7	0.05 0.34 0.68	— — —	Alveolar and bronchiolar epithelial metaplasia in rats at 3.5 and 7.0 mg/m^3, fibrosis at 7.0 mg/m^3 in rats and mice, inflammatory changes	Mauderly et al. (1987a) Henderson et al. (1988a)

Table 5-6. Histopathological effects of diesel exhaust in the lungs of laboratory animals (continued)

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rats, SPF 344	7 h/day 5days/week 104 weeks	2 mg/m^3 coal dust (CD) 2 mg/m^3 DPM 1 mg/m^3 CD + 1 mg/m^3 DPM	—	—	—	—	• Assessed pharmacological responses of rat airway smooth muscle in vitro • Maximal contractile responses to acetylcholine of tissues from CD-, DPM-, and CD + DPM- exposed animals significantly increased; effects of CD and DPM were additive • Maximal relaxation response to isoproterenol increased significantly by CD + DPM exposure, but not by individual treatments • The results indicate that chronic exposure to CD, DPM, and CD + DPM produce differential modifications in the behavior of rat airway smooth muscle	Feden et al. (1985)
Rat, Wistar, F; Mouse, NMRI, F (7 mg/m^3 only)	18 h/day 5 days/week 24 mo	0.8 2.5 6.98	7,400 21,800 61,700	2.6 8.3 21.2	0.3 1.2 3.8	0.3 1.1 3.4	Bronchioalveolar hyperplasia, interstitial fibrosis in all groups. Severity and incidence increase with exposure concentration	Heinrich et al. (1995)
Mouse, NMRI, F; C57BL/6N, F	18 h/day 5 days/week 13.5 mo (NMRI) 24 mo (C57BL/N)	6.98	35,500 - NMRI 38,300 - C57	14.2	2.3	2.8	No increase in tumors. Noncancer effects not discussed	
Mouse		4.5					No increase in tumors Noncancer effects not discussed	
Rat, M, F, F344/Jcl.	16 h/day 6 days/week 130 weeks	0.11[a] 0.41[a] 1.08[a] 2.31[a] 3.72[b]	1,373 5,117 13,478 28,829 46,336	1.23 2.12 3.96 7.10 12.9	0.08 0.26 0.70 1.41 3.00	0.38 1.06 2.42 4.70 4.57	Inflammatory changes Type II cell hyperplasia and lung tumors seen at >0.4 mg/m^3; shortening and loss of cilia in trachea and bronchi	Research Committee for HERP Studies (1988)
Mouse, NMRI, F	19 h/day 5 days/week 120 weeks	4.24	48,336	12.5	1.5	1.1	Inflammatory changes, bronchiolo-alveolar hyperplasia, alveolar lipo-proteinosis, fibrosis	Heinrich et al. (1986a)

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Table 5-6. Histopathological effects of diesel exhaust in the lungs of laboratory animals (continued)

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, Wistar, F	19 h/day 5 days/week 140 weeks	4.24	56,392	12.5	1.5	1.1	Thickened alveolar septa; AM aggregation; inflammatory changes; hyperplasia; lung tumors	Heinrich et al. (1986a)
Guinea Pig, Hartley, M	20 h/day 5.5 days/week 104 weeks	0.25 0.75 1.5 6.0	2,860 8,580 17,160 68,640	— — — —	— — — —	— — — —	Minimal response at 0.25 and ultrastructural changes at 0.75 mg/m^3; thickened alveolar membranes; cell proliferation; fibrosis at 6.0 mg/m^3; increase in PMN at 0.75 mg/m^3 and 1.5 mg/m^3	Barnhart et al. (1981, 1982) Vostal et al. (1981) Wallace et al. (1987)
Cat, inbred, M	8 h/day 7 days/week 124 weeks	6.0[c] 12.0[d]	41,664 83,328	20.2 33.2	2.7 4.4	2.1 5.0	Inflammatory changes, AM aggregation, bronchiolar epithelial metaplasia, Type II cell hyperplasia, peribronchiolar fibrosis	Plopper et al. (1983) Hyde et al. (1985)
Rat, F344, M	16 h/day 5 days/week 23 mo	2.44 6.33	19,520 50,640	— —	— —	— —	AM hyperplasia, epithelial hyperplasia, inflammation, septal fibrosis, bronchoalveolar metaplasia	Nikula et al. (1995)
Mouse, CD-1, M,F	7 h/day 5 days/week 104 weeks	0.35 3.5 7.1 0.25 µm MDD	1,274 12,740 25,844	3 17 30	0.1 0.3 0.7	— — —	Exposure-related increase in lung soot, pigment-laden macrophages, lung lesions. Bronchiolization in alveolar ducts at 7.1 mg/m^3	Mauderly et al. (1996)

[a]Light-duty engine.
[b]Heavy-duty engine.
[c]1 to 61 weeks exposure.
[d]62 to 124 weeks of exposure.

AM = Alveolar macrophage.
PMN = Polymorphonuclear leukocyte.

adjacent to collections of pigmented macrophages showed a marked Type II cell hyperplasia; degenerative changes were not observed in Type I cells. Histological examination of lung tissue from monkeys exposed for 24 mo in the same regimen as used for rats revealed aggregates of black particles, principally in the distal airways of the lung. Particles were present within the cytoplasm of macrophages in the alveolar spaces as well as the interstitium. Fibrosis, focal emphysema, or inflammation was not observed. No specific histopathological lesions were reported for the monkey.

Nikula et al. (1997a,b) reevaluated the lung tissue from this study. They concluded that there were no significant differences in the amount of retained particulate matter between monkeys and rats exposed under the same conditions. The rats, however, retained a greater portion of the particulate matter in lumens of the alveolar ducts and alveoli than did the monkeys. Conversely, monkeys retained a greater portion of the particulate material in the interstitium than did rats. Aggregations of particle-laden macrophages in the alveoli were rare, and there were few signs of particle-associated inflammation in the monkeys. Minimal histopathologic lesions were detected in the interstitium.

Histopathological effects of DE on the lungs of rats have been investigated by the Health Effects Research Program on Diesel Exhaust (HERP) in Japan (Ishinishi et al., 1986, 1988). Both light-duty (LD) and heavy-duty (HD) diesel engines were used. The exhaust was diluted to achieve nominal concentrations of 0.1 (LD only), 0.4 (LD and HD), 1 (LD and HD), 2 (LD and HD), and 4 (HD only) mg/m^3 DPM. Rats were exposed for 16 h/day, 6 days/week for 30 mo. No histopathological changes were observed in the lungs of rats exposed to 0.4 mg/m^3 DPM or less. At concentrations above 0.4 mg/m^3 DPM, severe morphological changes were observed. These changes consisted of shortened and absent cilia in the tracheal and bronchial epithelium, marked hyperplasia of the bronchiolar epithelium, and swelling of the Type II cellular epithelium. These lesions appeared to increase in severity with increases in exhaust concentration and duration of exposure. There was no difference in the degree of changes in pulmonary pathology at the same concentrations between the LD and the HD series.

Heinrich et al. (1982) investigated histological changes occurring in the respiratory tract of hamsters exposed to DE. Exposures were for 7 to 8 h/day, 5 days/week for 104 weeks to DE diluted to achieve a concentration of 3.9 mg/m^3 DPM. Significantly higher numbers of hamsters in the group exposed to DE exhibited definite proliferative changes in the lungs compared with the groups exposed to particle-free DE or clean air. Sixty percent of these changes were described as adenomatous proliferations.

Heinrich et al. (1995) reported increased incidence and severity of bronchioloalveolar hyperplasia in rats exposed to 0.8, 2.5, and 7 mg/m^3. The lesion in the lowest concentration group was described as very slight to moderate. Slight to moderate interstitial fibrosis also increased in incidence and severity in all exposed groups, but incidences were not reported. This

chronic study also exposed NMRI mice to 7 mg/m^3 for 13.5 mo and both NMRI and C56BL/6N mice to 4.5 mg/m^3 for 24 mo. Noncancer histological endpoints are not discussed in any detail in the report, which is focused on the carcinogenicity of diesel as compared with titanium dioxide and carbon black.

Iwai et al. (1986) performed serial histopathology on the lungs of rats at 1, 3, 6, 12, and 24 mo of exposure to DE. Exposures were for 8 h/day, 7 days/week for 24 mo; the exposure atmosphere contained 4.9 mg/m^3 DPM. At 1 and 3 mo of exposure, there were minimal histological changes in the lungs of the exposed rats. After 6 mo of exposure, there were particle-laden macrophages distributed irregularly throughout the lung and a proliferation of Type II cells with adenomatous metaplasia in areas where the macrophages had accumulated. After 1 year of exposure, foci of heterotrophic hyperplasia of ciliated or nonciliated bronchiolar epithelium on the adjacent alveolar walls were more common, the quantity of deposited particulate matter increased, and the number of degenerative AMs and proliferative lesions of Type II or bronchiolar epithelial cells increased. After 2 years of exposure, there was a fibrous thickening of the alveolar walls, mast-cell infiltration with epithelial hyperplasia in areas where the macrophages had accumulated, and neoplasms.

Heinrich et al. (1986a; see also Stöber, 1986) performed histopathologic examinations of the respiratory tract of hamsters, mice, and rats exposed to DE that had 4 mg/m^3 DPM. Exposures were for 19 h/day, 5 days/week; the maximum exposure period was 120 weeks for hamsters and mice and 140 weeks for rats. Histological examination revealed different levels of response among the three species. In hamsters, the exhaust produced thickened alveolar septa, bronchioloalveolar hyperplasia, and what were termed emphysematous lesions (diagnostic methodology not described). In mice, bronchoalveolar hyperplasia occurred in 64% of the mice exposed to the exhaust and in 5% of the controls. Multifocal alveolar lipoproteinosis occurred in 71% and multifocal interstitial fibrosis occurred in 43% of the mice exposed to exhaust but in only 4% of the controls. In exposed rats, there were severe inflammatory changes in the lungs, as well as thickened septa, foci of macrophages, and hyperplastic and metaplastic lesions.

Nikula et al. (1995) reported in detail the nonneoplastic effects in male and female F344 rats exposed to 2.4 or 6.3 mg/m^3 of DPM. At 3 mo in the low-concentration group, enlarged particle-containing macrophages were found with minimal aggregation. With higher concentration and longer duration of exposure, the number and size of macrophages and aggregates increased. Alveolar epithelial hyperplasia was found starting at 3 mo and in all rats at 6 mo. These lesions progressed to chronic active inflammation, alveolar proteinosis, and septal fibrosis at 12 mo. Other lesions observed late in the study included bronchiolar-alveolar metaplasia, squamous metaplasia, and squamous cysts. This study reports in detail the progression of lesions in DE exposure and finds relatively little difference between the lesions caused by DE exposure and exposure to similar levels of carbon black particles.

The effects of DE on the lungs of rats exposed to 8.3 ± 2.0 mg/m^3 DPM were investigated by Karagianes et al. (1981). Exposures were for 6 h/day, 5 days/week, for 4, 8, 16, or 20 mo. Histological examinations of lung tissue noted focal aggregation of particle-laden AMs, alveolar histiocytosis, interstitial fibrosis, and alveolar emphysema (diagnostic methodology not described). Lesion severity was related to length of exposure. No significant differences were noted in lesion severity among the DE, the DE plus coal dust (5.8 ± 3.5 mg/m^3), or the high-concentration (14.9 ± 6.2 mg/m^3) coal dust exposure groups following 20 mo of exposure.

Histological changes in the lungs of guinea pigs exposed to diluted DE containing either 0.25, 0.75, 1.5, or 6.0 mg/m^3 DPM were reported by Barnhart et al. (1981; 1982). Exposures at 0.75 and 1.5 mg/m^3 for 2 weeks to 6 mo resulted in an uptake of exhaust particles by three alveolar cell types (AMs, Type I cells, and interstitial macrophages) and also by granulocytic leukocytes (eosinophils). The alveolar-capillary membrane increased in thickness as a result of an increase in the absolute tissue volume of interstitium and Type II cells. In a continuation of these studies, guinea pigs were exposed to DE (up to 6.0 mg/m^3 DPM) for 2 years (Barnhart et al., 1982). A minimal tissue response occurred at a concentration of 0.25 mg/m^3. After 9 mo of exposure, there was a significant increase, about 30%, in Type I and II cells, endothelial cells, and interstitial cells over concurrent age-matched controls; by 24 mo only macrophages and Type II cells were significantly increased. As in the earlier study, ultrastructural evaluation showed that Type I cells, AMs, and eosinophils phagocytized the diesel particles. Exposure to 0.75 mg/m^3 for 6 mo resulted in fibrosis in regions of macrophage clusters and in focal Type II cell proliferation. No additional information was provided regarding the fibrotic changes with increasing concentration or duration of exposure. With increasing concentration/duration of DE exposure, Type II cell clusters occurred in some alveoli. Intraalveolar debris was particularly prominent after exposures at 1.5 and 6.0 mg/m^3 and consisted of secretory products from Type II cells.

In studies conducted on hamsters, Pepelko (1982b) found that the lungs of hamsters exposed for 8 h/day, 7 days/week for 6 mo to 6 or 12 mg/m^3 DPM were characterized by large numbers of black AMs in the alveolar spaces, thickening of the alveolar epithelium, hyperplasia of Type II cells, and edema.

Lungs from rats and mice exposed to 0.35, 3.5, or 7.1 mg/m^3 (0.23 to 0.26 μm mass median diameter [MMD]) for 7 h/day and 5 days/week showed pathologic lesions (Mauderly et al., 1987a; Henderson et al., 1988a). After 1 year of exposure at 7.1 mg/m^3, the lungs of the rats exhibited focal areas of fibrosis; fibrosis increased with increasing duration of exposure and was observable in the 3.5-mg/m^3 group of rats at 18 mo. The severity of inflammatory responses and fibrosis was directly related to the exposure level. In the 0.35 mg/m^3 group of rats, there was no inflammation or fibrosis. Although the mouse lungs contained higher burdens

of diesel particles per gram of lung weight at each equivalent exposure concentration, there was substantially less inflammatory reaction and fibrosis than was the case in rats. Fibrosis was observed only in the lungs of mice exposed at 7.1 mg/m^3 and consisted of fine fibrillar thickening of occasional alveolar septa.

Histological examinations were performed on the lungs of cats initially exposed to 6 mg/m^3 DPM for 61 weeks and subsequently increased to 12 mg/m^3 for Weeks 62 to 124 of exposure. Plopper et al. (1983; see also Hyde et al., 1985) concluded from the results of this study that exposure to DE produced changes in both epithelial and interstitial tissue compartments and that the focus of these lesions in the peripheral lung was the centriacinar region where the alveolar ducts join the terminal conducting airways. This conclusion was based on the following evidence. The epithelium of the terminal and respiratory bronchioles in exposed cats consisted of three cell types (ciliated, basal, and Clara cells) compared with only one type (Clara cells) in the controls. The proximal acinar region showed evidence of peribronchial fibrosis and bronchiolar epithelial metaplasia. Type II cell hyperplasia was present in the proximal interalveolar septa. The more distal alveolar ducts and the majority of the rest of the parenchyma were unchanged from controls. Peribronchial fibrosis was greater at the end of 6 mo in clean air following exposure, whereas the bronchiolar epithelial metaplasia was most severe at the end of exposure. Following an additional 6 mo in clean air, the bronchiolar epithelium more closely resembled the control epithelial cell population.

Wallace et al. (1987) used transmission electron microscopy (TEM) to determine the effect of DE on the intravascular and interstitial cellular populations of the lungs of exposed rats and guinea pigs. Exposed animals and matched controls were exposed to 0.25, 0.75, 1.5, or 6.0 mg/m^3 DPM for 2, 6, or 10 weeks or 18 mo. The results inferred the following: (1) exposure to 6.0 mg/m^3 for 2 weeks was insufficient to elicit any cellular response, (2) both species demonstrated an adaptive multicellular response to DE, (3) increased numbers of fibroblasts were found in the interstitium from week 6 of exposure through month 18, and (4) there was no significant difference in either cell type or number in alveolar capillaries, but there was a significant increase at 18 mo in the mononuclear population in the interstitium of both species.

Additional means for assessing the adverse effects of DE on the lung are to examine biochemical and cytological changes in bronchoalveolar lavage fluid (BALF) and in lung tissue. Fedan et al. (1985) performed studies to determine whether chronic exposure of rats affected the pharmacologic characteristics of rat airway smooth muscle. Concentration-response relationships for tension changes induced with acetylcholine, 5-hydroxytryptamine, potassium chloride, and isoproterenol were assessed in vitro on isolated preparations of airway smooth muscle (trachealis). Chronic exposure to DE significantly increased the maximal contractile responses to acetylcholine compared with control values; exposure did not alter the sensitivity

(EC_{50} values) of the muscles to the agonists. Exposures were to DE containing 2 mg/m^3 DPM for 7 h/day, 5 days/week for 2 years.

Biochemical studies of BALF obtained from hamsters and rats revealed that exposures to DE caused significant increases in lactic dehydrogenase, alkaline phosphatase, glucose-6-phosphate dehydrogenase (G6P-DH), total protein, collagen, and protease (pH 5.1) after approximately 1 year and 2 years of exposure (Heinrich et al., 1986a). These responses were generally much greater in rats than in hamsters. Exposures were to DE containing 4.24 mg/m^3 DPM for 19 h/day, 5 days/week for 120 (hamsters) to 140 (rats) weeks.

Protein, β-glucuronidase activity, and acid phosphatase activity were significantly elevated in BALF obtained from rats exposed to DE containing 0.75 or 1.5 mg/m^3 DPM for 12 mo (Strom, 1984). Exposure for 6 mo resulted in significant increases in acid phosphatase activity at 0.75 mg/m^3 and in protein, β-glucuronidase, and acid phosphatase activity at the 1.5 mg/m^3 concentration. Exposure at 0.25 mg/m^3 DPM did not affect the three indices measured at either time period. The exposures were for 20 h/day, 5.5 days/week for 52 weeks.

Additional biochemical studies (Misiorowski et al., 1980) were conducted on laboratory animals exposed under the same conditions and at the same site as reported on by Strom (1984). In most cases, exposures at 0.25 mg/m^3 did not cause any significant changes. The DNA content in lung tissue and the rate of collagen synthesis were significantly increased at 1.5 mg/m^3 DPM after 6 mo. Collagen deposition was not affected. Total lung collagen content increased in proportion to the increase in lung weight. The activity of prolyl hydroxylase was significantly increased at 12 weeks at 0.25 and 1.5 mg/m^3; it then decreased with age. Lysal oxidase activity did not change. After 9 mo of exposure, there were significant increases in lung phospholipids in rats and guinea pigs exposed to 0.75 mg/m^3 and in lung cholesterol in rats and guinea pigs exposed to 1.5 mg/m^3. Pulmonary prostaglandin dehydrogenase activity was stimulated by an exposure at 0.25 mg/m^3 but was not affected by exposure at 1.5 mg/m^3 (Chaudhari et al., 1980, 1981). Exposures for 12 or 24 weeks resulted in a concentration-dependent lowering of this enzyme activity. Exposure of male rats and guinea pigs at 0.75 mg/m^3 for 12 weeks did not cause any changes in glutathione levels of the lung, heart, or liver. Rats exposed for 2 mo at 6 mg/m^3 showed a significant depletion of hepatic glutathione, whereas the lung showed an increase of glutathione (Chaudhari and Dutta, 1982). Schneider and Felt (1981) reported that similar exposures did not substantially change adenylate cyclase and guanylate cyclase activities in lung or liver tissue of exposed rats and guinea pigs.

Bhatnagar et al. (1980; see also Pepelko, 1982a) evaluated changes in the biochemistry of lung connective tissue of diesel-exposed rats and mice. The mice were exposed for 8 h/day and 7 days/week for up to 9 mo to exhaust containing 6 mg/m^3 DPM. Total lung protein content was measured, as was labeled proline and labeled leucine. Leucine incorporation is an index of total protein synthesis, although collagen is very low in leucine. Proline incorporation reflects

collagen synthesis. Amino acid incorporation was measured in vivo in the rat and in short-term organ culture in mice. Both rats and mice showed a large increase in total protein (41% to 47% in rats), while leucine incorporation declined and proline incorporation was unchanged. These data are consistent with an overall depression of protein synthesis in diesel-exposed animals and also with a relative increase in collagen synthesis compared to other proteins. The increase in collagen synthesis suggested proliferation of connective tissue and possible fibrosis (Pepelko, 1982a).

A number of reports (McClellan et al., 1986; Mauderly et al., 1987a, 1990a; Henderson et al., 1988a) have addressed biochemical and cytological changes in lung tissue and BALF of rodents exposed for 7 h/day, 5 days/week for up to 30 mo at concentrations of 0, 0.35, 3.5, or 7.1 mg/m^3 DPM. At the lowest exposure level (0.35 mg/m^3), no biochemical or cytological changes occurred in the BALF or in lung tissue in either Fischer 344 rats or CD-1 mice. Henderson et al. (1988a) provide considerable time-course information on inflammatory events taking place throughout a chronic exposure. A chronic inflammatory response was seen at the two higher exposure levels in both species, as evidenced by increases in inflammatory cells (macrophages and neutrophils), cytoplasmic and lysosomal enzymes (lactate dehydrogenase, glutathione reductase, and β-glucuronidase), and protein (hydroxyproline) in BALF. Analysis of lung tissue indicated similar changes in enzyme levels as well as an increase in total lung collagen content. After 18 mo of exposure, lung tissue glutathione was depleted in a concentration-dependent fashion in rats but was slightly increased in mice. Lavage fluid levels of glutathione and glutathione reductase activity increased in a concentration-dependent manner and were higher in mice than in rats.

Rats exposed for up to 17 days to diluted DE (3.5 mg/m^3 DPM) had a fivefold increase in the bronchoconstrictive prostaglandin $PGF_{2\alpha}$ and a twofold increase in the inflammatory leukotriene LTB_4. In similarly exposed mice, there was a twofold increase in both parameters. These investigators (Henderson et al., 1988a,b) concluded that the release of larger amounts of such mediators of inflammation from the alveolar phagocytic cells of rats accounted for the greater fibrogenic response seen in that species.

Biochemical analysis of lung tissue from cats exposed for 124 weeks and held in clean air for an additional 26 weeks indicated increases of lung collagen; this finding was confirmed by an observed increase in total lung wet weight and in connective tissue fibers estimated morphometrically (Hyde et al., 1985). Exposures were for 7 h/day, 5 days/week at 6 mg/m^3 DPM for 61 weeks and at 12 mg/m^3 for weeks 62 to 124.

Heinrich et al. (1995) reported on bronchoalveolar lavage in animals exposed for 24 mo and found exposure-related increases in lactate dehydrogenase, β-glucuronidase, protein, and hydroxyproline in groups exposed to 2.5 or 7 mg/m^3, although detailed data are not presented. Lavage analyses were not carried out in concurrent studies in mice.

The pathogenic sequence following the inhalation of DE as determined histopathologically and biochemically begins with the interaction of diesel particles with airway epithelial cells and phagocytosis by AMs. The airway epithelial cells and activated macrophages release chemotactic factors that attract neutrophils and additional AMs. As the lung burden of DPM increases, there is an aggregation of particle-laden AMs in alveoli adjacent to terminal bronchioles, increases in the number of Type II cells lining particle-laden alveoli, and the presence of particles within alveolar and peribronchial interstitial tissues and associated lymph nodes. The neutrophils and macrophages release mediators of inflammation and oxygen radicals that deplete a biochemical defense mechanism of the lung (i.e., glutathione). As will be described later in more detail, other defense mechanisms are affected, particularly the decreased viability of AMs, which leads to decreased phagocytic activity and death of the macrophage. The latter series of events may result in the presence of pulmonary inflammatory, fibrotic, or emphysematous lesions. The data suggest that there may be a threshold of exposure to DE below which adverse structural and biochemical effects may not occur in the lung; however, differences in the anatomy and pathological responses of laboratory animals coupled with their lifespans compared with humans make a determination of human levels of exposure to DE without resultant pulmonary injury a difficult and challenging endeavor.

5.1.3.3.4. ***Effects on pulmonary defense mechanisms.*** The respiratory system has a number of defense mechanisms that negate or compensate for the effects produced by the injurious substances that repeatedly insult the upper respiratory tract, the tracheobronchial airways, and the alveoli. The effects of exposure to DE on the pulmonary defense mechanisms of laboratory animals as well as more details on exposure atmosphere are summarized in Table 5-7 and ranked by cumulative exposure (C × T).

Several studies have been conducted investigating the effect of inhaled DE on the deposition and fate of inert tracer particles or diesel particles themselves. Lung clearance of deposited particles occurs in two distinct phases: a rapid phase (hours to days) from the tracheobronchial region via the mucociliary escalator and a much slower phase (weeks to months) from the nonciliated pulmonary region via, primarily but not solely, AMs. Battigelli et al. (1966) reported impaired tracheal mucociliary clearance in vitro in excised trachea from rats exposed for single or repeated exposures of 4 to 6 h at two dilutions of DE that resulted in exposures of approximately 8 and 17 mg/m^3 DPM. The exposure to 17 mg/m^3 resulted in

Table 5-7. Effects of exposure to diesel exhaust on the pulmonary defense mechanisms of laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
				Alveolar macrophage status				
Guinea Pig, Hartley	20 h/day 5.5 days/week 8 weeks	0.25 1.5 0.19 µm MDD	220 1,320	2.9 7.5	— —	— —	No significant changes in absolute numbers of AMs	Chen et. al. (1980)
Rat, F344, M	7 h/day 5 days/week 104 weeks	2.0 0.23–0.36 µm MDD	7,280	11.5	1.5	0.81	Little effect on viability, cell number, oxygen consumption, membrane integrity, lyzomal enzyme activity, or protein content of AMs; decreased cell volume and ruffling of cell membrane and depressed luminescence of AM	Castranova et al. (1985)
Rat, F344, M	20 h/day 5.5 days/week 26, 48, or 52 weeks	0.25[a] 0.75[a] 1.5[b] 0.19 µm MDD	715-8,580	2.9 4.8 7.5	— — —	— — —	AM cell counts proportional to concentration of DPM at 0.75 and 1.5 mg/m^3; AM increased in lungs in response to rate of DPM mass entering lung rather than total DPM burden in lung; increased PMNs were proportional to inhaled concentrations and/or duration of exposure; PMNs affiliated with clusters of aggregated AM rather than DPM	Strom (1984) Vostal et al. (1982)
Rat F344/Crl, M, F Mouse, CD, M, F	7 h/day 5 days/week 104 weeks (rat), 78 weeks (mouse)	0.35 3.5 7.0 0.25 µm MDD	1,274[c] 12,740[c] 25,480[c]	2.9 16.5 29.7	0.05 0.34 0.68	— — —	Significant increases of AM in rats and mice exposed to 7.0 mg/m^3 DPM for 24 and 18 mo, respectively, but not at concentrations of 3.5 or 0.35 mg/m^3 DPM for the same exposure durations; PMNs increased in a dose-dependent fashion in both rats and mice exposed to 3.5 or 7.0 mg/m^3 DPM and were greater in mice than in rats	Henderson et al. (1988a)
Rat, Wistar, F	18 h/day 5 days/week 24 mo	0.8 2.5 7.1	7,400 21,800 61,700	2.6 8.3 21.2	0.3 1.1 3.4	— — —	Changes in differential cell counts in lung lavage	Heinrich et al. (1995)
Rat, F344/Crl, M	7 h/day 5 days/week 24 mo	3.49	12,704	9.8	1.2	—	Significantly reduced AM in lavage at 24 mo	Mauderly et al. (1990a)

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Table 5-7. Effects of exposure to diesel exhaust on the pulmonary defense mechanisms of laboratory animals (continued)

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
					Clearance			
Rat, M, F	7 h/day 5 days/week 12 weeks	0.2 1.0 4.5 0.25µm MDD	84 420 1,890	— — —	— — —	— — —	Evidence of apparent speeding of tracheal clearance at the 4.5 mg/m^3 level after 1 week of ^{99m}Tc macroaggregated-albumin and reduced clearance of tracer aerosol in each of the three exposure levels at 12 weeks; indication of a lower percentage of ciliated cells at the 1.0 and 4.5 mg/m^3 levels	Wolff and Gray (1980)
Rat, Wistar, F	18 h/day 5 days/week 24 mo	0.8 2.5 7.1	7,400 21,800 61,700	2.6 8.3 21.2	0.3 1.2 3.8	0.3 1.1 3.4	Significant increase in clearance half-time of inhaled labeled aerosols in all groups at 3-18 mo	Heinrich et al. (1995)
Rat, F344, M, developing 0-6 mo adult 6-12 mo	7 h/day 5 days/week 6 mo	3.55	3,321	7.9	9.5		Clearance of 2 µm, aluminosilicate particles. Half-time significantly increased in adult, not different in developing rats	Mauderly et al. (1987b)
Rat, F344, M, F	7 h/day 5 days/week 18 weeks	0.15 0.94 4.1 <0.5 µm MDD	94.5 592 2,583	— — —	— — —	— — —	Lung burdens of DPM were concentration-related; clearance half-time of DPM almost double in 4.1 mg/m^3 group compared to 0.15 mg/m^3 group	Griffis et al. (1983)
Rat, F344, M	7 h/day 5 days/week 26-104 weeks	2.0 0.23-0.36 µm MDD	1,820-7,280	11.5	1.5	0.8	No difference in clearance of $^{59}Fe_3O_4$ particles 1 day after tracer aerosol administration; 120 days after exposure tracer aerosol clearance was enhanced; lung burden of DPM increased significantly between 12 and 24 mo of exposure	Lewis et al. (1989)
Rat, Sprague-Dawley, M	4-6 h/day 7 days/week 0.1 to 14.3 weeks	0.9 8.0 17.0	2.5-10,210	— — —	5.0 2.7 8.0	0.2 0.6 1.0	Impairment of tracheal mucociliary clearance in a concentration-response manner	Battigelli et al. (1966)

Table 5-7. Effects of exposure to diesel exhaust on the pulmonary defense mechanisms of laboratory animals (continued)

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, F344, M, F	7 h/day 5 days/week 130 weeks	0.35 3.5 7.1 0.25 µm MDD	1,593 15,925 31,850	2.9 16.5 29.7	0.1 0.3 0.7	— — —	No changes in tracheal mucociliary clearance after 6, 12, 18, 24, or 30 mo of exposure; increases in lung clearance half-times as early as 6 mo at 7.0 mg/m^3 level and 18 mo at 3.5 mg/m^3 level; no changes seen at 0.35 mg/m^3 level; after 24 mo of diesel exposure, long-term clearance half-times were increased in the 3.5 and 7.0 mg/m^3 groups	Wolff et al. (1987)
Rat, F344/Crl, M	7 h/day 5 days/week 24 mo	3.49	12,704	9.8	1.2	—	Doubling of long-term clearance half-time for clearance of 1.0 µm aluminosilicate particles. Less effect on clearance in animals with experimentally induced emphysema	Mauderly et al. (1990a)
				Microbial-induced mortality				
Mice CD-1, F	7 h/day 5 days/week 4, 12, or 26 weeks	2.0 0.23–0.36 µm MDD	280-1,820	11.5	1.5	0.8	Mortality similar at each exposure duration when challenged with Ao/PR/8/34 influenza virus; in mice exposed for 3 and 6 mo, but not 1 mo, there were increases in the percentages of mice having lung consolidation, higher virus growth, depressed interferon levels, and a fourfold reduction in hemagglutinin antibody levels	Hahon et al. (1985)
Mice, CR/CD-1, F	8 h/day 7 days/week 2 h up to 46 weeks	5.3 to 7.9	11-20,350	19 to 22	1.8 to 3.6	0.9 to 2.8	Enhanced susceptibility to lethal effects of *S. pyogenes* infections at all exposure durations (2 and 6 h; 8, 15, 16, 307, and 321 days); inconclusive results with *S. typhimurium* because of high mortality rates in controls; no enhanced mortality when challenged with A/PR8-3 influenza virus	Campbell et al. (1980, 1981)

[a]Chronic exposure lasted 52 weeks.
[b]Chronic exposure lasted 48 weeks.
[c]Calculated for 104-week exposure.
DPM = Diesel particulate matter.
AM = Alveolar macrophage.
PMN = Polymorphonuclear leukocyte.

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decreased clearance after a single exposure as well as after a cumulative exposure of 34 or 100 h. Clearance was reduced to a lesser extent and in fewer tracheas from animals exposed to 8 mg/m^3 for a cumulative exposure of 40 h. Lewis et al. (1989) found no difference in the clearance of $^{59}Fe_3O_4$ particles (1.5 μm MMAD, σ_g 1.8) 1 day after dosing control and DE-exposed rats (2 mg/m^3, 7 h/day, 5 days/week for 8 weeks).

Wolff et al. (1987) and Wolff and Gray (1980) studied the effects of both subchronic and chronic DE exposure on the tracheal clearance of particles. Tracheal clearance assessments were made by measuring the retention of radiolabeled technetium macroaggregated-albumin remaining 1 h after instillation in the distal trachea of rats. In the subchronic studies, rats were exposed to 0.2, 1.0, or 4.5 mg/m^3 DPM on a 7 h/day, 5 days/week schedule for up to 12 weeks. After 1 week there was an apparent speeding of tracheal clearance at the 4.5 mg/m^3 exposure level (p=0.10), which returned toward baseline after 6 weeks and was slightly below the baseline rate at 12 weeks. In the 1.0 mg/m^3 group, there was a progressive significant reduction in the clearance rate at 6 and 12 weeks of exposure. There was a trend toward reduced clearance in the 0.2 mg/m^3 group. Scanning electron micrographs indicated minimal changes in ciliary morphology; however, there was an indication of a lower percentage of ciliated cells at the 1.0 and 4.5 mg/m^3 levels. In the chronic studies, rats were exposed to 0, 0.35, 3.5, or 7.1 mg/m^3 for 7 h/day, 5 days/week for 30 mo. There were no significant differences in tracheal clearance rates between the control group and any of the exposure groups after 6, 12, 18, 24, or 30 mo of exposure. The preexposure measurements for all groups, however, were significantly lower than those during the exposure period, suggesting a possible age effect. The preexposure value for the 3.5-mg/m^3 group was also significantly lower than the control group.

There is a substantial body of evidence for an impairment of particle clearance from the bronchiole-alveolar region of rats following exposure to DE. Griffis et al. (1983) exposed rats 7 h/day, 5 days/week for 18 weeks to DE at 0.15, 0.94, or 4.1 mg/m^3 DPM. Lung burdens of the 0.15, 0.94, and 4.1 mg/m^3 levels were 35, 220, and 1,890 μg/g lung, respectively, 1 day after the 18-week exposure. The clearance half-time of the DPM was significantly greater, almost double, for the 4.1 mg/m^3 exposure group than for those of the lower exposure groups, 165 ± 8 days versus 99 ± 8 days (0.94 mg/m^3) and 87 ± 28 days (0.15 mg/m^3), respectively.

Chan et al. (1981) showed a dose-related slowing of ^{14}C-diesel particle clearance in rats preexposed to DE at 0.25 or 6 mg/m^3 particulate matter for 20 h/day, 7 days/week for 7 to 112 days. Clearance was inhibited in the 6 mg/m^3 group when compared by length of exposure or compared with the 0.25 mg/m^3 or control rats at the same time periods.

Heinrich et al. (1982) evaluated lung clearance in rats exposed for approximately 18 mo at 3.9 mg/m^3 DPM for 7 to 8 h/day, 5 days/week. Following exposure to $^{59}Fe_2O_3$-aerosol, the rats were returned to the DE exposure and the radioactivity was measured over the thoracic area

at subsequent times. The biological half-life of the iron oxide deposited in the rats' lungs was nearly twice that of controls.

Heinrich also used labeled iron oxide aerosols to study clearance in rats exposed to 0.8, 2.5, or 7 mg/m^3 diesel DPM for 24 mo (Heinrich et al., 1995). Clearance measurements were carried out at 3, 12, and 18 mo of exposure. Half-times of clearance were increased in a concentration- and duration-related manner in all exposed groups, with a range of a 50% increase in the 0.8 mg/m^3 group at 3 mo to an 11-fold increase in the 7 mg/m^3 group at 19 mo. The differential cell counts in these animals were stated to have shown clear effects in the 2.5 and 7 mg/m^3 groups, but specific information about the changes is not reported.

Wolff et al. (1987) investigated alterations in DPM clearance from the lungs of rats chronically exposed to DE at 0, 0.35, 3.5, or 7.1 mg/m^3 DPM for 7 h/day, 5 days/week for up to 24 mo. Progressive increases in lung burdens were observed over time in all groups; levels of DPM in terms of milligrams per lung were 0.60, 11.5, and 20.5 after 24 mo of exposure at the 0.35, 3.5, or 7.1 mg/m^3 exposure levels, respectively. There were significant increases in 16-day clearance half-times of inhaled radiolabeled particles of $^{67}Ga_2O_3$ (0.1 μm MMD) as early as 6 mo at the 7.1 mg/m^3 level and 18 mo at the 3.5 mg/m^3 level; no significant changes were seen at the 0.35 mg/m^3 level at any time point examined. Rats inhaled fused aluminosilicate particles (2 μm MMAD) labeled with ^{134}Cs after 24 mo of DE exposure; long-term clearance half-times were 79, 81, 264, and 240 days for the 0, 0.35, 3.5, and 7.1 mg/m^3 groups, respectively. Differences were significant between the control and the 3.5 and 7.1 mg/m^3 groups ($p < 0.01$), but not between the control and the 0.35 mg/m^3 group.

Mauderly et al. (1987b) compared the effects of DE in the developing lung to the adult lung by exposing groups of male F344 rats to 3.5 mg/m^3 for 7 h/day, 5 days/week for 6 mo. One group (adult) was exposed between 6 and 12 mo of age, and the other was exposed beginning in utero and until 6 mo of age. Clearance of an inhaled monodisperse 2 μm aluminosilicate particle was measured after exposure for 6 mo. The clearance half-time of the slow phase was found to be doubled in the diesel-exposed adult rats compared with age-matched controls and was not significantly affected in developing rat lungs.

Mauderly et al. (1990a) compared the effects of DE in normal lungs with rats in which emphysema had been induced experimentally by instillation of elastase 6 weeks before DE exposures. The rats were exposed to 3.5 mg/m^3 DPM for 7 h/day, 5 days/week for 24 mo. Measurements included histopathology, clearance, pulmonary function, lung lavage, and immune response. In the rats that were not pretreated with elastase, there was a significant reduction in the number of macrophages recovered by pulmonary lavage in contrast to the increases in macrophages reported by Strom (1984) and Henderson et al. (1988). The half-time of the slow phase of clearance of inhaled, 1 μm, monodisperse particles was doubled in the animals without elastase pretreatment. The elastase pretreatment did not affect clearance in

unexposed animals but significantly reduced the effect of diesel. The clearance half-time was significantly less in elastase-pretreated, diesel-exposed animals than in diesel-exposed normal animals. Many other effects measured in this study were also less affected by diesel exposure in elastase-treated animals. Measurements of lung burden of DPM showed that elastase-pretreated animals accumulated less than half as much DPM mass as normal animals exposed at the same time, suggesting that the difference in effect could be explained by differences in dose to the lung. The composite results of this study indicate that, at least in a murine laboratory animal species, the presence of a pulmonary restrictive disease such as emphysema does not seem to exacerbate the effects of chronic exposure to diesel.

Lewis et al. (1989) conducted lung burden and $^{59}Fe_3O_4$ tracer studies in rats exposed for 12 and 24 mo to 2 mg/m^3 DPM (7 h/day, 5 days/week). The slope of the Fe_3O_4 clearance curve of the DPM-exposed animals was significantly steeper than that of the controls, indicating a more rapid alveolar clearance of the deposited $^{59}Fe_3O_4$. After 120 days from the inhalation of the tracer particle, 19% and 8% of the initially deposited $^{59}Fe_3O_4$ were present in the lungs of control and DE-exposed rats, respectively. The lung burden of DPM, however, increased significantly between 12 and 24 mo of exposure (0.52 to 0.97% lung dry weight), indicating a later dose-dependent inhibition of clearance.

Alveolar macrophages, because of their phagocytic and digestive capabilities, are one of the prime defense mechanisms of the alveolar region of the lung against inhaled particles. Thus, characterization of the effects of DE on various properties of AMs provides information on the integrity or compromise of a key pulmonary defense mechanism. The physiological viability of AMs from diesel-exposed rats was assessed after 2 years of exposure by Castranova et al. (1985). The 7 h/day, 5 days/week exposure at 2 mg/m^3 DPM had little effect on the following: viability, cell number, oxygen consumption, membrane integrity, lysosomal enzyme activity, or protein content of the AMs. A slight decrease in cell volume, a decrease in chemiluminescence indicative of a decreased secretion of reactive oxygen species, and a decrease in ruffling of the cell membrane were observed. These latter findings could be reflective of an overall reduction in phagocytic activity.

Exposure to DE has been reported both to increase the number of recoverable AMs from the lung (Strom, 1984; Vostal et al., 1982; Henderson et al., 1988a) or to produce no change in numbers (Chen et al., 1980; Castranova et al., 1985). Strom (1984) found that in rats exposed to 0.25 mg/m^3 DPM for 20 h/day, 5.5 days/week for 6 mo or 1 year, as well as in the controls, BAL cells consisted entirely of AMs, with no differences in the cell counts in the lavage fluid. At the higher concentrations, 0.75 or 1.5 mg DPM/m^3, the count of AM increased proportionally with the exposure concentration; the results were identical for AMs at both 6 and 11 or 12 mo of exposure. The increase in AM counts was much larger after exposure to 1.5 mg/m^3 DPM for 6 mo than after exposure to 0.75 mg/m^3 for 1 year, although the total mass (calculated as C × T)

of deposited particulate burden was the same. These data suggested to the authors that the number of lavaged AMs was proportional to the mass influx of particles rather than to the actual DPM burden in the lung. These results further implied that there may be a threshold for the rate of mass influx of DPM into the lungs of rats above which there was an increased recruitment of AMs. Henderson et al. (1988a) reported similar findings of significant increases of AMs in rats and mice exposed to 7.1 mg/m^3 DPM for 18 and 24 mo, respectively, for 7 h/day, 5 days/week, but not at concentrations of 3.5 or 0.35 mg/m^3 for the same exposure durations. Chen et al. (1980), using an exposure regimen of 0.25 and 1.5 mg/m^3 DPM for 2 mo and 20 h/day and 5.5 days/week, found no significant changes in absolute numbers of AMs from guinea pig BALF, nor did Castranova et al. (1985) in rat BALF following exposure to 2 mg/m^3 DPM for 7 h/day, 5 days/week for 2 years.

A similar inflammatory response was noted by Henderson et al. (1988a) and Strom (1984), as evidenced by an increased number of PMNs present in BALF from rodents exposed to DE. Henderson et al. (1988) found these changes in rats and mice exposed to 7.1 and 3.5 mg/m^3 DPM for 7 h/day, 5 days/week. Significant increases in BALF PMNs were observed in mice at 6 mo of exposure and thereafter at the 7.1 and 3.5 mg/m^3 exposure levels, but in rats only the 7.1 mg/m^3 exposure level showed an increase in BALF PMNs at 6 mo of exposure and thereafter. Significant increases in BALF PMNs occurred in rats at 12, 18, and 24 mo of exposure to 3.5 mg/m^3 DPM. Although increases in PMNs were usually greater in mice in terms of absolute numbers, the PMN response in terms of increase relative to controls was only about one-third that of rats. Strom (1984) reported that the increased numbers of PMNs in BALF were proportional to the inhaled concentrations and/or duration of exposure. The PMNs also appeared to be affiliated with clusters of aggregated AMs rather than to the diesel particles per se. Proliferation of Type II cells likewise occurred in response to the formed aggregates of AMs (White and Garg, 1981).

The integrity of pulmonary defense mechanisms can also be ascertained by assessing if exposure to DE affects colonization and clearance of pathogens and alters the response of the challenged animals to respiratory tract infections. Campbell et al. (1980, 1981) exposed mice to DE followed by infectious challenge with *Salmonella typhimurium, Streptococcus pyogenes*, or A/PR8-3 influenza virus and measured microbial-induced mortality. Exposures to DE were to 6 mg/m^3 DPM for 8 h/day, 7 days/week for up to 321 days. Exposure to DE resulted in enhanced susceptibility to the lethal effects of *S. pyogenes* infection at all exposure durations (2 h, 6 h; 8, 15, 16, 307, and 321 days). Tests with *S. typhimurium* were inconclusive because of high mortality rates in the controls. Mice exposed to DE did not exhibit an enhanced mortality when challenged with the influenza virus. Hatch et al. (1985) found no changes in the susceptibility of mice to Group C *Streptococcus* sp. infection following intratracheal injection of 100 μg of DPM suspended in unbuffered saline.

Hahon et al. (1985) assessed virus-induced mortality, virus multiplication with concomitant IFN levels (lungs and sera), antibody response, and lung histopathology in mice exposed to DE prior to infectious challenge with Ao/PR/8/34 influenza virus. Weanling mice were exposed to DE containing 2 mg/m^3 DPM for 7 h/day, 5 days/week. In mice exposed for 1, 3, and 6 mo, mortality was similar between the exposed and control mice. In mice exposed for 3 and 6 mo, however, there were significant increases in the percentage of mice having lung consolidation, higher virus growth, depressed IFN levels, and a fourfold reduction in hemagglutinin antibody levels; these effects were not seen after the 1-mo exposure.

The effects of DE on the pulmonary defense mechanisms appear to be determined by three critical factors related to exposure: the concentrations of the pollutants, the exposure duration, and the exposure pattern. Higher doses of DE as determined by an increase in one or more of these three variables have been reported to increase the numbers of AMs, PMNs, and Type II cells in the lung, whereas lower doses fail to produce such changes. In rats, the single most significant contributor to the impairment of the pulmonary defense mechanisms appears to be an excessive accumulation of DPM, particularly as particle-laden aggregates of AMs. Such an accumulation would result from an increase in deposition and/or a reduction in clearance. The deposition of particles does not appear to change significantly following exposure to equivalent DE doses over time. Because of the significant nonlinearity in particle accumulation between low and high doses of DE exposure, coupled with no evidence of increased particle deposition, an impairment in one or more of the mechanisms of pulmonary defense appears to be responsible for the DPM accumulation and subsequent pathological sequelae. The time of onset of pulmonary clearance impairment was dependent both on the magnitude and on the duration of exposures. For example, for rats exposed for 7 h/day, 5 days/week for 104 weeks, the concentration needed to induce pulmonary clearance impairment appears to lie between 0.35 and 2.0 mg/m^3 DPM.

5.1.3.3.5. ***Effects on the immune system—inhalation studies.*** The effects of DE on the immune system of guinea pigs were investigated by Dziedzic (1981). Exposures were to 1.5 mg/m^3 DPM for 20 h/day, 5.5 days/week for up to 8 weeks. There was no effect of diesel exposure when compared with matched controls for the number of B and T lymphocytes and null cells isolated from the tracheobronchial lymph nodes, spleen, and blood. Cell viability as measured by trypan blue exclusion was comparable between the exposed and control groups. The results of this study and others on the effects of exposure to DE on the immune system are summarized in Table 5-8.

Mentnech et al. (1984) examined the effect of DE on the immune system of rats. Exposures were to 2 mg/m^3 DPM for 7 h/day, 5 days/week for up to 2 years. Rats exposed for 12 and 24 mo were tested for immunocompetency by determining antibody-producing cells in

the spleen 4 days after immunization with sheep erythrocytes. The proliferative response of splenic T-lymphocytes to the mitogens concanavalin A and phytohemagglutinin was assessed in rats exposed for 24 mo. There were no significant differences between the exposed and control animals. Results obtained from these two assays indicate that neither humoral immunity (assessed by enumerating antibody-producing cells) nor cellular immunity (assessed by the lymphocyte blast transformation assay) were markedly affected by the exposures.

Bice et al. (1985) evaluated whether or not exposure to DE would alter antibody immune responses induced after lung immunization of rats and mice. Exposures were to 0.35, 3.5, or 7.1 mg/m^3 DPM for 7 h/day, 5 days/week for 24 mo. Chamber controls and exposed animals were immunized by intratracheal instillation of SRBCs after 6, 12, 18, or 24 mo of exposure. No suppression in the immune response occurred in either species. After 12, 18, and 24 mo of exposure, the total number of anti-SRBC IgM antibody forming cells (AFCs) was elevated in rats, but not in mice, exposed to 3.5 or 7.1 mg/m^3 DPM; after 6 mo of exposure, only the 7.1 mg/m^3 level was found to have caused this response in rats. The number of AFCs per 10^6 lymphoid cells in lung-associated lymph nodes and the levels of specific IgM, IgG, or IgA in rat sera were not significantly altered. The investigators concluded that the increased cellularity and the presence of DPM in the lung-associated lymph nodes had only a minimal effect on the immune and antigen filtration function of these tissues.

The effects of inhaled DE and DPM have been studied in a murine model of allergic asthma (Takano et al., 1998a,b). ICR mice were exposed for 12 h/day, 7 days/week for 40 weeks to DE (0.3, 1.0, or 3.0 mg/m^3). The mice were sensitized with ovalbumin (OA) after 16 weeks exposure and subsequently challenged with aerosol allergen (1% OA in isotonic saline for 6 min) at 3-week intervals during the last 24 weeks of exposure. Exposure to DE enhanced allergen-related eosinophil recruitment to the submucosal layers of the airways and to the bronchoalveolar space, and increased protein levels of GM-CSF and IL-5 in the lung in a dose-dependent manner. In the DE-exposed mice, increases in eosinophil recruitment and local cytokine expression were accompanied by goblet-cell proliferation in the bronchial epithelium and airwayhyperresponsiveness to inhaled acetylcholine. In contrast, mice exposed to clean air or DE without allergen provocation showed no eosinophil recruitment to the submucosal layers of the airways or to the bronchoalveolar space, and few goblet-cells in the bronchial epithelium. The

Table 5-8. Effects of inhalation of diesel exhaust on the immune system of laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Guinea Pig, Hartley, M	20 h/day 5.5 days/week 4 or 8 weeks	1.5 0.19 µm MDD	660 or 7,280	7.5	—	—	No alterations in numbers of B, T, and null lymphocytes or cell viability among lymphocytes isolated from tracheobronchial lymph nodes, spleen, or blood	Dziedzic (1981)
Rat, F344, M	7 h/day 5 days/week 52 or 104 weeks	2.0 0.23–0.36 µm MDD	3,640 or 7,280	11.5	1.5	0.8	Neither humoral immunity (assessed by enumerating antibody-producing cells) nor cellular immunity (assessed by the lymphocyte blast transformation assay) were markedly affected	Mentnech et al. (1984)
Rat, F344; Mouse, CD-1	7 h/day 5 days/week 104 weeks	0.35 3.5 7.1 0.25 µm MDD	1,274 12,740 25,480	2.9 16.5 29.7	0.05 0.34 0.68	— — —	Total number of anti-sheep red blood cell IgM AFC in the lung-associated lymph nodes was elevated in rats exposed to 3.5 or 7.0 mg/m^3 DPM (no such effects in mice); total number of AFC per 10^6 lymphoid cells in lung-associated lymph nodes and level of specific IgM, IgG, or IgA in rat sera were not altered	Bice et al. (1985)
Mouse, BALB/C, M	12 h/day, 7 days/week, 3 weeks Mice administered OA intranasally before, immediately after, and 3 weeks after exposure	3.0 6.0 0.4 µm	756 1,512	— —	2.8 4.1	1.7 2.7	Spleen weights in mice exposed to DE (6 mg/m^3) increased significantly. Serum anti-OA IgE antibody titers in mice exposed to 6 mg/m^3 significantly higher than control. Antigen-stimulated IL-4 and IL-10 production increased while IFN-g production decreased significantly in spleen cells from DE-exposed (6 mg/m^3) mice stimulated with OA in vitro. DE inhalation may affect antigen-specific IgE antibody production through alteration of the cytokine network.	Fujimaki et al. (1997)
Mouse, C3H/Hen, M	12 h /day, for 12 weeks. Before exposure mice injected IP with OA. After 3 weeks and every 3 weeks thereafter, mice challenged with OA aerosol.	1.0 3.0	1,008 3,024	—	1.42 4.02	0.87 1.83	DE + antigen challenge induced airway hyperresponsiveness and inflammation with increased eosinophils, mast cells, and goblet cells. DE alone induced airway hyperresponsiveness, but not eosinophilic infiltration or increased goblet cells. DE inhalation enhanced airway hyperresponsiveness and airway inflammation caused by OA sensitization.	Miyabara et al. (1998a)

Table 5-8. Effects of inhalation of diesel exhaust on the immune system of laboratory animals (continued)

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Mouse, C3H/HeN, M	12 h/day, for 5 weeks. After 7 days mice injected IP with OA. At end of exposure mice challenged with OA aerosol for 15 minutes.	3.0	1,260	—	4.08	1.26	DE alone increased neutrophils and macrophages in BAL fluid; after DE + OA challenge eosinophils increased. OA alone increased eosinophils but the increase was enhanced by DE. DE + OA, but not DE alone, increased goblet cells, respiratory resistance, production of OA-specific IgE and Ig1 in the serum, and overexpression of IL-5 in lung tissue.	Miyabara et al. (1998b)
Mouse, ICR (murine model of allergic asthma)	12 h/day, 7days/week, 40 weeks. After 16 weeks sensitized to OA and challenged with OA aerosol for 6 min, at 3-week intervals during the last 24 weeks of exposure.	0.3 1.0 3.0	1,008 3,360 10,080	—	—	—	DE exposure enhanced allergen-related recruitment to the submucosal layers of the airways and the bronchoalveolar space, and increased GM-CSF and IL-5 in the lung in a dose-dependent manner. Increases in eosinophil recruitment and local cytosine expression accompanied by goblet cell proliferation in the bronchial epithelium and airway hyperresponsiveness to inhaled acetylcholine. Mice exposed to clean air or DE without allergen provocation showed no eosinophil recruitment to the submucosal layers of the airways nor to the bronchoalveolar space, and few goblet cells in the bronchial epithelium. Daily inhalation of DE may enhance allergen-related respiratory diseases such as allergic asthma, and effect may be mediated by the enhanced local expression of IL-5 and GM-CSF.	Takano et al. (1998a)

DPM = Diesel particulate matter.
AFC = Antibody-forming cells.

authors concluded that daily inhalation of DE can enhance allergen-related respiratory diseases such as allergic asthma, and that this effect may be mediated by the enhanced local expression of IL-5 and GM-CSF. The effect of DPM on a second characteristic of allergic asthma, airway hyperresponsiveness, was examined by Takano et al. (1998b). Laboratory mice were administered OA, DPM, or OA and DPM combined by intratracheal instillation for 6 wk. Respiratory resistance (Rrs) after acetylcholine challenge was measured 24 h after the final instillation. Rrs was significantly greater in the mice treated with OA and DPM than in the other treatments. The authors concluded that DPM can enhance airway responsiveness associated with allergen exposure.

In a series of inhalation studies following earlier instillation studies, Miyabara and co-workers investigated whether inhalation of DE could enhance allergic reactions in laboratory mice. C3H/HeN mice were exposed to DE (3 mg DPM/m^3) by inhalation for 5 weeks (Miyabara et al., 1998b) and, after 7 days of exposure, were sensitized to OA injected intraperitoneally. At the end of the DE exposure, the mice were challenged with an OA aerosol for 15 min. DE caused an increase in the numbers of neutrophils and macrophages in bronchoalveolar lavage fluid independent of OA sensitization, whereas a significant increase in eosinophil numbers occurred only after DE exposure was combined with antigen challenge. Even though OA alone caused an increase in eosinophil numbers in lung tissue, this response was enhanced further by DE. DE exposure combined with OA sensitization enhanced the number of goblet-cells in lung tissue, respiratory resistance, production of OA-specific IgE and IgG_1 in the serum, and overexpression of IL-5 in lung tissue. In a second study, C3H/HeN mice were sensitized with OA injected intraperitoneally and then exposed to DE by inhalation for 12 h/day for 3 mo at either 1 or 3 mg/m^3 (Miyabara et al., 1998a). After 3 weeks of DE exposure, and every 3 weeks thereafter, the mice were challenged with an OA aerosol. Exposure to DE with antigen challenge induced airway hyperresponsiveness and airway inflammation, which was characterized by increased numbers of eosinophils and mast cells in lung tissue. The increase in inflammatory cells was accompanied by an increase in goblet cells in the bronchial epithelium. Airway hyperresponsiveness, but not eosinophilic infiltration or increased goblet cells, was increased by DE exposure alone. These workers concluded that inhalation of DE can enhance airway hyperresponsiveness and airway inflammation caused by OA sensitization in mice.

The effects of DE on IgE antibody production were investigated in BALB/c mice sensitized with OA and exposed by inhalation to DE (3.0 and 6.0 mg/m^3) for 3 weeks (Fujimaki et al., 1997). The mice were sensitized by intranasal administration of OA alone before, immediately after, and 3 weeks after DE inhalation. While body and thymus weights were unchanged in the DE-exposed and control mice, spleen weights in mice exposed to 6 mg/m^3 DE increased significantly. Anti-OA IgE antibody titers in the sera of mice exposed to 6 mg/m^3 DE were significantly higher than control. Total IgE and anti-OA IgG in sera from DE-exposed and

control mice remained unchanged. Cytokine production was measured in vitro stimulated with OA in spleen cells from mice exposed to DE (6 mg/m^3). Antigen-stimulated interleukin-4 (IL-4) and -10 (IL-10) production increased significantly in vitro in spleen cells from DE-exposed mice compared with controls, while IFN-γ production decreased markedly. The authors concluded that DE inhalation in mice may affect antigen-specific IgE antibody production through alteration of the cytokine network.

5.1.3.3.6. ***Effects on the immune system—noninhalation studies.*** The immune response of laboratory animals to DPM has been studied in various noninhalation models, and the results of these studies are presented in Table 5-9. Takafuji et al. (1987) evaluated the IgE antibody response of mice inoculated intranasally at intervals of 3 weeks with either 0.5 or 25 μg of DPM in ovalbumin per mouse. Antiovalbumin IgE antibody titers, assayed by passive cutaneous anaphylaxis, were enhanced by doses as low as 1 μg of particles compared with immunization with ovalbumin alone.

Muranaka et al. (1986) studied the effects of DPM on IgE antibody production in immunized mice. A greater IgE antibody response was noted in mice immunized by ip injection of ovalbumin (OA) mixed with DPM, either 0.02, 0.2, or 2mg per mouse, than in animals immunized with OA alone. This effect of DPM on IgE antibody production in mice was also demonstrated in mice immunized with repeated injections of dinitrophenylated-OA. Moreover, a persistent IgE-antibody response to Japanese cedar pollen (JCPA), a common pollen allergen causing allergic rhinitis in Japan, was observed in mice immunized with JCPA mixed with DPM but not in animals immunized with JCPA alone. The results suggest an association between the adjuvant activity of DPM and allergic rhinitis caused by JCPA.

Takano et al. (1997) designed a study to evaluate the effects of DPM on the manifestations of allergic asthma in mice, with emphasis on antigen-induced airway inflammation; the local expression of IL-5, GM-CSF, IL-2, and IFN-γ; and the production of antigen-specific IgE and IgG. Male ICR mice were intratracheally instilled with ovalbumin (OVA), DPM, and DPM+OVA. DPM was obtained from a 4JB1-type, light-duty 2.74 L, four-cylinder Isuzu diesel engine operated at a steady speed of 1,500 rpm under a load of 10 torque (kg/m). The OVA-group mice were instilled with 1 μg OVA at 3 and 6 weeks. The mice receiving DPM alone were instilled with 100 μg DPM weekly for 6 weeks. The OVA + DPM group received the combined treatment in the same protocol as the OVA and the DPM groups, respectively. Additional groups were exposed for 9 weeks. DPM aggravated OVA-induced airway inflammation, characterized by infiltration of eosinophils and lymphocytes and an

Table 5-9. Effects of diesel particulate matter on the immune response of laboratory animals

Model	Treatment	Effects	Reference
Mouse, BDFI, F		Intranasally delivered doses of DPM as low as 1 mg exerted an adjuvant activity for IgE antibody production.	Takafuji et al. (1987)
Mouse, ICR, w/w, M	Intratracheal instillation of DPM, once/week for 16 weeks	Infiltration of inflammatory cells, proliferation of goblet cells, increased mucus secretion, respiratory resistance, and airway constriction. Increased eosinophils in the submucosa of the proximal bronchi and medium bronchioles. Eosinophil infiltration suppressed by pretreatment with PEG-SOD. Bound sialic acid, an index of mucus secretion, in bronchial alveolar lavage fluids increased, but was suppressed by PEG-SOD. Increased respiratory resistance suppressed by PEG-SOD. Oxygen radicals produced by instilled DPM may cause features characteristic of bronchial asthma in mice.	Sagai et al. (1996)
Mouse, A/J, M	Mice immunized intranasally with Der f II + pyrene, or Der f II + DPM 7 times at 2-week intervals	IgE antibody responses to Der f II enhanced in mice immunized with Der f II+ pyrene or Der f II + DPM compared with Der f II alone. Response was dose related. DPM and pyrene contained in DPM have adjuvant activity on IgE and IgG1 antibody production in mice immunized with house dust mite allergen.	Suzuki et al. (1996)
Mouse, BDF_1, M	Mice were administered 25 mg of each of 5 fine particles (Kanto loam dust, fly ash, CB, DPM, and aluminum hydroxide [alum]) intranasally and exposed to aerosolized Japanese cedar pollen allergens (JCPA) for intervals up to 18 wk	Measurements were made of JCPA-specific IgE and IgG antibody titers, the protein-adsorbing capacity of each type of particle, and nasal rubbing movements (a parameter of allergic rhinitis in mice). The increases in anti-JPCA IgE and IgG antibody titers were significantly greater in mice treated with particles and aerosolized JCPA than in mice treated with aerosolized JCPA alone. In a subsequent experiment, the mice received the particles as before, but about 160,000 grains of Japanese cedar pollen (JCP) were dropped onto the tip of the nose of each mouse twice a week for 16 wk. After 18 wk there were no significant differences in the anti-JCPA IgE and IgG production, nasal rubbing, or histopathological changes. The workers concluded that the nature of the particle, the ability of the particle to absorb antigens, and/or particle size is not related to the enhancement of IgE antibody production or symptoms of allergic rhinitis. However, IgE antibody production did appear to occur earlier in mice treated with particles than in mice immunized with allergens alone.	Maejima et al. (1997)
Mouse, BALB/C, nu/nu, F	Inoculated OA with DPM or CB into hind footpad measured response using popliteal lymph node assay	Increased response (increased weight, cell numbers, cell proliferation) and longer response observed with DPM and OA, compared to DPM or OA alone. Response was specific and not an unspecific inflammatory response. CB was slightly less potent than DPM. Nonextractable carbon core contributes substantially to adjuvant activity of DPM.	Løvik et al. (1997)
Mouse, BALB/cA, F	Intranasal administration of DPM. Mice immunized with OA or OA combined with DPM or CB	Increased response to antigen in animals receiving DPM or CB. Increased number of responding animals and increased serum anti OA IgE antibody. Both DPM and CB have adjuvant activity for IgE production. DPM response more pronounced than CB, indicating both organic matter adsorbed to DPM and the nonextractable carbon core responsible for adjuvant activity.	Nilsen et al. (1997)
Mouse, ICR, M	Intratracheal instillation of OA, DPM, or OVA and DPM combined, once/week for 6 wk	Respiratory resistance (Rrs) measured 24 h after the final instillation. Rrs after acetylcholine challenge was significantly greater in the mice treated with OVA and DPM than other treatments. DPM can enhance airway responsiveness associated with allergen exposure.	Takano et al. (1998b)

OA - Ovalbumin.
DPM - Diesel particulate matter.
CB - Carbon black.

PEG-SOD - Polyethyleneglycol-conjugated superoxide dismutase.
IL-4 - Interleukin-4.
IL-5 - Interleukin-5.
IL-10 - Interleukin-10.
IFN - Interferon-g.
GM-CSF -Granulocyte-colony stimulating factor.
IP - Intraperitoneally.

increase in goblet cells in the bronchial epithelium. DPM in combination with antigen markedly increased IL-5 protein levels in lung tissue and bronchoalveolar lavage supernatants compared with either antigen or DPM alone. The combination of DPM and antigen induced significant increases in local expression of IL-4, GM-CSF, and IL-2, whereas expression of IFN-γ was not affected. In addition, DPM exhibited adjuvant activity for the antigen-specific production of IgG and IgE.

The potential role of oxygen radicals in injury caused by DPM was investigated by Sagai et al. (1996). These workers reported that repeated intratracheal instillation of DPM (either 0.1 or 0.2 mg per mouse, once/week for 16 weeks) in mice caused marked infiltration of inflammatory cells, proliferation of goblet cells, increased mucus secretion, respiratory resistance, and airway constriction. Eosinophils in the submucosa of the proximal bronchi and medium bronchioles increased eightfold following instillation. Eosinophil infiltration was significantly suppressed by pretreatment with polyethyleneglycol-conjugated superoxide dismutase (PEG-SOD), an inhibitor of oxygen radicals. Bound sialic acid concentrations in bronchial alveolar lavage fluids, an index of mucus secretion, increased with DPM, but were also suppressed by pretreatment with PEG-SOD. Goblet cell hyperplasia, airway narrowing, and airway constriction also were observed with DPM.

Respiratory resistance to acetylcholine in the DPM group was 11 times higher than in controls, and the increased resistance was significantly suppressed by PEG-SOD pretreatment. These findings indicate that oxygen radicals caused by intratracheally instilled DPM elicit responses characteristic of bronchial asthma.

Potential adjuvant effects of DPM on the response to the model allergen OA were investigated in BALB/c mice using the popliteal lymph node (PLN) assay (Løvik et al., 1997). DPM inoculated together with OA into one hind footpad (0.02 mL of a 5 mg/mL DPM suspension) gave a significantly augmented response (increase in weight, cell numbers, and cell proliferation) in the draining popliteal lymph node as compared to DPM or OA alone. The duration of the local lymph node response was also longer when DPM was given with the allergen. The lymph node response appeared to be of a specific immunologic character and not an unspecific inflammatory reaction. The OA-specific response IgE was increased in mice receiving OA together with DPM as compared with the response in mice receiving OA alone. Further studies using carbon black (CB) as a surrogate for the nonextractable core of DPM found that while CB resembled DPM in its capacity to increase the local lymph node response and serum-specific IgE response to OA, CB appeared to be slightly less potent than DPM. The results indicate that the nonextractable particle core contributes substantially to the adjuvant activity of DPM.

Nilsen et al. (1997) investigated which part of the particle was responsible, the carbon core and/or the adsorbed organic substances, for the adjuvant activity of DPM. Female

BALB/cA mice were immunized with OA alone or in combination with DPM or CB particles by intranasal administration a total of four times, once weekly, at 25 μg/inoculation. There was an increased response to the antigen in animals receiving OA together with DPM or CB, compared with animals receiving OA alone. The response was seen as both an increased number of responding animals and increased serum anti OA IgE response. The workers concluded that both DPM and CB have an adjuvant activity for specific IgE production, but that the activity of DPM may be more pronounced than that of CB. The results suggest that both the organic matter adsorbed to DPM and the nonextractable carbon are responsible for the observed adjuvant effect of DPM.

The effects of DPM and its components (extracted particles and particle extracts) on the release of proinflammatory cytokines, interleukin-1 (IL-1), and tumor necrosis factor-α (TNF-α) by alveolar macrophages (AMs) were investigated by Yang et al. (1997). Rat AMs were incubated with 0, 5, 10, 20, 50, or 100 μg/10^6 AM/mL of DPM, methanol-extracted DPM, or equivalent concentrations of DPM at 37 °C for 24 h. At high concentrations, both DPM and DPM extracts were shown to increase IL-1-like activity secreted by AMs, whereas extracted particles had no effect. Neither particles, particle extracts, or extracted particles stimulated secretion of TNF-α. DPM inhibited lipid polysaccharide (LPS)-stimulated production of IL-1 and TNF-α. In contrast, interferon (IFN)-γ-stimulated production of TNF-α was not affected by DPM. Results of this study indicate that the organic fraction of exhaust particles is responsible for the effects noted. Stimulation of IL-1 but not TNF-α suggests that IL-1, but not TNF-α, may play an important role in the development of DPM-induced inflammatory and immune responses. The cellular mechanism involved in inhibiting increased release of IL-1 and TNF-α by LPS is unknown, but may be a contributing factor to the decreased AM phagocytic activity and increased susceptibility to pulmonary infection after prolonged exposure to DPM.

Fujimaki et al. (1994) investigated the relationship between DPM and IgE antibody production, interleukin 4 (IL-4) production in BALB/c mice treated with DPM mixed with antigen OA or JCP antigen by intratracheal instillation. BALB/c mice were injected with DPM (300 μg) plus OA or OA alone and, after the last instillation, the proliferative response and lymphokine production by mediastinal lymph node cells (LNC) were examined in vitro. The proliferative response to OA in mediastinal LNC from mice injected with DPM plus OA was enhanced to 4-17 times that of control mice. IL-4 production by OA stimulation was also enhanced in mediastinal LNC from mice injected with DPM plus OA. A significantly larger amount of anti-OA IgE antibody was detected in sera from DPM- and OA-injected mice compared with those from control mice. The levels of IL-4, estimated by JCP antigen in mediastinal LNC, from mice injected with DPM plus JCP antigen were twofold higher than those from mice injected with JCP antigen alone. These results suggest that intratracheal

instillation of DPM affects antigen-specific IgE antibody responses via local T-cell activation, especially enhanced IL-4 production.

Suzuki et al. (1993) investigated the adjuvant activity of pyrene, one of many PAHs contained in DPM, on IgE antibody production in mice. In the first experiment, mice were immunized with 1 mg of OA alone, 1 mg of OA plus 1 mg of pyrene, or 1 mg of OA plus 1 mg of DPM, respectively. The IgE antibody responses to OA in mice immunized with OA plus pyrene or OA plus DPM were enhanced as compared to those in mice immunized with OA alone; the highest responses were observed in mice immunized with OA plus DPM. In the second experiment, mice were immunized with 10 mg of JCPA alone or 10 mg of JCPA plus 5 mg of pyrene. The IgE antibody responses to JCPA in mice immunized with JCPA plus pyrene were higher than those in mice immunized with JCPA alone. The results indicate that pyrene contained in DPM acts as an adjuvant in IgE antibody production in immunized mice.

Suzuki et al. (1996) investigated the effect of pyrene on IgE and IgG1 antibody production in mice to clarify the relation between mite allergy and adjuvancy of the chemical compounds in DPM. The mite allergen was Der f II, one of the major allergens of house dust mite (*Dermatophagoides farinae*). Allergen mice were grouped and immunized with Der f II (5 μg), Der f II (5 μg) plus pyrene (200 μg), and Der f II (5 μg) plus DPM (100 μg) intranasally seven times at 2-week intervals. The separate groups of mice were also immunized with Der f II (10 μg) plus the same dose of adjuvants in the same way. The IgE antibody responses to Der f II in mice immunized with Der f II plus pyrene or Der f II plus DPM were markedly enhanced compared with those immunized with Der f II alone. The anti-Der f II IgE antibody production increased with increasing the dose of Der f II from 5 μg to 10 μg in mice immunized with Der f II plus the same dose of adjuvants. The IgG1 antibody responses to Der f II in mice immunized with Der f II (10 μg) plus pyrene (200 μg) or Der f II (10 μg) plus DPM (100 μg) were greater than those immunized with 10 μg of Der f II alone. In addition, when peritoneal macrophages obtained from normal mice were incubated with pyrene or DPM in vitro, an enhanced IL-1a production by the macrophages was observed. When spleen lymphocytes obtained from the mice immunized with Der f II (10 μg) plus DPM (100 μg) or Der f II (10 μg) plus pyrene (200 μg) were stimulated with 10 μg of Der f II in vitro, an enhanced IL-4 production of the lymphocytes was also observed compared with those immunized with Der f II alone. This study indicates that DPM and pyrene (one of the many PAHs adsorbed onto DPM) have an adjuvant activity on IgE and IgG1 antibody production in mice immunized intranasally with a house dust mite allergen.

Maejima et al. (1997) examined the potential adjuvant activity of several different fine particles. These workers administered 25 μg of each of 5 particles (Kanto loam dust, fly ash, CB, DPM, and aluminum hydroxide [alum]) intranasally in mice and exposed them to aerosolized JCPA for intervals up to 18 weeks. Measurements were made of JCPA-specific IgE

and IgG antibody titers, the protein-adsorbing capacity of each type of particle, and nasal rubbing movements (a parameter of allergic rhinitis in mice). The increases in anti-JPCA IgE and IgG antibody titers were significantly greater in mice treated with particles and plus aerosolized JCPA than in mice treated with aerosolized JCPA alone. In a subsequent experiment, the mice received the particles as before, but about 160,000 grains of JCP were dropped onto the tip of the nose of each mouse twice a week for 16 weeks. After 18 weeks there were no significant differences in the anti-JCPA IgE and IgG production, nasal rubbing, or histopathological changes. The workers concluded that the nature of the particle, the ability of the particle to absorb antigens, and particle size are not related to the enhancement of IgE antibody production or symptoms of allergic rhinitis. However, IgE antibody production did appear to occur earlier in mice treated with particles than in mice immunized with allergens alone.

The potential for DPM to modulate cytokine production has been demonstrated in cultured mouse bone marrow-derived mast cells (BMMC). Saneyoshi et al. (1997) examined the production of cytokines in BMMC treated with DPM (0.8, 2 and 4 mg/mL). Production of interleukin-4 (IL-4) and IL-6 was higher in BMMC stimulated with A23187 and treated with low concentrations of DPM than in controls, but no increase was seen in BMMC treated with high DPM. After pretreatment with low DPM for 24 h, IL-4 production in BMMC stimulated with A23187 was lower than in controls. Antigen-induced IL-4 production increased significantly in BMMC treated with 0.4 or 0.8 mg/mL DPM, but did not increase with low DPM. Although the enhancement of IL-4 production of BMMC stimulated with A23187 plus DPM was not completely inhibited by 2-mercaptoethanol, treatment with dexamethasone inhibited further IL-4 production. Thus, DPM may affect the immune response via the modulation of cytokine production in mast cells.

Ormstad et al. (1998) investigated the potential for DPM as well as other suspended particulate matter (SPM) to act as a carrier for allergens into the airways. These investigators found both Can f 1 (dog) and Bet v 1 (birch pollen) on the surface of SPM collected in air from different homes. In an extension of the study, they found that DPM adhered to polycarbonate filters had the potential of binding both of these allergens as well as Fel d 1 (cat) and Der p 1 (house mite). The authors conclude that soot particles in indoor air house dust may act as carrier of several allergens in indoor air.

Knox et al. (1997) investigated whether free grass pollen allergen molecules, released from pollen grains by osmotic shock (Suphioglu et al., 1992) and dispersed in microdroplets of water in aerosols, can bind to DPM mounted on copper grids in air. Using natural highly purified Lol p 1, immunogold labeling with specific monoclonal antibodies, and a high-voltage transmission electron-microscopic imaging technique, these workers demonstrated binding of the major grass pollen allergen, Lol p 1, to DPM in vitro. These workers conclude that binding of

DPM with Lol p 1 might be a mechanism by which allergens can become concentrated in air and trigger attacks of asthma.

Murphy et al. (1999) examined the comparative toxicities to the lung of four different-sized CB particles and DPM, in primary cultures of mouse Clara and rat type II epithelial cells. Particle toxicity was assessed by cell attachment to an extracellular matrix substratum. The CB particles varied in toxicity to Clara and type II cells. DPM stored for 2 weeks was equally toxic to both cell types. DPM became progressively less toxic to type II cells with time of storage. Both primary epithelial cell types internalized the particles in culture. These workers concluded that bioreactivity was related to CB particle size and surface area, with the smaller particles having the larger surface area being the more toxic. Although freshly prepared DPM was equally toxic to type II and Clara cells, DPM became progressively less toxic to the type II cells with time.

Exposure studies in laboratory animals and isolated cell systems derived from animals also indicate that DPM can elicit both inflammatory and immunological changes. Moreover, the effects appear to be due to both the nonextractable carbon core and the adsorbed organic fraction of the diesel particle. Changes in IgE, goblet cell hyperplasia, mast cell influx, and cytokines in various animal models and in vitro model systems are all key markers of asthma. The data further indicate a role for oxygen radicals in DPM injury because the extent of the injury can be reduced by treatment with antioxidants. DPM also has the capacity to bind and transport airborne allergens.

5.1.3.3.7. ***Effects on the liver.*** Meiss et al. (1981) examined alterations in the hepatic parenchyma of hamsters by using thin-section and freeze-fracture histological techniques. Exposures to DE were for 7 to 8 h/day, 5 days/week, for 5 mo at about 4 or 11 mg/m^3 DPM. The livers of the hamsters exposed to both concentrations of DE exhibited moderate dilatation of the sinusoids, with activation of the Kupffer cells and slight changes in the cell nuclei. Fatty deposits were observed in the sinusoids, and small fat droplets were occasionally observed in the peripheral hepatocytes. Mitochondria often had a loss of cristae and exhibited a pleomorphic character. Giant microbodies were seen in the hepatocytes, which were moderately enlarged, and gap junctions between hepatocytes exhibited a wide range in structural diversity. The results of this study and others on the effect of exposure of DE on the liver of laboratory animals are summarized in Table 5-10.

Table 5-10. Effects of exposure to diesel exhaust on the liver of laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, F344, M, F	7 h/day 5 days/week 52 weeks	2.0 0.23–0.36 µm MDD	3,640	12.7	1.6	0.83	No changes in absolute liver weight or liver/body weight ratio	Green et al. (1983)
Hamster, Syrian	7-8 h/day 5 days/week 22 weeks	4.0 8.0 11.0	3,080-9,680	12.0 19.0 25.0	0.5 1.0 1.5	3.0 6.0 7.0	Enlarged sinusoids, with activated Kupffer's cells and slight changes of nuclei; fatty deposits; mitochondria, loss of cristae and pleomorphic character; gap junctions between hepatocytes had wide range in structural diversity	Meiss et al. (1981)
Cat, inbred, M	8 h/day 7 days/week 124 weeks	6.0[a] 12.0[b]	41,664 83,328	20.2 33.3	2.7 4.4	2.1 5.0	No change in the absolute liver weight	Plopper et al. (1983)

[a]1 to 61 weeks of exposure.
[b]62 to 124 weeks of exposure.

Green et al. (1983) and Plopper et al. (1983) reported no changes in liver weights of rats exposed to 2 mg/m^3 DPM for 7 h/day, 5 days/week for 52 weeks or of cats exposed to 6 to 12 mg/m^3, 8 h/day, 7 days/week for 124 weeks. The use of light and electron microscopy revealed that long-term inhalation of varying high concentrations of DE caused numerous alterations to the hepatic parenchyma of guinea pigs. A less sensitive index of liver toxicity, increased liver weight, failed to detect an effect of DE on the liver of the rat and cat following long-term exposure to DE. These results are too limited to understand potential impacts on the liver.

5.1.3.3.8. ***Blood and cardiovascular systems.*** Several studies have evaluated the effects of DE exposure on hematological and cardiovascular parameters of laboratory animals. These studies are summarized in Table 5-11. Standard hematological indices of toxicological effects on red and white blood cells failed to detect dramatic and consistent responses. Erythrocyte (RBC) counts were reported as being unaffected in cats (Pepelko and Peirano, 1983), rats and monkeys (Lewis et al., 1989), guinea pigs and rats (Penney et al., 1981), and rats (Karagianes et al., 1981); lowered in rats (Heinrich et al., 1982); and elevated in rats (Ishinishi et al., 1988; Brightwell et al., 1986). Mean corpuscular volume was significantly increased in monkeys, 69 versus 64 (Lewis et al., 1989), and hamsters (Heinrich et al., 1982), and lowered in rats (Ishinishi et al., 1988). The only other parameters of erythrocyte status and related events were lowered mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration in1 rats (Ishinishi et al., 1988), a 3% to 5% increase in carboxyhemoglobin saturation in rats (Karagianes et al., 1981), and a suggestion of an increase in prothrombin time (Brightwell et al., 1986). The biological significance of these findings regarding adverse health effects is deemed to be inconsequential.

Three investigators (Pepelko and Peirano, 1983; Lewis et al., 1989; Brightwell et al., 1986) reported an increase in the percentage of banded neutrophils in cats and rats. This effect was not observed in monkeys (Lewis et al., 1989). The health implications of an increase in abnormal maturation of circulating neutrophils are uncertain but indicate a toxic response of leukocytes following exposures to DE. Leukocyte counts were reported to be reduced in hamsters (Heinrich et al., 1982); increased in rats (Brightwell et al., 1986); and unaffected in cats, rats, and monkeys (Pepelko and Peirano, 1983; Ishinishi et al., 1988; Lewis et al., 1989). These inconsistent findings indicate that the leukocyte counts are more indicative of the clinical status of the laboratory animals than any direct effect of exposure to DE.

No significant changes in heart mass were found in guinea pigs or rats exposed to DE (Wiester et al., 1980; Penney et al., 1981; Lewis et al., 1989). Rats exposed to DE showed a greater increase in the medial wall thickness of pulmonary arteries of differing diameters and

Table 5-11. Effects of exposure to diesel exhaust on the hematological and cardiovascular systems of laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Monkey, Cynomolgus, M	7 h/day 5 days/week 104 weeks	2 0.23–0.36 µm MDD	7,280	11.5	1.5	0.8	Increased MCV	Lewis et al. (1989)
Rat, F344, M, F	7 h/day 5 days/week 104 weeks	2 0.23–0.36 µm MDD	7,280	11.5	1.5	0.8	Increase in banded neutrophils; no effect on heart or pulmonary arteries	Lewis et al. (1989) Vallyathan et al. (1986)
Guinea Pig, Hartley, M, F	20 h/day 7 days/week 8 weeks	6.3[a] 6.8[b]	7,056 7,616	17.4 16.7	2.3 2.9	2.1 1.9	No effect on heart mass or ECG; small decrease in heart rate (IE only)	Wiester et al. (1980)
Hamster, Syrian, M, F	7-8 h/day 5 days/week 75 weeks	3.9 0.1 µm MDD	10,238-11,700	18.5	1.2	3.1	At 29 weeks, lower erythrocyte count; increased MCV; reduced leukocyte count	Heinrich et al. (1982)
Rat, F344; Guinea Pig, Hartley	20 h/day 5.5 days/week 78 weeks	0.25 0.75 1.5 0.19 µm MDD	2,145 6,435 12,870	3.0 4.8 6.9	0.11 0.27 0.49	— — —	No changes in heart mass or hematology at any exhaust level or duration of exposure in either species	Penney et al. (1981)
Rat, Wistar, M	6 h/day 5 days/week 78 weeks	8.3 0.71 µm MDD	19,422	50.0	4-6	—	3% increase in COHb	Karagianes et al. (1981)
Rat, F3444/Jcl, M, F	16 h/day 6 days/week 130 weeks	0.11[c] 0.41[c] 1.08[c] 2.31[c] 3.72[d] 0.1 µm MDD	1,373 5,117 13,478 28,829 46,426	1.23 2.12 3.96 7.10 12.9	0.08 0.26 0.70 1.41 3.00	0.38 1.06 2.42 4.70 4.57	At higher concentrations, RBC, Hb, Hct slightly elevated; MCV and mean corpuscular hemoglobin and concentration were lowered	Ishinishi et al. (1988)
Rat, F344	16 h/day 5 days/week 104 weeks	0.7 2.2 6.6	5,824 18,304 54,912	— — 32.0	— — —	— — —	Increases in RBC, Hb, Hct, and WBC, primarily banded neutrophils; suggestion of an increase in prothrombin time; increased heart/body weight and right ventricular/heart ratios and decreased left ventricular contractility in 6.6 mg/m^3 group	Brightwell et al. (1986)
Cat, Inbred, M	8 h/day 7 days/week 124 weeks	6.0[e] 12.0[f]	41,664 83,328	20.2 33.3	2.7 4.4	2.1 5.0	Increases in banded neutrophils; significant at 12 mo, but not 24 mo	Pepelko and Peirano (1983)

[a]Nonirradiated DE.
[b]Irradiated DE.
[c]Light-duty engine.
[d]Heavy-duty engine.
[e]1 to 61 weeks of exposure.
[f]62 to 124 weeks of exposure.

Key: MCV = Mean corpuscular volume.

right ventricular wall thickness; these increases, however, did not achieve statistically significant levels (Vallyathan et al., 1986). Brightwell et al. (1986) reported increased heart/body weight and right ventricular/heart weight ratios and decreased left ventricular contractility in rats exposed to 6.6 mg/m^3 DPM for 16 h/day, 5 days/week for 104 weeks.

The effects of DPM on the endothelium-dependent relaxation (EDR) of vascular smooth muscle cells have been investigated (Ikeda et al., 1995, 1998). Incubation of rat thoracic aortae with suspensions of DPM (10-100 μg/mL) markedly attenuated acetylcholine-induced EDR. The mechanism of this effect was studied further in cultured porcine endothelial cells (CPE). A 10-min incubation of CPE with DPM (0.1-100 μg/mL) inhibited endothelium-dependent relaxing factor (EDRF) or nitric oxide (NO) release. A 10-min incubation of DPM with NO synthase inhibited formation of NO_2^-, a product of NO metabolism. The authors concluded that DPM, at the concentrations tested, neither induced cell damage nor inhibited EDRF release from CPE, but scavenged and thereby blocked the physiological action of NO.

5.1.3.3.9. ***Serum chemistry.*** A number of investigators have studied the effects of exposure to DE on serum biochemistry, and no consistent effects have been found. Such studies are summarized in Table 5-12.

The biological significance of changes in serum chemistry reported by Lewis et al. (1989) in female but not male rats exposed at 2 mg/m^3 DPM for 7 h/day, 5 days/week for 104 weeks is difficult to interpret. Not only were the effects noted in one sex (females) only, but the serum enzymes, lactate dehydrogenase (LDH), serum glutamic-oxaloacetic transaminase (SGOT), and serum glutamic-pyruvic transaminase (SGPT), were elevated in the control group, a circumstance contrary to denoting organ damage in the exposed female rats. The elevations of liver-related serum enzymes in the control versus the exposed female rats appear to be a random event among these aged subjects. The incidence of age-related disease, such as mononuclear cell leukemia, can markedly affect such enzyme levels, seriously compromising the usefulness of a comparison to historical controls. The serum sodium values of 144 versus 148 mmol/L in control and exposed rats, respectively, although statistically different, would have no biological significance.

The increased serum enzyme activities, alkaline phosphatase, SGOT, SGPT, gamma-glutamyl transpeptidase, and decreased cholinesterase activity suggest an impaired liver; however, such an impairment was not established histopathologically (Heinrich et al., 1982; Ishinishi et al., 1988; Brightwell et al., 1986). The increased urea nitrogen, electrolyte levels, and gamma globulin concentration and reduction in total blood proteins are indicative of impaired kidney function. Again, there was no histopathological confirmation of impaired kidneys in these studies.

Table 5-12. Effects of chronic exposures to diesel exhaust on serum chemistry of laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, F344, M, F	7 h/day 5 days/week 104 weeks	2.0 0.23 0.36 µm MDD	7,280	11.5	1.5	0.8	Decreased phosphate, LDH, SGOT, and SGPT; increased sodium in females but not males	Lewis et al. (1989)
Hamster, Syrian, M, F	7-8 h/day 5 days/week 75 weeks	3.9 0.1 µm MDD	10,238-11,700	18.5	1.2	3.1	After 29 weeks, increases in SGOT, LDH, alkaline phosphatase, gamma-glutamyl transferase, and BUN	Heinrich et al. (1982)
Rat, F344/JcL, M, F	16 h/day 6 days/week 130 weeks	0.11[a] 0.41[a] 1.08[a] 2.31[a] 3.72[b] 0.19–0.28 µm MDD	1,373 5,117 13,478 28,829 46,426	1.23 2.12 3.96 7.10 12.9	0.08 0.26 3.96 7.10 3.00	0.38 1.06 2.42 4.70 4.57	Lower cholinesterase activity in males in both the light-and heavy-duty series and elevated gamma globulin and electrolyte levels in males and females in both series	Research Committee for HERP Studies (1988)
Rat, F344; Hamster, Syrian	16 h/day 5 days/week 104 weeks	0.7 2.2 6.6	5,824 18,304 54,912	— — 32.0	— — —	— — —	Rats, 6.6 mg/m^3, reduction in blood glucose, blood proteins, triglycerides, and cholesterol; increase in BUN, alkaline phosphate alamine, and aspartate aminotransferases (SGPT and SGOT); hamsters, 6.6 mg/m^3, decrease in potassium, LDH, aspartate amino-transferase; increase in albumin and gamma-glutamyl transferase	Brightwell et al. (1986)
Cat inbred, M	8 h/day 7 days/week 124 weeks	6.0[c] 12.0[d]	41,664 83,328	20.2 33.3	2.7 4.4	2.1 5.0	BUN unaltered; SGOT and SGPT unaffected; LHD increase after 1 year of exposure	Pepelko and Peirano (1983)

[a]Light-duty engine.
[b]Heavy-duty engine.
[c]1 to 61 weeks of exposure.
[d]62 to 124 weeks of exposure.

Key:
LDH = Lactate dehydrogenase.
SGOT = Serum glutamic-oxaloacetic transaminase.
BUN = Blood urea nitrogen.
SGPT = Serum glutamic-pyruvic transaminase.

Clinical chemistry studies suggest impairment of both liver and kidney functions in rats and hamsters chronically exposed to high concentrations of DE. The absence of histopathological confirmation, the appearance of such effects near the end of the lifespan of the laboratory animal, and the failure to find such biochemical changes in cats exposed to a higher dose, however, tend to discredit the probability of hepatic and renal hazards to humans exposed at atmospheric levels of DE.

5.1.3.3.10. ***Effects on microsomal enzymes.*** Several studies have examined the effects of DE exposure on microsomal enzymes associated with the metabolism and possible activation of xenobiotics, especially polynuclear aromatic hydrocarbons (PAH). These studies are summarized in Table 5-13. Lee et al. (1980) measured the activities of aryl hydrocarbon hydroxylase (AHH) and epoxide hydrase (EH) in liver, lung, testis, and prostate gland of adult male rats exposed to 6.32 mg/m^3 DPM 20 h/day for 42 days. Maximal significant AHH activities (pmol/min/mg microsomal protein) occurred at different times during the exposure period, and differences between controls and exposed rats, respectively, were as follows: prostate 0.29 versus 1.31, lung 3.67 versus 5.11, and liver 113.9 versus 164.0. There was no difference in AHH activity in the testis between exposed and control rats. Epoxide hydrase activity was not significantly different from control values for any of the organs tested.

Pepelko and Peirano (1983) found no statistically significant differences in liver microsomal cytochrome P448-450 levels and liver microsomal AHH between control and diesel-exposed mice at either 6 or 8 mo of exposure. Small differences were noted in the lung microsomal AHH activities, but these were believed to be artifactual differences, due to increases in nonmicrosomal lung protein present in the microsomal preparations. Exposures to 6 mg/m^3 DPM were for 8 h/day, 7 days/week.

Rabovsky et al. (1984) investigated the effect of chronic exposure to DE on microsomal cytochrome P450-associated benzo[*a*]pyrene (B[*a*]P) hydroxylase and 7-ethoxycoumarin deethylase activities in rat lung and liver. Male rats were exposed for 7 h/day, 5 days/week for 104 weeks to 2 mg/m^3 DPM. The exposure had no effect on B[*a*]P hydroxylase or 7-ethoxycoumarin deethylase activities in lung or liver. In related studies, Rabovsky et al. (1986) examined the effects of DE on viral induced enzyme activity and interferon production in female mice. The mice were exposed for 7 h/day, 5 days/week for 1 mo to DE diluted to achieve a concentration of 2 mg/m^3 DPM. After the exposure, the mice were inoculated intranasally with influenza virus. Changes in serum levels of interferon and liver microsomal activities of 7-ethoxycoumarin, ethylmorphine demethylase, and nicotinamide adenine dinucleotide phosphate

Table 5-13. Effects of chronic exposures to diesel exhaust on microsomal enzymes of laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × t ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, F344, M	—	—	—	—	—	—	Intratracheal administration of DPM extract required doses greater than 6 mg/m^3 before the lung AHH was barely doubled; liver AHH activity was unchanged	Chen (1986)
Mouse, CD-1, F	7 h/day 5 days/week 4 weeks	2.0 0.2–0.36 µm mdd	280	11.5	1.5	0.8	Mice inoculated intranasally with influenza virus had smaller increases in ethylmorphine demethylase activity on days 2 to 4 postvirus infection and abolition of day 4 postinfection increase in NADPH-dependent cytochrome c reductase	Rabovsky et al. (1986)
Rat, Sprague-Dawley, M	20 h/day 7 days/week 1-7 weeks	6.3	882-6,174	17.4	2.3	2.1	AHH induction occurred in lung, liver, and prostate gland but not in testes; maximum significant activities occurred at different times; liver has greatest overall activity, percent increase highest in prostate; expoxide hydrase activity was unaffected	Lee et al. (1980)
Rat, F344, M	20 h/day 5.5 days/week 4, 13, 26, or 39 weeks	0.75 1.5 0.19 µm mdd	330-6,435	4.8 7.5	— —	— —	Inhalation exposure had no significant effect on liver AHH activity; lung AHH activity was slightly reduced after 6-mo exposure to 1.5 mg/m^3 DPM; an ip dose of dp extract, estimated to be equivalent to inhalation exposure, had no effect on AHH activity in liver and lungs; cyt. P-50 was unchanged in lungs and liver following inhalation or ip administration	Chen and Vostal (1981)
	20 h/day 5.5 days/week 4, 13, 26, or 39 weeks	0.75 1.5 0.19 µm mdd	330-6,435	4.8 7.5	— —	— —		
Rat, F344, F	7 h/day 5 days/week 12, 26, or 104 weeks	2.0 0.23-0.36 µm mdd	840-7,280	11.5	1.5	0.8	No effect on B[*a*]p hydrolase or 7-exthoxycoumarin deethylase activities in the liver	Rabovsky et al. (1984)
Rat, F344, M	20 h/day 5.5 days/week 8-53 weeks	0.25 1.5 0.19 µm mdd	220-8,745	2.9 7.5	— —	— —	After 8 weeks, no induction of cyt. P-450, cyt. P-448, or NADPH-dependent cyt. c reductase; after 1 year of exposure, liver microsomal oxidation of B[*a*]p was not increased; 1 year of exposure to either 0.25 or 1.5 mg/m^3 DPM impaired lung microsomal metabolism of B[*a*]p	Navarro et al. (1981)
Mouse, A/J, M	8 days/week 7 days/week 26 or 35 weeks	6.0	17.4	17.4	2.3	2.1	No differences in lung and liver AHH activities and liver P-448, P-450 levels	Pepelko and Peirano (1983)

AHH = aryl hydrocarbon hydroxylase.
B[*a*]p = benzo[*a*]pyrene.

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(NADPH)-dependent cytochrome c reductase were measured. In the absence of viral inoculation, exposure to DE had no significant effects on the activity levels of the two liver microsomal monooxygenases and NADPH-dependent cytochrome c reductase. Exposure to DE produced smaller increases in ethylmorphine demethylase activity on days 2 to 4 postvirus infection and also abolished the day 4 postinfection increase in NADPH-dependent cytochrome c reductase when compared with nonexposed mice. These data suggested to the authors that the relationship that exists between metabolic detoxification and resistance to infection in unexposed mice was altered during a short-term exposure to DE.

Chen and Vostal (1981) measured the activity of AHH and the content of cytochrome P450 in the lungs and livers of rats exposed by inhalation of DE or intraperitoneal (i.p.) injection of a dichloromethane extract of DPM. In the inhalation exposures, the exhaust was diluted to achieve concentrations of 0.75 or 1.5 mg/m^3 DPM, and the exposure regimen was 20 h/day, 5.5 days/week for up to 9 mo. The concentration of total hydrocarbons and particle-phase hydrocarbons was not reported. Parenteral administration involved repeated injections at several dose levels for 4 days. Inhalation exposure had no significant effect on liver microsomal AHH activity; however, lung AHH activity was slightly reduced after 6 mo exposure to 1.5 mg/m^3. An i.p. dose of DPM extract, estimated to be equivalent to the inhalation exposure, had no effect on AHH activity in liver or lungs. No changes were observed in cytochrome P450 contents in lungs or liver following inhalation exposure or i.p. treatment. Direct intratracheal administration of a dichloromethane DPM extract required doses greater than 6 mg/kg body weight before the activity of induced AHH in the lung was barely doubled; liver AHH activity remained unchanged (Chen, 1986).

In related studies, Navarro et al. (1981) evaluated the effect of exposure to DE on rat hepatic and pulmonary microsomal enzyme activities. The same exposure regimen was employed (20 h/day, 5.5 days/week, for up to 1 year), and the exhaust was diluted to achieve concentrations of 0.25 and 1.5 mg/m^3 DPM (a few studies were also conducted at 0.75 mg/m^3). After 8 weeks of exposure, there was no evidence for the induction of cytochrome P450, cytochrome P448, or NADPH-dependent cytochrome c reductase in rat liver microsomes. One year of exposure had little, if any, effect on the hepatic metabolism of B[*a*]P. However, 1 year of exposure to 0.25 and 1.5 mg/m^3 significantly impaired the ability of lung microsomes to metabolize B[*a*]P (0.15 and 0.02 nmole/30 min/mg protein, respectively, versus 0.32 nmole/30 min/mg protein for the controls).

There are conflicting results regarding the induction of microsomal AHH activities in the lungs and liver of rodents exposed to DE. One study reported induction of AHH activity in the lungs, liver, and prostate of rats exposed to DE containing 6.32 mg/m^3 DPM for 20 h/day for 42 days; however, no induction of AHH was observed in the lungs of rats and mice exposed to 6 mg/m^3 DPM for 8 h/day, 7 days/week for up to 8 mo or to 0.25 to 2 mg/m^3 for periods up to 2

years. Exposure to DE has not been shown to produce adverse effects on microsomal cytochrome P450 in the lungs or liver of rats or mice. The weight of evidence suggests that the absence of enzyme induction in the rodent lung exposed to DE is caused either by the unavailability of the adsorbed hydrocarbons or by their presence in quantities insufficient for enzyme induction.

5.1.3.3.11. ***Effects on behavior and neurophysiology***. Studies on the effects of exposure to DE on the behavior and neurophysiology of laboratory animals are summarized in Table 5-14. Laurie et al. (1978) and Laurie et al. (1980) examined behavioral alterations in adult and neonatal rats exposed to DE. Exposure for 20 h/day, 7 days/week, for 6 weeks to exhaust containing 6 mg/m^3 DPM produced a significant reduction in adult spontaneous locomotor activity (SLA) and in neonatal pivoting (Laurie et al., 1978). In a follow-up study, Laurie et al. (1980) found that shorter exposure (8 h/day) to 6 mg/m^3 DPM also resulted in a reduction of SLA in adult rats. Laurie et al. (1980) conducted additional behavioral tests on adult rats exposed during their neonatal period. For two of three exposure situations (20 h/day for 17 days postparturition, or 8 h/day for the first 28 or 42 days postparturition), significantly lower SLA was observed in the majority of the tests conducted on the adults after week 5 of measurement. When compared with control rats, adult 15-month-old rats that had been exposed as neonates (20 h/day for 17 days) also exhibited a significantly slower rate of acquisition of a bar-pressing task to obtain food. The investigators noted that the evidence was insufficient to determine whether the differences were the result of a learning deficit or due to some other cause (e.g., motivational or arousal differences).

These data are difficult to interpret in terms of health hazards to humans under ambient environmental conditions because of the high concentration of DE to which the laboratory rats were exposed. Additionally, there are no further concentration-response studies to assess at what exposure levels these observed results persist or abate. A permanent alteration in both learning ability and activity resulting from exposures early in life is a health hazard whose significance to humans should be pursued further.

Neurophysiological effects from exposure to DE were investigated in rats by Laurie and Boyes (1980, 1981). Rats were exposed to diluted DE containing 6 mg/m^3 DPM for 8 h/day, 7 days/week from birth up until 28 days of age. Somatosensory evoked potential, as elicited by a 1 mA electrical pulse to the tibial nerve in the left hind limb, and visual evoked potential, as elicited by a flash of light, were the endpoints tested. An increased pulse latency was reported for the rats exposed to DE, and this was thought to be caused by a reduction in the degree of

Table 5-14. Effects of chronic exposures to diesel exhaust on behavior and neurophysiology

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, Sprague-Dawley, M	8 h/day 7 days/week 1-4 weeks	6	336-1,344	19	2.5	1.8	Somatosensory and visual evoked potentials revealed longer pulse latencies in pups exposed neonatally	Laurie and Boyes (1980, 1981)
Rat, Sprague Dawley, F	20 h/day 7 days week 6 weeks	6	5,040	19	2.5	1.8	Reduction in adult SLA and in neonatal pivoting	Laurie et al. (1978)
Rat, Sprague-Dawley, F	8 or 20 h/day 7 days/week 3, 4, 6, or 16 weeks	6	1,008-13,440	19	2.5	1.8	Reduction in SLA in adults; neonatal exposures for 20 or 8 h/day caused reductions in SLA. Neonatal exposures for 20 h/day for 17 days resulted in a slower rate of a bar-pressing task to obtain food	Laurie et al. (1980)

SLA = Spontaneous locomotor activity.

nerve myelinization. There was no neuropathological examination, however, to confirm this supposition.

Based on the data presented, it is not possible to specify the particular neurological impairment(s) induced by the exposure to DE. Again, these results occurred following exposure to a high level of DE and no additional concentration-response studies were performed.

5.1.3.3.12. ***Effects on reproduction and development.*** Studies of the effects of exposure to DE on reproduction and development are summarized in Table 5-15. Twenty rats were exposed 8 h/day on days 6 through 15 of gestation to diluted DE containing 6 mg/m^3 DPM (Werchowski et al., 1980a,b; Pepelko and Peirano, 1983). There were no signs of maternal toxicity or decreased fertility. No skeletal or visceral teratogenic effects were observed in 20-day-old fetuses (Werchowski et al., 1980a). In a second study, 42 rabbits were exposed to 6 mg/m^3 DPM for 8 h/day on gestation days 6 through 18. No adverse effects on body weight gain or fertility were seen in the does exposed to DE. No visceral or skeletal developmental abnormalities were observed in the fetuses (Werchowski et al., 1980b).

Pepelko and Peirano (1983) evaluated the potential for DE to affect reproductive performance in mice exposed from 100 days prior to exposure throughout maturity of the F_2 generation. The mice were exposed for 8 h/day, 7 days/week to 12 mg/m^3 DPM. In general, treatment-related effects were minimal. Some differences in organ and body weights were noted, but overall fertility and survival rates were not altered by exposure to DE. The only consistent change, an increase in lung weights, was accompanied by a gross pathological diagnosis of anthracosis. These data denoted that exposure to DE at a concentration of 12 mg/m^3 did not affect reproduction. See Section 5.3, which reports a lack of effects of exposure to DE on rat lung development (Mauderly et al., 1987b).

Several studies have evaluated the effect of exposure to DE on sperm. Lewis et al. (1989) found no adverse sperm effects (sperm motility, velocity, densities, morphology, or incidence of abnormal sperm) in monkeys exposed for 7 h/day, 5 days/week for 104 weeks to 2 mg/m^3 DPM. In another study in which A/Strong mice were exposed to DE containing 6 mg/m^3 DPM for 8 h/day for 31 or 38 weeks, no significant differences were observed in sperm morphology between exposed and control mice (Pereira et al., 1981). It was noted, however, that there was a high rate of spontaneous sperm abnormalities in this strain of mice, and this may have masked any small positive effect. Quinto and De Marinis (1984) reported a statistically significant and dose-related increase in sperm abnormalities in mice injected intraperitoneally for 5 days with 50, 100, or 200 mg/kg of DPM suspended in corn oil. A significant decrease in sperm number was seen at the highest dose, but testicular weight was unaffected by the treatment.

Table 5-15. Effects of chronic exposures to diesel exhaust on reproduction and development in laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Mouse, [C57BL]/6XC3H]F_1, M	5 days	50, 100, or 200 mg/kg in corn oil; i.p. injection	—	—	—	—	Dose-related increase in sperm abnormalities; decrease in sperm number at highest dose; testicular weights unaffected	Quinto and De Marinis (1984)
Rat, Sprague-Dawley, F	8 h/day 7 days/week 1.7 weeks	6	571	20	2.7	2.1	No signs of maternal toxicity or decreased fertility; no skeletal or visceral teratogenic effects in 20-day-old fetuses	Werchowski et al. (1980a) Pepelko and Peirano (1983)
Rabbit, New Zealand Albino, F	8 h/day 7 days/week 1.9 weeks	6	638	20	2.7	2.1	No adverse effects on maternal weight gain or fertility; no skeletal or visceral teratogenic effects in the fetuses	Werchowski et al. (1980a) Pepelko and Peirano (1983)
Monkey, Cynomolgus, M	7 h/day 5 days/week 104 weeks	2	7,280	11.5	1.5	0.8	No effects on sperm motility, velocity, density, morphology, or incidence of abnormalities	Lewis et al. (1989)
Mouse, A/Strong, M	8 h/day 7 days/week 31 or 38 weeks	6	10,416-12,768	20	2.7	2.1	No effect on sperm morphology; high rate of spontaneous sperm abnormalities may have masked small effects	Pereira et al. (1981)
Mouse, CD-1, M, F	8 h/day 7 days/week 6 to 28 weeks	12	4,032-18,816	33	4.4	5.0	Overall fertility and survival rates were unaffected in the three-generation reproductive study; only consistent change noted, an increase in lung weights, was diagnosed as anthracosis	Pepelko and Peirano (1983)

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Watanabe and Oonuki (1999) investigated the effects of diesel engine exhaust on reproductive endocrine function in growing rats. The rats were exposed to whole diesel engine exhaust (5.63 mg/m^3 DPM, 4.10 ppm NO_2, and 8.10 ppm NO_x); a group was exposed to filtered exhaust without DPM, and a group was exposed to clean air. Exposures were for 3 mo beginning at birth (6 h/day for 5 days/week).

Serum levels of testosterone and estradiol were significantly higher and follicle-stimulating hormone significantly lower in animals exposed to whole DE and filtered exhaust compared to controls. Luteinizing hormone was significantly decreased in the whole-exhaust-exposed group as compared to the control and filtered groups. Sperm production and activity of testicular hyaluronidase were significantly reduced in both exhaust-exposed groups as compared to the control group. This study suggests that DE stimulates hormonal secretion of the adrenal cortex, depresses gonadotropin-releasing hormone, and inhibits spermatogenesis in rats. Because these effects were not inhibited by filtration, the gaseous phase of the exhaust appears more responsible than particulate matter for disrupting the endocrine system.

The effects of freshly generated DE particles on the reproductive system of male Fischer 344 rats were investigated by Tsukue et al. (2001). Groups (n=25) of 13-mo-old male rats were exposed to whole DE diluted to 0.33, 0.99 or 3.24 mg/m^3 (MMAD = 0.4 μm) for 8 months 12/h/d, 7 d/wk. Subsequent to this exposure, evaluation of potential reproductive effect was performed, including measurement of reproductive organ weights, sperm characteristics and number, gonadotrophins, testosterone, and inhibin. Results showed either no effect or effects with an inconsistent dose-response character that typically were not different from controls even at the highest exposure concentration.

No teratogenic, embryotoxic, fetotoxic, or female reproductive effects were observed in mice, rats, or rabbits at exposure levels up to 12 mg/m^3 DPM. Effects on sperm morphology and number were reported in hamsters and mice exposed to high doses of DPM; however, no adverse effects were observed in sperm obtained from monkeys exposed at 2 mg/m^3 for 7 h/day, 5 days/week for 104 weeks. Concentrations of 12 mg/m^3 DPM did not affect male rat reproductive fertility in the F_0 and F_1 generation breeders. Thus, exposure to DE would not appear to be a reproductive or developmental hazard.

5.2. MODE OF ACTION OF DIESEL EXHAUST-INDUCED NONCANCER EFFECTS

5.2.1. Comparison of Health Effects of Filtered and Unfiltered Diesel Exhaust

There exist a total of four chronic toxicity studies of DE, in which the experimental protocol included exposing test animals to exhaust containing no particles. Comparisons were then made between the effects caused by whole, unfiltered exhaust and those caused by the gaseous components of the exhaust. Concentrations of components of the exposure atmospheres in these four studies are given in Table 5-16.

Heinrich et al. (1982) compared the toxic effects of whole and filtered DE on hamsters and rats. Exposures were at 3.9 mg/m^3 for 7 to 8 h/day and 5 days/week. Rats exposed for 24 mo to either whole or filtered exhaust exhibited no significant changes in respiratory frequency, respiratory minute volume, compliance or resistance as measured by a whole-body plethysmography, or heart rate. In the hamsters, histological changes (adenomatous proliferations) were seen in the lungs of animals exposed to either whole or filtered exhaust; however, in all groups exposed to the whole exhaust the number of hamsters exhibiting such lesions was significantly higher than for the corresponding groups exposed to filtered exhaust or clean air. Severity of the lesions was, however, not reported.

In a second study, Heinrich et al. (1986a, see also Stöber, 1986) compared the toxic effects of whole and filtered DE on hamsters, rats, and mice. The test animals (96 per test group) were exposed to 4.24 mg DPM/m^3 for 19 h/day, 5 days/week for 120 (hamsters and mice) or 140 (rats) weeks. Body weights of hamsters were unaffected by either exposure. Body weights of rats and mice were reduced by the whole exhaust but not by the filtered exhaust. Exposure-related higher mortality rates occurred in mice after 2 years of exposure to whole exhaust. After 1 year of exposure to the whole exhaust, hamsters exhibited increased lung weights, a significant increase in airway resistance, and a nonsignificant reduction in lung compliance. For the same time period, rats exhibited increased lung weights, a significant decrease in dynamic lung compliance, and a significant increase in airway resistance. Test animals exposed to filtered exhaust did not exhibit such effects. Histopathological examination indicated that different levels of response occurred in the three species. In hamsters, filtered exhaust caused no significant histopathological effects in the lung; whole exhaust caused thickened alveolar septa, bronchioloalveolar hyperplasia, and emphysematous lesions. In mice, whole exhaust, but not filtered exhaust, caused multifocal bronchioloalveolar hyperplasia, multifocal alveolar lipoproteinosis, and multifocal interstitial fibrosis. In rats, there were no significant morphological changes in the lungs following exposure to filtered exhaust. In rats exposed to whole exhaust, there were severe inflammatory changes in the lungs, thickened alveolar septa, foci of macrophages, crystals of cholesterol, and hyperplastic and metaplastic lesions. Biochemical studies of lung lavage fluids of hamsters and mice indicated that exposure to filtered exhaust caused fewer changes than did exposure to whole exhaust. The latter produced significant increases in lactate dehydrogenase, alkaline phosphatase, glucose-6-phosphate dehydrogenase (G6PDH), total protein, protease (pH 5.1), and collagen. The filtered exhaust had a slight but nonsignificant effect on G6PDH, total protein, and collagen. Similarly, cytological studies showed that while the filtered exhaust had no effect on differential cell counts, the whole

Table 5-16. Composition of exposure atmospheres in studies comparing unfiltered and filtered diesel exhaust[a]

Species/sex	Exposure[b] period		Particles (mg/m^3)	C × t ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, Wistar, F; Hamster, Syrian	7 h/day 5 days/week 104 weeks	Uf	3.9	14,196	18.5	1.2	3.1	No effect on pulmonary function or heart rate in rats; increases in pulmonary adenomatous proliferations in hamsters, UF significantly higher than F or C	Heinrich et al. (1982)
		F	—		18.0	1.0	2.8		
		C	—		—	—	—		
Rat, F344, F	8 h/day 7 days/week 104 weeks	Uf	4.9	28,538	7.0	1.8	13.1	Body weight decrease after 6 mo in UF, 18 mo in f; lung/body rate weight rate higher in both groups at 24 mo; at 2 years, fibrosis and epithelial hyperplasia in lungs of uf; nominal lung and spleen histologic changes	Iwai et al. (1986)
		F[c]	—		—	—	—		
		C	—		—	—	—		
Rat, F344, M, F; Hamster, Syrian, M, F	16 h/day 5 days/week 104 weeks	Uf	0.7	5,824	—	—	—	Uf: elevated red and white cell counts, hematocrit and hemoglobin; increased heart/body weight and right ventricular/heart weight ratios; lower left ventricular contractility; changes in blood chemistry; obstructive and restrictive lung disease; F: no effects	Brightwell et al. (1986)
		Uf	2.2	18,304	—	—	—		
		Uf	6.6	54,912	32.0	—	—		
		F[d]	—		32.0	—	—		
		C	—		1.0	—	—		
Rat, Wistar, F; Hamster, Syrian, F; Mouse NMRI, F	19 h/day 5 days/week 120 to 140 weeks	Uf	4.24	48,336	12.5	1.5	3.1	Uf: decreased body wt in rats and mice but not hamsters; increased mortality, mice only; decreased lung compliance and increased airway resistance, rats and hamsters; species differences in lung lavage enzymes and cell counts and lung histopathology and collagen content, most pronounced in rats; F: no effect on glucose-6-phosphate dehydrogenase, total protein, and lung collagen	Heinrich et al. (1986a)
		F[d]	—	56,392	11.1	1.2	1.02		
		C	—		0.16	—	—		
Mouse, NMRI, F, C57BL/6N, F	18 h/day 5 days/week 23 mo (NMRI) 24 mo (C57BL/6N)	Uf	4.5	40,365	14.2	2.3	2.8	Uf: increased lung wet weight starting at 3 mo	Heinrich et al. (1995)
		F	0.01		14.2	2.9	2.4		
		C	0.01		0.2	0.01	0.1	F: no noncancer effects reported	

[a]Man values.
[b]UF= unfiltered whole exhaust, F = filtered exhaust, C = control.
[c]Reported to have the same component concentrations as the unfiltered, except particles were present in undetectable amounts.
[d]Concentrations reported for high concentration level only.

exhaust resulted in an increase in leukocytes (161 ± 43.3/μL versus 55.7 ± 12.8/μL in the controls), a decrease in AMs (30.0 ± 12.5 versus 51.3 ± 12.5/μL in the controls), and an increase in granulocytes (125 ± 39.7 versus 1.23 ± 1.14/μL in the controls). All values presented for this study are the mean with its standard deviation. The differences were significant for each cell type. There was also a small increase in lymphocytes (5.81 ± 4.72 versus 3.01 ± 1.23/μL in the controls).

Iwai et al. (1986) exposed rats (24 per group) to whole or filtered DE 8 h/day, 7 days/week for 24 mo. The whole exhaust was diluted to achieve a concentration of 4.9 ± 1.6 mg/m^3 DPM. Body weights in the whole exhaust group began to decrease after 6 mo and in both exposed groups began to decrease after 18 mo when compared with controls. Lung-to-body weight ratios of the rats exposed to the whole exhaust showed a significant increase (p<0.01) after 12 mo in comparison with control values. Spleen-to-body weight ratios of both exposed groups were higher than control values after 24 mo. After 6 mo of exposure to whole exhaust, DPM accumulated in AMs, and Type II cell hyperplasia was observed. After 2 years of exposure, the alveolar walls had become fibrotic with mast cell infiltration and epithelial hyperplasia. In rats exposed to filtered exhaust, after 2 years there were only minimal histologic changes in the lungs, with slight hyperplasia and stratification of bronchiolar epithelium and infiltration of atypical lymphocytic cells in the spleen.

Brightwell et al. (1986) evaluated the toxic effects of whole and filtered DE on rats and hamsters. Three exhaust dilutions were tested, producing concentrations of 0.7, 2.2, and 6.6 mg/m^3 DPM. The test animals (144 rats and 312 hamsters per exposure group) were exposed for five 16-h periods per week for 2 years. The four exposure types were gasoline, gasoline catalyst, diesel, and filtered diesel. The results presented were limited to statistically significant differences between exhaust-exposed and control animals. The inference from the discussion section of the paper was that there was a minimum of toxicity in the animals exposed to filtered DE: "It is clear from the results presented that statistically significant differences between exhaust-exposed and control animals are almost exclusively limited to animals exposed to either gasoline or unfiltered diesel exhaust." Additional results are described in Section 5.1.3.3.

Heinrich et al. (1995) exposed female NMRI and C57BL/6N mice to a DE dilution that resulted in a DPM concentration of 4.5 mg/m^3 and to the same dilution after filtering to remove the particles. This study is focused on the carcinogenic effects of DPM exposure, and inadequate information was presented to compare noncancer effects in filtered versus unfiltered exhaust.

A comparison of the toxic responses in laboratory animals exposed to whole exhaust or filtered exhaust containing no particles demonstrates across studies that when the exhaust is sufficiently diluted to limit the concentrations of gaseous irritants (NO_2 and SO_2), irritant vapors (aldehydes), CO, or other systemic toxicants, the diesel particles are the prime etiologic agents

of noncancer health effects, although additivity or synergism with the gases cannot be ruled out. These toxic responses are both functional and pathological and represent cascading sequelae of lung pathology based on concentration and species. The diesel particles plus gas exposures produced biochemical and cytological changes in the lung that are much more prominent than those evoked by the gas phase alone. Such marked differences between whole and filtered DE are also evident from general toxicological indices, such as decreases in body weight and increases in lung weights, pulmonary function measurements, and pulmonary histopathology (e.g., proliferative changes in Type II cells and respiratory bronchiolar epithelium, fibrosis). Hamsters, under equivalent exposure regimens, have lower levels of retained DPM in their lungs than rats and mice do and, consequently, less pulmonary function impairment and pulmonary pathology. These differences may result from lower DPM inspiration and deposition during exposure, greater DPM clearance, or lung tissue less susceptible to the cytotoxicity of deposited DPM.

5.2.2. Mode of Action for the Noncarcinogenic Effects of DPM

As noted in Chapter 2, diesel emissions are a complex mixture that includes both a vapor phase and a particle phase. The particle phase consists of poorly soluble carbon particles on the surfaces of which are adsorbed a large number of organic and inorganic compounds. Although the effects to be discussed are considered attributable to the particle phase (termed diesel particulate matter or DPM), additive or synergistic effects due to the vapor phase cannot be totally discounted. This may be especially so in the human studies and the animal toxicology studies where exposure is to various dilutions of diesel emissions, or in the in vitro studies in which the test material was captured by filtration.

The mechanisms by which DPM is inhaled, deposited, and cleared from the respiratory tract are discussed in Chapter 3. DPM deposited upon airway surfaces may be cleared from the respiratory tract completely, or may be translocated to other sites within the respiratory system. In rats, the pathogenic sequence following the deposition of inhaled DPM begins with the interaction of DPM with airway epithelial cells and phagocytosis by AMs. The airway epithelial cells and activated AMs release chemotactic factors that attract neutrophils and additional AMs. As the lung burden of DPM increases, there is an aggregation of particle-laden AMs in alveoli adjacent to terminal bronchioles, increases in the number of Type II cells lining particle-laden alveoli, and the presence of particles within alveolar and peribronchial interstitial tissues and associated lymph nodes.

The macrophages engulfing the DPM may release cytokines, growth factors, and proteases, which may cause inflammation, cell injury, cell proliferation, hyperplasia, and fibrosis. This is especially true under lung overload conditions occurring in laboratory rats when the rate of deposition exceeds the rate of alveolar clearance. This phenomenon is described in

Chapter 3. The mechanisms leading to the generation of oxygen radicals and subsequent lung injury are described in Chapter 7, Section 7.4.3.

DPM is a poorly soluble particle whose rate of clearance by dissolution is likely insignificant compared to its rate of clearance as an intact particle. The organic material adsorbed to the surface is desorbed from the DPM and may enter into metabolic reactions and be activated and enter into reactions with other macromolecules or be detoxified and excreted (Figure 7-1). The diesel particle may be cleared directly by the clearance mechanisms described in Chapter 3.

The organic material desorbed from the particle (described in Chapter 7, Section 7.4.7) appears to be associated with the immunological changes described above. The potential adjuvant effects of DPM have also been studied. The results indicate that the nonextractable particle core and the organic matter adsorbed to the core both contribute to the adjuvant activity of DPM. Further, it is possible that any of the plethora of compounds present in the organic fraction of DPM, including various PAH, may elicit this response.

Thus, the available evidence indicates that DPM has the potential to produce pathological and immunological changes in the respiratory tract. Moreover, the magnitude of these responses is determined by the dose delivered to the respiratory tract and is attributable to both the carbon core and the adsorbed organic materials.

5.3. INTERACTIVE EFFECTS OF DIESEL EXHAUST

A multitude of factors may influence the susceptibility to exposure to DE as well as the resulting response. Some of these have already been discussed in detail (e.g., the composition of DE and concentration-response data); others will be addressed in this section (e.g., the interaction of DE with factors particular to the exposed individual and the interaction of DE components with other airborne contaminants).

In a study discussed already in this chapter, Mauderly et al. (1990a) compared the susceptibility of normal rats and rats with preexisting laboratory-induced pulmonary emphysema exposed for 7 h/day, 5 days/week for 24 mo to DE containing 3.5 mg/m^3 DPM or to clean air (controls). Emphysema was induced in one-half of the rats by intratracheal instillation of elastase 6 weeks before exhaust exposure. Measurements included lung burdens of DPM, respiratory function, bronchoalveolar lavage, clearance of radiolabeled particles, pulmonary immune responses, lung collagen, excised lung weight and volume, histopathology, and mean linear intercept of terminal air spaces. None of the data for the 63 parameters measured suggest that rats with emphysematous lungs were more susceptible than rats with normal lungs to the effects of DE exposure. In fact, each of the 14 emphysema-exhaust interactions detected by statistical analysis of variance indicated that emphysema acted to reduce the effects of DE exposure. DPM accumulated much less rapidly in the lungs of emphysematous rats than in those

of normal rats. The mean lung burdens of DPM in the emphysematous rats were 39%, 36%, and 37% of the lung burdens of normal rats at 12, 18, and 24 mo, respectively. No significant interactions were observed among lung morphometric parameters. Emphysema prevented the exhaust-induced increase for three respiratory indices of expiratory flow rate at low lung volumes, reduced the exhaust-induced increase in nine lavage fluid indicators of lung damage, prevented the expression of an exhaust-induced increase in lung collagen, and reduced the exhaust-induced delay in DPM clearance.

Mauderly et al. (1987b) evaluated the relative susceptibility of developing and adult rat lungs to damage by exposure to DE. Rats (48 per test group) were exposed to DE containing 3.5 mg/m^3 DPM and about 0.8 ppm NO_2. Exposures were for 7 h/day, 5 days/week through gestation to the age of 6 mo, or from the age of 6 to 12 mo. Comparative studies were conducted on respiratory function, immune response, lung clearance, airway fluid enzymes, protein and cytology, lung tissue collagen, and proteinases in both age groups. After the 6-mo exposure, adult rats, compared with controls, exhibited (1) more focal aggregates of particle-containing AMs in the alveolar ducts near the terminal bronchioles, (2) a sixfold increase in the neutrophils (as a percentage of total leukocytes) in the airway fluids, (3) a significantly higher number of total lymphoid cells in the pulmonary lymph nodes, (4) delayed clearance of DPM and radiolabeled particles ($t_{1/2}$ = 90 days versus 47 days for controls), and (5) increased lung weights. These effects were not seen in the developing rats. On a weight-for-weight (milligrams of DPM per gram of lung) basis, DPM accumulation in the lungs was similar in developing and adult rats immediately after the exposure. During the 6-mo postexposure period, DPM clearance was much more rapid in the developing rats, approximately 2.5-fold. During postexposure, diesel particle-laden macrophages became aggregated in the developing rats, but these aggregations were located primarily in a subpleural position. The authors concluded that exposure to DE, using pulmonary function, structural (qualitative or quantitative) biochemistry as the indices, did not affect the developing rat lung more severely than the adult rat lung.

As a result of the increasing trend of using diesel-powered equipment in coal mining operations and the concern for adverse health effects in coal miners exposed to both coal dust or coal mine dust and DE, Lewis et al. (1989) and Karagianes et al. (1981) investigated the interaction of coal dust and DE. Lewis et al. (1989) exposed rats, mice, and cynomolgus monkeys to (1) filtered ambient air, (2) 2 mg/m^3 DPM, (3) 2 mg/m^3 respirable coal dust, and (4) 1 mg/m^3 of both DPM and respirable coal dust. Gaseous and vapor concentrations were identical in both DE exposures. Exposures were for 7 h/day, 5 days/week for up to 24 mo. Synergistic effects between DE and coal dust were not demonstrated; additive toxic effects were the predominant effects noted.

Karagianes et al. (1981) exposed rats (24 per group) to DE containing 8.3 mg/m^3 of DPM alone or in combination with about 6 mg/m^3 of coal dust. No synergistic effects were found

between DE and coal dust; additive effects in terms of visual dust burdens in necropsied lungs were related to dose (i.e., length of exposure and airborne particulate concentrations).

The health effects of airborne contaminants from sources other than diesel engines may be altered in the presence of DPM by their adsorption onto the diesel particles. When adsorbed onto diesel particles, the gases and vapors can be transported and deposited deeper into the lungs, and because they are more concentrated on the particle surface, the resultant cytotoxic effects or physiological responses may be enhanced. Nitrogen dioxide adsorbed onto carbon particles caused pulmonary parenchymal lesions in mice, whereas NO_2 alone produced edema and inflammation but no lesions (Boren, 1964). Exposure to formaldehyde and acrolein adsorbed onto carbon particles (1 to 4 μm) resulted in the recruitment of PMNs to tracheal and intrapulmonary epithelial tissues but not when the aldehydes were tested alone (Kilburn and McKenzie, 1978).

Madden et al. (2000) observed that O_3 exposure increased the bioactivity of DPM. DPM, preexposed to O_3 for 48 h or nonozone-exposed DPM (1 to 500 μg), was instilled into the lungs of laboratory rats. Lung inflammation and injury were examined 24 h after instillation by lung lavage. DPM pre-exposed to 0.1 PPM O_3 was more potent in increasing neutrophilia, lavage total protein, and LDH compared to unexposed DPM. Treatment of DPM with higher concentrations of O_3 (1.0 PPM) decreased the bioactivity of the particles.

There is no direct evidence that DE, at concentrations found in the ambient environment, interacts with other substances in the exposure environment or the physiological status of the exposed subject other than impaired resistance to respiratory tract infections. Although there is experimental evidence that gases and vapors can be adsorbed onto carbonaceous particles, enhancing the toxicity of these particles when deposited in the lung, there is no evidence for an increased health risk from such interactions with DPM under urban atmospheric conditions. Likewise, there is no experimental evidence in laboratory animals that the youth or preexisting emphysema of an exposed individual enhances the risk of exposure to DE.

5.4. COMPARATIVE RESPONSIVENESS AMONG SPECIES TO THE HISTOPATHOLOGIC EFFECTS OF DIESEL EXHAUST

There is some evidence indicating that species may differ in pulmonary responses to DE. Mauderly (1994) compared the pulmonary histopathology of rats and mice after 18 mo of exposure to DE. There was less aggregation of macrophages in mice. Diffuse septal thickening was noted in the mice, but there were few inflammatory cells, no focal fibrosis, little epithelial hyperplasia, and no epithelial metaplasia, as was observed in rats. Heinrich et al. (1986a) reported that wet lung weight of hamsters increased only 1.8-fold following chronic exposure to DE, compared with an increase of 3.4-fold in rats. Smaller increases in neutrophils, lactic acid dehydrogenase, collagen, and protein supported the conclusion of a lesser inflammatory response

in Syrian hamsters. The histopathologic changes in the lungs of Chinese hamsters after 6 mo exposure to DE, on the other hand, was similar to that of rats (Pepelko and Peirano, 1983). Guinea pigs respond to chronic DE exposure with a well-defined epithelial proliferation, but it is based on an eosinophilic response in contrast to the neutrophil-based responses in other species. Epithelial hyperplasia and metaplasia were quite striking in the terminal and respiratory bronchioles of cats exposed for 27 mo to DE (Plopper et al., 1983). This study is of particular interest because the terminal airways of cats are more similar to those of humans than rodent species are. It should be noted, however, that exposure concentrations were very high (12 mg/m^3) for most of the period. Lewis et al. (1989) exposed rats and cynomolgus monkeys 8 h per day, 5 days per week for 2 years to DE at a particle concentration of 2 mg/m^3. Unfortunately, this exposure rate was sufficiently low that few effects were noted in either species other than focal accumulations of particles, primarily in the alveolar macrophages, interstitium, and lymphoid tissue. It is apparent that species do vary in their pulmonary responses to DE exposure, despite the difficulty in making direct comparisons because of differences in exposure regimes, lifespans, and pulmonary anatomy. Most species do respond, however, suggesting that humans are likely to be susceptible to induction of pulmonary pathology during chronic exposure to DE at some level.

5.5. DOSE-RATE AND PARTICULATE CAUSATIVE ISSUES

The purpose of animal toxicological experimentation is to elucidate mechanisms of action and identify the hazards and dose-response effects posed by a chemical substance or complex mixture and to extrapolate these effects to humans for subsequent health assessments. The cardinal principle in such a process is that the intensity and character of the toxic action are a function of the dose of the toxic agent(s) that reaches the critical site of action. The considerable body of evidence reviewed clearly denotes that major noncancerous health hazards may be presented to the lung following the inhalation of DE. Based on pulmonary function and histopathological and histochemical effects, a determination can be made concerning which dose/exposure rates of DE (expressed in terms of the DPM concentration) result in injury to the lung and which appear to elicit no effect. The inhalation of poorly soluble particles, such as those found in DE, increases the pulmonary particulate burden. When the dosing rate exceeds the ability of the pulmonary defense mechanisms to achieve a steady-state lung burden of particles, there is a slowing of clearance and the progressive retention of particles in the lung that can ultimately approach a complete cessation of lung clearance (Morrow, 1988). This phenomenon, which is reviewed in Chapter 3, has practical significance both for the interpretation of experimental inhalation data and for the prevention of disease in humans exposed to airborne particles.

The data for exposure intensities that cause adverse pulmonary effects demonstrate that they are less than the exposure intensities reported to be necessary to induce lung tumors. Using the most widely studied laboratory animal species and the one reported to be the most sensitive to tumor induction, the laboratory rat, the no-adverse-effect exposure intensity for adverse pulmonary effects was 56 $mg \cdot h \cdot m^{-3}$/week (Brightwell et al., 1986). The lowest-observed-effect level for adverse pulmonary effects (noncancer) in rats was 70 $mg \cdot h \cdot m^{-3}$/week (Lewis et al., 1989), and for pulmonary tumors, 122.5 $mg \cdot h \cdot m^{-3}$/week (Mauderly et al., 1987a). The results clearly show that noncancerous pulmonary effects are produced at lower exposure intensities than are pulmonary tumors. Such data support the position that inflammatory and proliferative changes in the lung may play a key role in the etiology of pulmonary tumors in exposed rats (Mauderly et al., 1990b).

The effects of DE on the developing lung and on a model of a preexisting disease state have been studied in rats (Mauderly et al., 1990a, 1987b). Mauderly et al. (1987b) showed that diesel did not affect the developing lung more severely than the adult rat lung, and in fact, that clearance was faster in the younger lung. Mauderly et al. (1990a) compared the pulmonary response to inhalation of DE in rats with elastase-induced emphysema with normal rats. They found that respiratory tract effects were not more severe in emphysematous rats and that the lung burden of particles was less in the compromised rat. These studies provide limited evidence that some factors that are often considered to result in a wider distribution of sensitivity among members of the population may not have this effect with diesel exposure. However, these studies have no counterpart in human studies and extrapolation to humans remains uncertain.

There is also the issue of whether the noncancerous health effects related to exposure to DE are caused by the carbonaceous core of the particle or substances adsorbed onto the core, or both.

Current understanding, derived primarily from studies in rats, suggests that much of the toxicity resulting from the inhalation of DE relates to the carbonaceous core of the particles. Several studies on inhaled aerosols demonstrate that lung reactions characterized by an appearance of particle-laden AMs and their infiltration into the alveolar ducts, adjoining alveoli, and tracheobronchial lymph nodes; hyperplasia of Type II cells; and the impairment of pulmonary clearance mechanisms are not limited to exposure to diesel particles. Such responses have also been observed in rats following the inhalation of coal dust (Lewis et al., 1989; Karagianes et al., 1981), titanium dioxide (Heinrich et al., 1995; Lee et al., 1985), CB (Nikula et al., 1995; Heinrich et al., 1995), titanium tetrachloride hydrolysis products (Lee et al., 1986), quartz (Klosterkötter and Bünemann, 1961), volcanic ash (Wehner et al., 1986), amosite (Bolton et al., 1983), and manmade mineral fibers (Lee et al., 1988) among others. In more recent studies, animals have been exposed to CB that is similar to the carbon core of the DE particle. Nikula et al. (1995) exposed rats for 24 mo to CB or DE at target exposure concentrations of 2.5

and 6 mg/m^3 (exposure rates of 200 or 520 mg·h·m^{-3}/week). Both concentrations induced AM accumulation, epithelial proliferation, inflammation, and fibrosis. They observed essentially no difference in potency of nonneoplastic or in tumor responses based on a regression analysis.

Dungworth et al. (1994) reported moderate to severe inflammation characterized by multifocal bronchoalveolar hyperplasia, alveolar histiocytosis, and focal segmental fibrosis in rats exposed to CB for up to 20 mo at exposure rates of 510 to 540 mg·h·m^{-3}/week. The observed lung pathology reflects notable dose-response relationships and usually evolves in a similar manner. With increasing dose, there is an increased accumulation and aggregation of particle-laden AMs, Type II cell hyperplasia, a foamy (degenerative) macrophage response, alveolar proteinosis, alveolar bronchiolization, cholesterol granulomas, and often squamous cell carcinomas and bronchioalveolar adenomas derived from metaplastic squamous cells in the areas of alveolar bronchiolization.

Heinrich et al. (1995) compared effects of diesel exposure in rats and mice with exposure to titanium dioxide or carbon black. Exposures to TiO_2 and carbon black were adjusted during the exposure to result in a similar lung burden for the three types of particles. At similar lung burdens in the rat, DPM, TiO_2, and CB had nearly identical effects on lung weights and on the incidence of lesions, both noncancer and cancer. Also, a similar effect on clearance of a labeled test aerosol was measured for the different particles. A comparison of the effect of DPM, TiO_2, and carbon black exposures in mice also showed a similar effect on lung weight, but noncancer effects were not reported and no significant increase in tumors was observed.

Murphy et al. (1998) compared the toxicological effects of DPM with three other particles chosen for their differing morphology and surface chemistry. One mg each of well-characterized crystalline quartz, amorphous silica, CB, and DPM was administered to laboratory rats by a single intratracheal instillation. The laboratory rats were sacrificed at 48 h, and 1, 6, and 12 weeks after instillation. Crystalline quartz produced significant increases in lung permeability, persistent surface inflammation, progressive increases in pulmonary surfactant and activities of epithelial marker enzymes up to 12 wk after primary exposure. Amorphous silica did not cause progressive effects but did produce initial epithelial damage with permeability changes that regressed with time after exposure. By contrast, CB had little if any effect on lung permeability, epithelial markers, or inflammation. Similarly, DPM produced only minimal changes, although the individual particles were smaller and differed in surface chemistry from CB. The authors concluded that DPM is less damaging to the respiratory epithelium than is silicon dioxide, and that the surface chemistry of the particle is more important than ultrafine size in explaining biological activity.

These experiments provide strong support for the idea that DE toxicity results from a mechanism that is analogous to that of other relatively inert particles in the lung. This

qualitative similarity exists along with some apparent quantitative differences in the potency of various particles for producing effects on the lung or on particle clearance.

The exact relationship between toxicity and particle size within the ultrafine particle mode, including DPM (BéruBé et al., 1999), remains unresolved. Studies reviewed in the PM CD (U.S. EPA, 1996) suggest a greater inherent potential toxicity of inhaled ultrafine particles. Exposure to ultrafine particles may increase the release of proinflammatory mediators that could be involved in lung disease. For example, Driscoll and Maurer (1991) compared the effects of fine (0.3 μm) and ultrafine (0.02 μm) TiO_2 particles instilled into the lungs of laboratory rats. Although both size modes caused an increase in the numbers of AMs and PMNs in the lungs, and release of TNF and fibronectin by AMs, the responses were greater and more persistent with the ultrafine particles. While fine particle exposure resulted in a minimally increased prominence of particle-laden macrophages associated with alveolar ducts, ultrafine particle exposure produced a somewhat greater prominence of macrophages, some necrosis of macrophages, and slight interstitial inflammation of the alveolar duct region. Moreover, collagen increased only with exposure to ultrafine particles.

Oberdörster et al. (1992) compared the effects of fine (0.25 μm) and ultrafine (0.02 μm) TiO_2 particles instilled into the lungs of laboratory rats on various indicators of inflammation. Instillation of ultrafine particles increased the number of total cells recovered by lavage, decreased the percentage of AMs, and increased the percentage of PMNs and protein. Instillation with fine particles did not cause statistically significant effects. Thus, the ultrafine particles had greater pulmonary inflammatory potency than did larger sizes of this material. The investigators attributed the enhanced toxicity to greater interaction of the ultrafine particles with their large surface area, with alveolar and interstitial macrophages, which resulted in enhanced release of inflammatory mediators. They suggested that ultrafine particles of low in vitro solubility appear to enter the interstitium more readily than do larger sizes of the same material, which accounted for the increased contact with macrophages in this compartment of the lung. Driscoll and Maurer (1991) noted that the pulmonary retention of ultrafine TiO_2 particles instilled into rat lungs was greater than for the same mass of fine-mode TiO_2 particles. Thus, the available evidence tends to suggest a potentially greater toxicity for inhaled ultrafine particles.

Particle size, volume, surface area, and composition may be the critical elements in the overload phenomenon following exposure to particles, which could explain those quantitative differences. The overloaded AMs secrete a variety of cytokines, oxidants, and proteolytic enzymes that are responsible for inducing particle aggregation and damaging adjacent epithelial tissue (Oberdörster, 1994). For a more detailed discussion of mechanism, see Chapter 3.

On the basis of currently available laboratory animal data, the principal noncancerous health hazard to humans posed by exposure to DE is a structural or functional injury to the lung. Such effects are demonstrable at dose rates or cumulative doses of DPM lower than those

reported to be necessary to induce lung tumors in rats. An emerging human health issue concerning short-term exposure to ambient DE/DPM is the potential for allergenic responses in several studies. Heightened allergenic responses including increased cytokine production as well as increased numbers of inflammatory cells have been detected in nasal lavage from humans exposed to inhaled or instilled DE/DPM. In individuals already allergic to ragweed, exposure to DE/DPM with the allergen was observed to result in an enhanced allergenic response, particularly IgE production. Current knowledge indicates that the carbonaceous core of diesel particles is the major causative factor in the injury to the lung and that other factors such as the cytotoxicity of adsorbed substances on the particles also may play a role. The lung injury appears to be mediated through effects on pulmonary AMs. Because noncancerous pulmonary effects occur at lower doses than tumor induction does in the rat, and because these effects may be cofactors in the etiology of DE-induced tumors, noncancerous pulmonary effects must be considered in the total evaluation of DE, notably the particulate component.

5.6. SUMMARY AND DISCUSSION

5.6.1. Effects of Diesel Exhaust on Humans

The most readily identified acute noncancer health effect of DE on humans is its ability to elicit subjective complaints of eye, throat, and bronchial irritation and neurophysiological symptoms such as headache, lightheadedness, nausea, vomiting, and numbness and tingling of the extremities. Studies of the perception and offensiveness of the odor of DE and a human volunteer study in an exposure chamber have demonstrated that the time of onset of the human subjective symptoms is inversely related to increasing concentrations of DE and the severity is directly related to increasing concentrations of DE. In one study in which a diesel engine was operated under varying load conditions, a dilution factor of 140 to 475 was needed to reduce the exhaust level to an odor-detection threshold level.

A public health issue is whether short-term exposure to DE might result in an acute decrement in ventilatory function and whether the frequent repetition of such acute respiratory effects could result in chronic lung function impairment. One convenient means of studying acute decrements in ventilatory function is to monitor differences in pulmonary function in occupationally exposed workers at the beginning and end of a workshift. In studies of underground miners, bus garage workers, dockworkers, and locomotive repairmen, increases in respiratory symptoms (cough, phlegm, and dyspnea) and decreases in lung function (FVC, FEV_1, PEFR, and FEF_{25-75}) over the course of a workshift were generally found to be minimal and not statistically significant. In a study of acute respiratory responses in diesel bus garage workers, there was an increased reporting of cough, labored breathing, chest tightness, and wheezing, but no reductions in pulmonary function were associated with exposure to DE. Pulmonary function was affected in stevedores over a workshift exposure to DE but normalized

after a few days without exposure to DE fumes. In a third study, there was a trend toward greater ventilatory function changes during a workshift among coal miners, but the decrements were similar in miners exposed and not exposed to DE.

Smokers appeared to demonstrate larger workshift respiratory function decrements and increased incidence of respiratory symptoms. Acute sensory and respiratory symptoms were earlier and more sensitive indicators of potential health risks from diesel exposure than were decrements in pulmonary function. Studies on the acute health effects of exposure to DE in humans, experimental and epidemiologic, have failed to demonstrate a consistent pattern of adverse effects on respiratory morbidity; the majority of studies offer, at best, equivocal evidence for an exposure-response relationship. The environmental contaminants have frequently been below permissible workplace exposure limits; in those few cases where health effects have been reported, the authors have failed to identify conclusively the individual or collective causative agents in the DE.

Chronic effects of DE exposure have been evaluated in epidemiologic studies of occupationally exposed workers (metal and nonmetal miners, railroad yard workers, stevedores, and bus garage mechanics). Most of the epidemiologic data indicate an absence of an excess risk of chronic respiratory disease associated with exposure to DE. In a few studies, a higher prevalence of respiratory symptoms, primarily cough, phlegm, or chronic bronchitis, was observed among the exposed. These increased symptoms, however, were usually not accompanied by significant changes in pulmonary function. Reductions in FEV_1 and FVC and, to a lesser extent, FEF_{50} and FEF_{75}, also have been reported. Two studies detected statistically significant decrements in baseline pulmonary function consistent with obstructive airway disease. One study of stevedores had a limited sample size of 17 exposed and 11 controls. The second study in coal miners showed that both underground and surface workers at diesel-use mines had somewhat lower pulmonary performance than their matched controls. The proportion of workers in or at diesel-use mines, however, showed equivalent evidence of obstructive airway disease, and for this reason the authors of the second paper felt that factors other than diesel exposure might have been responsible. A doubling of the prevalence of minor restrictive airway disease was also observed in workers in or at diesel-use mines. These two studies, coupled with other reported nonsignificant trends in respiratory flow-volume measurements, suggest that exposure to DE may impair pulmonary function among occupational populations. Epidemiologic studies of the effects of DE on organ systems other than the pulmonary system are scant. Whereas a preliminary study of the association of cardiovascular mortality and exposure to DE found a fourfold higher risk ratio, a more comprehensive epidemiologic study by the same investigators found no significant difference between the observed and expected number of deaths caused by cardiovascular disease.

Caution is warranted in the interpretation of results from the epidemiologic studies that have addressed noncarcinogenic health effects from exposure to DE. These investigations suffer from myriad methodological problems, including (1) incomplete information on the extent of exposure to DE, necessitating in some studies estimations of exposures from job titles and resultant misclassification; (2) the presence of confounding variables such as smoking or occupational exposures to other toxic substances (e.g., mine dusts); and (3) the short duration and low intensity of exposures. These limitations restrict drawing definitive conclusions as to the cause of any noncarcinogenic DE effect, observed or reported.

It is also apparent that at some level of exposure DE as measured by DPM appears to have the potential to induce airway inflammation in humans without disease. Also, in one other study peripheral blood changes were noted. An emerging area of concern is the immunological changes that have been documented in response to DE exposure and the potential relationship of these changes to the explosive growth of asthma in human populations.

5.6.2. Effects of Diesel Exhaust on Laboratory Animals

Laboratory animal studies of the toxic effects of DE have involved acute, subchronic, and chronic exposure regimens. In acute exposure studies, toxic effects appear to have been associated primarily with high concentrations of carbon monoxide, nitrogen dioxide, and aliphatic aldehydes. In short- and long-term studies, toxic effects have been associated with exposure to the complex exhaust mixture. Effects of DE in various animal species are summarized in Tables 5-2 to 5-15. In short-term studies, health effects related to function, when found, are mild and result from extremely high DPM concentrations of about 6 mg/m^3 and extensive durations of exposure approximating 20 h/day. There is ample evidence, however, that other pathophysiological effects such as accumulation of DPM in pulmonary tissues, evidence of inflammatory response, AM aggregation and accumulation near the terminal bronchioles, Type II cell proliferation, and the thickening of alveolar walls adjacent to AM aggregation do occur under short-term exposures at lower levels of DE. Little evidence exists, however, from short-term studies that exposure to DE impairs lung function. Chronic exposures cause lung pathology that results in altered pulmonary function and increased DPM retention in the lung. Exposures to DE have also been associated with increased susceptibility to respiratory tract infection, neurological or behavioral changes, an increase in banded neutrophils, and morphological alterations in the liver.

5.6.2.1. *Effects on Survival and Growth*

The data presented in Table 5-3 show limited effects on survival in mice and rats and some evidence of reduced body weight in rats following chronic exposures to concentrations of 1.5 mg/m^3 DPM or higher and exposure durations of 16 to 20 h/day, 5 days/week for 104 to

130 weeks. Increased lung weights and lung to body-weight ratios in rats, mice, and hamsters; an increased heart to body weight ratio in rats; and decreased lung and kidney weights in cats have been reported following chronic exposure to DE. No evidence was found of an effect of DE on other body organs (Table 5-4). The lowest-observed-effect level in rats approximated 1 to 2 mg/m^3 DPM for 7 h/day, 5 days/week for 104 weeks.

5.6.2.2. *Effects on Pulmonary Function*

Pulmonary function impairment has been reported in rats, hamsters, cats, and monkeys exposed to DE and included lung mechanical properties (compliance and resistance), diffusing capacity, lung volumes, and ventilatory performance (Table 5-5). The effects generally appeared only after prolonged exposures. The lowest exposure levels (expressed in terms of DPM concentrations) that resulted in impairment of pulmonary function occurred at 2 mg/m^3 in cynomolgus monkeys (the only level tested), 1.5 and 3.5 mg/m^3 in rats, 4.24 and 6 mg/m^3 in hamsters, and 11.7 mg/m^3 in cats. Exposures in monkeys, cats, and rats (3.5 mg/m^3) were for 7 to 8 h/day, 5 days/week for 104 to 130 weeks. While this duration is considered to constitute a lifetime study in rodents, it is a small part of the lifetime of a monkey or cat. Exposures in hamsters and rats (1.5 mg/m^3) varied in hours per day (8 to 20) and weeks of exposure (26 to 130). In all species but the monkey, the testing results were consistent with restrictive lung disease; alteration in expiratory flow rates indicated that 1.5 mg/m^3 DPM was a LOAEL for a chronic exposure (Gross, 1981). Monkeys demonstrated evidence of obstructive airway disease. The nature of the pulmonary impairment is dependent on the dose of toxicants delivered to and retained in the lung, the site of deposition and effective clearance or repair, and the anatomy and physiology of the affected species; these variables appear to be factors in the disparity of the airway disease in monkey versus the other species tested.

5.6.2.3. *Histopathological and Histochemical Effects*

Histological studies have demonstrated that chronic exposure to DE can result in effects on respiratory tract tissue (Table 5-6). Typical findings include alveolar histiocytosis, AM aggregation, tissue inflammation, increase in PMNs, hyperplasia of bronchiolar and alveolar Type II cells, thickened alveolar septa, edema, fibrosis, and emphysema. Lesions in the trachea and bronchi were observed in some studies. Associated with these histopathological findings were various histochemical changes in the lung, including increases in lung DNA, total protein, alkaline and acid phosphatase, glucose-6-phosphate dehydrogenase; increased synthesis of collagen; and release of inflammatory mediators such as leukotriene LTB and prostaglandin $PGF_{2\alpha}$. Although the overall laboratory evidence is that prolonged exposure to DPM results in histopathological and histochemical changes in the lungs of exposed animals, some studies have also demonstrated that there may be a threshold of exposure to DPM below which pathologic

changes do not occur. These no-observed-adverse-effect levels for histopathological effects were reported to be 2 mg/m^3 for cynomolgus monkeys (the only concentration tested), 0.11 to 0.35 mg/m^3 for rats, and 0.25 mg/m^3 DPM for guinea pigs exposed for 7 to 20 h/day, 5 to 5.5 days/week for 104 to 130 weeks.

5.6.2.4. *Effects on Airway Clearance*

The pathological effects of DPM appear to be strongly dependent on the relative rates of pulmonary deposition and clearance (Table 5-7). Clearance of particles from the alveolar region of the lungs is a multiphasic process involving phagocytosis by AMs. Chronic exposure to DPM concentrations of about 1 mg/m^3 or above, under varying exposure durations, causes pulmonary clearance to be reduced, with concomitant focal aggregations of particle-laden AMs, particularly in the peribronchiolar and alveolar regions, as well as in the hilar and mediastinal lymph nodes. The exposure concentration at which focal aggregates of particle-laden AMs occur may vary from species to species, depending on rate of uptake and pulmonary deposition, pulmonary clearance rates, the relative size of the AM population per unit of lung tissue, the rate of recruitment of AMs and leukocytes, and the relative efficiencies for removal of particles by the mucociliary and lymphatic transport system. The principal means by which PM clearance is reduced is through a decrease in the function of pulmonary AMs. Impairment of particle clearance seems to be nonspecific and applies primarily to dusts that are persistently retained in the lungs. Lung dust levels of approximately 0.1 to 1 mg/g lung tissue appear to produce this effect in the Fischer 344 rat (Health Effects Institute, 1995). Morrow (1988) suggested that the inability of particle-laden AMs to translocate to the mucociliary escalator is correlated to an average composite particle volume per AM in the lung. When this particle volume exceeds approximately 60 μm^3 per AM in the Fischer 344 rat, impairment of clearance appears to be initiated. When the particulate volume exceeds approximately 600 μm^3 per cell, evidence suggests that AM-mediated particulate clearance virtually ceases, agglomerated particle-laden macrophages remain in the alveolar region, and increasingly nonphagocytized dust particles translocate to the pulmonary interstitium. Data for other laboratory animal species and humans are, unfortunately, limited.

5.6.2.5. *Neurological and Behavioral Effects*

Behavioral effects have been observed in rats exposed to DE from birth to 28 days of age (Table 5-14). Exposure caused a decreased level of spontaneous locomotor activity and a detrimental effect on learning in adulthood. In agreement with the behavioral changes was physiological evidence for delayed neuronal maturation. Exposures were to 6 mg/m^3 DPM for 8 h/day, 7 days/week from birth to about 7, 14, 21, or 28 days of age.

5.6.2.6. *Effects on Immunity and Allergenicity*

Several laboratory animal studies have indicated that exposure to DPM can reduce an animal's resistance to respiratory infection. This effect, which can occur even after only 2 or 6 h of exposure to DE containing 5 to 8 mg/m^3 DPM, does not appear to be caused by direct impairment of the lymphoid or splenic immune systems; however, in one study of influenza virus infection, interferon levels and hemaglutinin antibody levels were adversely affected in the exposed mice.

As with humans, there are animal data suggesting that DPM is a possible factor in the increasing incidence of allergic hypersensitivity. The effects have been demonstrated primarily in acute human and laboratory animal studies and appear to be associated with both the nonextractable carbon core and the organic fraction of DPM. It also appears that synergies with DPM may increase the potency of known airborne allergens. Both animal and human cell culture studies indicate that DPM also has the potential to act as an adjuvant.

5.6.2.7. *Other Noncancer Effects*

Essentially no effects (based on the weight of evidence of a number of studies) were noted for reproductive and teratogenic effects in mice, rats, rabbits, and monkeys; clinical chemistry and hematology in the rat, cat, hamster, and monkeys; and enzyme induction in the rat and mouse (Tables 5-11 through 5-13 and 5-15).

5.6.3. Comparison of Filtered and Unfiltered Diesel Exhaust

The comparison of the toxic responses in laboratory animals exposed to whole DE or filtered exhaust containing no particles demonstrates across laboratories that diesel particles are the principal etiologic agent of noncancerous health effects in laboratory animals exposed to DE (Table 5-16). Whether the particles act additively or synergistically with the gases cannot be determined from the designs of the studies. Under equivalent exposure regimens, hamsters have lower levels of retained DPM in their lungs than rats and mice do and consequently less pulmonary function impairment and pulmonary pathology. These differences may result from a lower intake rate of DPM, lower deposition rate and/or more rapid clearance rate, or lung tissue that is less susceptible to the cytotoxicity of DPM. Observations of a decreased respiration in hamsters when exposed by inhalation favor lower intake and deposition rates.

5.6.4. Interactive Effects of Diesel Exhaust

There is no direct evidence that DE interacts with other substances in an exposure environment, other than an impaired resistance to respiratory tract infections. Young animals were not more susceptible. In several ways, animals with laboratory-induced emphysema were more resistant. There is experimental evidence that both inorganic and organic compounds can

be adsorbed onto carbonaceous particles. When such substances become affiliated with particles, these substances can be carried deeper into the lungs where they might have a more direct and potent effect on epithelial cells or on AM ingesting the particles. Few specific studies to test interactive effects of DE with atmospheric contaminants, other than coal dust, have been conducted. Coal dust and DPM had an additive effect only.

5.6.5. Conclusions

Conclusions concerning the principal human hazard from exposure to DE are as follows:

- Allergenic inflammatory disorders of the airways to responses typical of asthma have been demonstrated under short-term exposure scenarios to either DE or DPM. The evidence indicates that the immunological changes appear to be due to the DPM component of DE and that the immunological changes are caused by both the nonextractable carbon core and the adsorbed organic fraction of the diesel particle. The toxicological significance of these effects has yet to be resolved.
- Some occupational studies of acute exposure to DE during work shifts suggest that increased acute sensory and respiratory symptoms (cough, phlegm, chest tightness, wheezing) are more sensitive indicators of possible health risks from exposure to DE than pulmonary function decrements (which were consistently found not to be significantly associated with DE exposure)
- Noncancer effects in humans from long-term chronic exposure to DPM are not evident. Noncancer effects from long-term exposure to DPM of several laboratory animal species, conducted to assess the pathophysiologic effects of DPM in humans showed pulmonary histopathology (principally fibrosis) and chronic inflammation.

Although the mode of action of DE is not clearly evident for any of the effects documented in this chapter, the respiratory tract effects observed under acute scenarios are suggestive of an irritant mechanism, while lung effects observed in chronic scenarios indicate an underlying inflammatory response. Current knowledge indicates that the carbonaceous core of the diesel particle is the causative agent of the lung effects, with the extent of the injury being mediated at least in part by a progressive impairment of AMs. It is noted that lung effects occur in response to DE exposure in several species and occur in rats at doses lower than those inducing particle overload and a tumorigenic response (see above); it follows that lung effects such as inflammation and fibrosis are relevant in the development of risk assessments for DE.

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6. ESTIMATING HUMAN NONCANCER HEALTH RISKS OF DIESEL EXHAUST

6.1. INTRODUCTION

As discussed earlier in this document (Chapter 2, Section 2.2.7, 2.2.8), diesel engine exhaust (DE) consists of a complex mixture of gaseous pollutants and particles. In attempting to estimate potential health risks associated with human exposure to DE, researchers have focused attention mostly on the particulate matter (PM) components. They have done so, in part, by comparing the relative toxicity of unfiltered versus filtered DE (with gaseous components removed), as discussed in Chapter 5.

Diesel particulate matter (DPM) consists mainly of: (a) elemental carbon (EC) particles having relatively large surface areas, (b) soluble organic carbon, including 5-ring or higher polycyclic aromatic hydrocarbons (PAHs) such as benzo(*a*)pyrene, and other 3- or 4-ring compounds distributed between gas and particle phases, and (c) metallic compounds. DPM also typically contains small amounts of sulfate/sulfuric acid and nitrates, trace elements, and water, plus some unidentified components. DPM is made up almost entirely of fine particles (i.e., all below 1–3 μm) with a significant subset of ultrafine particles (i.e., those with a mass median diameter below about 0.1 μm).

Health concerns have long focused on DPM. Toxicological data described in Chapter 5 (Section 5.2) indicate DPM to be the prime etiologic agent of noncancer health effects when DE is sufficiently diluted to limit the concentrations of gaseous irritants (NO_2 and SO_2), irritant vapors (aldehydes), CO, or other systemic toxicants. The large surface areas of DPM allow for adsorption of organics from the diesel combustion process and for adsorption of additional compounds during transport in ambient air. The small size of DPM, combined with their large surface area, likely enhance the potential for subcellular interactions with important cellular components of respiratory tissues once the particles are inhaled by humans or other species (Johnston et al., 2000; Oberdörster et al., 2000).

The content of DPM as described above and in Chapter 2 is of clear toxicological significance. The experimental evidence described in Chapter 5 concerning DPM's association with and etiology of noncancer effects is extensive and compelling. These points, along with the fact that DPM is easily and most frequently measured and reported in toxicological studies of diesel emissions, make DPM a reasonable choice as a measure of diesel emissions. As a surrogate, DPM is as valid as any other component of DE to show what is currently known—and probably what is not yet known—about diesel emissions. Therefore, DPM is the quantitative focus of this chapter.

The usual agency approach to evaluating noncancer risks from inhaled exposures to toxic air pollutants such as ambient DE has been documented by EPA in the methods for derivation of an inhalation reference concentration (RfC) (U.S. EPA, 1994). For DPM exposures, this means combining key elements derived from evaluations of specific DPM noncancer effects in animals and humans (described in Chapter 5) with the use of quantitative dosimetry models (described in Chapter 3). The goal is to estimate DPM concentrations to which humans might be exposed throughout their lives (i.e., chronically) without experiencing any untoward or adverse effects. Such an effort can be accomplished through analysis of dose-response relationships where the adverse response is considered as a function of a corresponding measure of dose. Chapter 5 is replete with dose-response information on adverse (but nonlethal) noncancer health effects observed in long-term (chronic/lifetime) exposure studies to DE in general and to DPM in particular, albeit mostly in animals. Chapter 3 analyzes available methods to convert external exposure concentrations of DPM in animal studies to estimates of a human-equivalent concentration (HEC). The following sections of this chapter (Sections 6.2, 6.3, and 6.5) assess and integrate this information to derive a chronic RfC, using the above-cited methodology in developing dose-response assessments of the noncancer effects of toxic air pollutants.

Yet another approach to consider in deriving quantitative estimates of potential human health risks associated with ambient (nonoccupational) DPM exposures is the extent to which DPM could contribute to the adverse health effects that have been associated with exposure to ambient fine PM, $PM_{2.5}$. Such associations with adverse health effects are based primarily on epidemiologic studies evaluated in EPA's Air Quality Criteria Document for Particulate Matter (PM CD) (U.S. EPA, 1996a).[1] This PM CD served as the scientific basis for the last periodic review of the national ambient air quality standards (NAAQS) for PM, which resulted in the establishment of revised PM standards in 1997, including standards for $PM_{2.5}$. DPM is a component of ambient fine PM (see Chapter 2) and should be considered as a toxicologically important component of ambient fine PM. Any guidelines established for DPM, then, should be concordant with information on fine PM in general, as presented in the PM CD. To more fully consider the implications of the relationship between ambient DPM and fine PM, the epidemiological evidence on fine PM and the basis for the $PM_{2.5}$ standards are summarized, and the relationship between ambient DPM and fine PM is discussed later in this chapter (Section 6.4). This relationship is of interest with respect to the noncancer assessment of DE. As is noted here , however, and reflected in Sections 6.2–6.4 below, the definitions, procedures, and statutory mandates that apply to criteria pollutants such as PM (regulated through the establishment of

[1]A new PM CD is now being prepared to reflect the latest scientific studies on ambient PM available since the last document was completed.

NAAQS under sections 108 and 109 of the Clean Air Act) are fundamentally different from those that apply to toxic air pollutants such as DE and to the derivation of RfCs for such pollutants. Thus, the ambient $PM_{2.5}$ concentrations that are specified as the levels of the $PM_{2.5}$ NAAQS should not be compared directly with any RfC that may be derived for DPM. It is reasonable to observe, however, that the annual $PM_{2.5}$ standard would be expected to provide a measure of protection from DPM, reflecting DPM's current approximate proportion to $PM_{2.5}$.

Estimates of DE levels associated with effects occurring under less than lifetime exposure scenarios (such as acute exposure) are not addressed in this chapter. Studies of acute exposure to DE are discussed in Chapter 5, but are accompanied by scant dose-response information, with single-exposure studies for various specialized endpoints (e.g., allergenicity/adjuvancy) and other multiple-exposure-level studies reporting data on mortality only. Based on currently available methodologies, these studies do not yet appear to provide a sufficient basis from which to derive a dose-response assessment for an acute DE exposure scenario.

6.2. THE INHALATION REFERENCE CONCENTRATION APPROACH

Historically, approaches such as the Acceptable Daily Intake (ADI) were developed whereby effect levels, such as no-observed-adverse-effect levels (NOAELs) or lowest-observed-adverse-effect levels (LOAELs) from human or animal data, were combined with certain "safety factors" to accommodate areas of uncertainty to make quantitative estimates of a safe dose, i.e., a level at which no adverse effect would be likely to occur. In response to the National Academy of Sciences (NAS) report entitled "Risk Assessment in the Federal Government: Managing the Process" (National Research Council, 1983), EPA developed two approaches similar to the ADI, i.e., the oral reference dose (RfD) (Barnes and Dourson, 1988) and the parallel inhalation reference concentration, the RfC, with its formal methodology (U.S. EPA, 1994). Similar to the ADI in intent, the RfD/C approach is used for dose-response assessment of noncancer effects, using an explicitly delineated, rigorous methodology that adheres to the principles set forth in the 1983 NRC report. The RfC methodology includes comprehensive guidance on a number of complex issues, including consistent application to effect levels of uncertainty factors (UFs) rather than the ADI safety factors for consideration of uncertainty. Basically, these approaches attempt to estimate a likely subthreshold concentration in the human population. Use of the RfD/C approach is one of the principal current agency methods for deriving dose-response assessments.

A chronic RfC is currently defined as:

An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious noncancer effects during a lifetime.

The RfC approach involves the following general steps:

- Identification of a critical effect relevant to humans, i.e., an adverse effect that occurs at the lowest exposure/dose in human or animal studies and whose prevention avoids the occurrence of all other adverse effects;
- Selection of appropriate dose-response data to derive a point of departure (POD) for extrapolation of a key study (or studies) that provides a NOAEL, LOAEL, or benchmark concentration ($BMCL_x$)[2];
- Estimation of HECs when animal exposure-response data are used (via use of PBPK/dosimetry models);
- Application of UFs to the point of departure (e.g., NOAEL, LOAEL, $BMCL_x$) to address extrapolation uncertainties (e.g., interindividual variability, interspecies differences, adequacy of database); and
- Characterization of the "confidence" in the dose-response assessment and resultant RfC.

The basic quantitative formula for derivation of an RfC, given in Equation 6-1, has as its basic components an effect level, here a NOAEL, expressed as an HEC, and UFs. The units of an RfC are typically mg/m^3 or $\mu g/m^3$.

Alternatively, the numerator in Equation 6-1 may be a LOAEL or $BMCL_x$. The

$$RfC = \frac{NOAEL_{HEC}}{UF} \tag{6-1}$$

benchmark concentration (BMC) approach and its application in this assessment are documented in Appendix B and described further below. Also, a modifying factor (MF) may be used in the denominator of this equation to account for scientific uncertainties, usually relating to the study chosen as the basis for the RfC. Further specifics of RfC derivation procedures are discussed as

[2]$BMCL_x$ is defined as the lower 95% confidence limit of the dose that will result in a level of "x" response (e.g., $BMCL_{10}$ is the lower 95% confidence limit of a dose for a 10% increase in a particular response). See Appendix B for further specifics.

they are used in the following sections. All such procedures are described in detail in the RfC Methodology (U.S. EPA, 1994).

6.3. CHRONIC REFERENCE CONCENTRATION FOR DIESEL EXHAUST

As concluded in Chapter 5, chronic respiratory effects are the principal noncancer hazard to humans from long-term environmental exposure to DE. Other effects (e.g., neurological, liver-related) are observed in animal studies at higher exposures than those producing the respiratory effects. The human and animal data for the immunological effects of DE are currently considered inadequate for dose-response evaluation. Thus, the respiratory effects are considered the "critical effect" for the derivation of a chronic RfC for DE.

The evidence for chronic respiratory effects is based mainly on animal studies showing consistent findings of inflammatory, histopathological (including fibrosis), and functional changes in the pulmonary and tracheobronchial regions of laboratory animals, including the rat, mouse, hamster, guinea pig, and monkey. Occupational studies of DE provide some corroborative evidence of possible respiratory effects (e.g., respiratory symptoms and possible lung function changes), although those studies are generally deficient in exposure information.

Mode-of-action information about respiratory effects from DE exposure indicates that, at least in rats, the pathogenic sequence following the inhalation of DPM begins with the phagocytosis of diesel particles by alveolar macrophages (AMs). These activated AMs release chemotactic factors that attract neutrophils and additional AMs. As the lung burden of DPM increases, there are aggregations of particle-laden AMs in alveoli adjacent to terminal bronchioles, increases in the number of Type II cells lining particle-laden alveoli, and the presence of particles within alveolar and peribronchial interstitial tissues and associated lymph nodes. The neutrophils and AMs release mediators of inflammation and oxygen radicals, and particle-laden macrophages are functionally altered, resulting in decreased viability and impaired phagocytosis and clearance of particles. This series of events may result in pulmonary inflammation, fibrosis, and eventually lesions like those described in the studies reviewed in Chapter 5. Although information describing the possible pathogenesis of respiratory effects in humans is not available, the effects reported in studies of humans exposed to DE are not inconsistent with the findings in controlled laboratory animal studies.

Several reasons explain why the dose-response data from rats are considered especially appropriate for use in characterizing noncancer health effects in humans and deriving a chronic RfC for DE. First, similar noncancer respiratory effects are seen in other species (mouse, hamster, guinea pig, and monkey). Second, rats and humans exhibit similar noncancer responses (macrophage response and interstitial fibrosis) to other particles such as coal mine dust, silica, and beryllium (Haschek and Witschi, 1991; Oberdörster, 1994). Third, relative to other species

there exists a plethora of long-term, specialized, and mechanistic studies in rats. Fourth, an expert panel convened by the International Life Sciences Institute (ILSI) recommended that response data on persistent, inflammatory processes may be used to assess nonneoplastic responses of poorly soluble particles (PSP) such as DPM (ILSI, 2000).

6.3.1. Principal Studies for Dose-Response Analysis: Chronic, Multiple-Dose Level Rat Studies

The experimental protocols and results from the long-term, repeated-exposure chronic studies demonstrating and characterizing the critical effects of pulmonary fibrotic changes and inflammation are discussed in Chapter 5. Salient points of these studies, including species/sex of the test species, the exposure regime and concentrations reported in mg DPM/m^3, and effect levels, are abstracted in Table 6-1 for further consideration. The effect levels are designated as N for no-observed-adverse-effect level, A for adverse-effect level, and $BMCL_{10}$.

The purpose of many of the chronic studies listed in this table was not the elucidation of the concentration-response character of DPM. The studies of Heinrich et al. (1982, 1986) in hamsters, mice, and rats; of Iwai et al. (1986) in rats; of Lewis et al. (1989) in monkeys; and of Pepelko (1982a) in rats are all single-dose-level analyses that have as their genesis mechanistic or species-comparative purposes. As discussed in Chapter 5, many of these studies do provide valuable supporting information for designation of the critical effect of pulmonary histopathology. The lack of any clear dose-response data, however, precludes consideration of these studies as a basis for RfC derivation.

Likewise, studies of chronic, multiple-level exposure involving species other than rats, i.e., hamsters (Pepelko, 1982b), cats (Plopper et al., 1983), and guinea pigs (Barnhart et al., 1981, 1982), provide cross-species corroboration of the critical effects of pulmonary histopathology and inflammatory alteration.

The remaining studies showing exposure-response relationships in rats for the critical effects include those of Ishinishi et al. (1986, 1988), Mauderly et al. (1987a), Heinrich et al. (1995), and Nikula et al. (1995). As described in Chapter 5, all of these studies were conducted and reported in a thorough, exhaustive manner on the critical effects and little, if any, basis exists for choosing one over another for purposes of RfC derivation. One way of taking advantage of this high degree of methodological and scientific merit would be to array data from all these studies and their effect levels (NOAEL, LOAEL, $BMCL_x$) subsequent to normalization of the exposure conditions, i.e., conversion of the exposure regimes to yield an HEC. This exercise would result in an interstudy concentration-response continuum normalized to a continuous human exposure to DPM that would facilitate the choice of a concentration to use as a point of departure in deriving an RfC.

Table 6-1. Histopathological effects of diesel exhaust in the lungs of laboratory animals

Study	Species/sex	Exposure period	Particles (mg/m^3)	Effect level[a]	Effects[b]
Lewis et al. (1989)	Monkey, Cynomolgus, M	7 h/day 5 days/wk 104 wks	2.0	N	AM aggregation; no fibrosis, inflammation, or emphysema
Bhatnagar et al. (1980) Pepelko (1982a)	Rat, F344, M, F	7 h/day 5 days/wk 104 wks	2.0		Multifocal histiocytosis; inflammatory changes; Type II cell proliferation; fibrosis
Pepelko (1982b)	Hamster, Chinese, M	8 h/day 5 days/wk 26 wks	6.0 12.0	A	Inflammatory changes; AM accumulation; thickened alveolar lining; Type II cell hyperplasia; edema; increase in collagen
Heinrich et al. (1982)	Hamster, Syrian, M, F	7-8 h/day 5 days/wk 120 wks	3.9	A	Inflammatory changes, 60% adenomatous cell proliferation
Iwai et al. (1986)	Rat, F344, F	8 h/day 7 days/wk 104 wks	4.9	A	Type II cell proliferation; inflammatory changes; bronchial hyperplasia; fibrosis
Mauderly et al. (1987a) Henderson et al. (1988)	Rat, F344, M, F; Mouse, CD-1, M, F	7 h/day 5 days/wk 130 wks	0.35 3.5 7.1	N A A	Alveolar and bronchiolar epithelial metaplasia in rats at 3.5 and 7.0 mg/m^3; fibrosis at 7.0 mg/m^3 in rats and mice; inflammatory changes; few quantitative data given
Heinrich et al. (1995)	Rat, Wistar, F; Mouse, NMRI, F (7 mg/m^3 only)	18 h/day 5 days/wk 24 mo	0.8 2.5 7.0	A A A	Bronchioalveolar hyperplasia, interstitial fibrosis in all groups; severity and incidence increase with exposure concentration; text given only
	Mouse, NMRI, F; C57BL/6N, F	18 h/day 5 days/wk 13.5 mo (NMRI) 24 mo (C57BL/N)	7.0	A	No increase in tumors; noncancer effects not discussed

Table 6-1. Histopathological effects of diesel exhaust in the lungs of laboratory animals (continued)

Study	Species/sex	Exposure period	Particles (mg/m^3)	Effect level[a]	Effects[b]
Ishnishi et al. (1986, 1988)	Rat, M, F, F344, /Jcl.	16 h/day 6 days/wk 130 wks	0.11[c] 0.41[c] 1.08[c] 2.32[c] 0.46[d] 0.96[d] 1.84[d] 3.72[d]	N N A A N A A A	Inflammatory changes; Type II cell hyperplasia and lung tumors seen at >0.4 mg/m^3; shortening and loss of cilia in trachea and bronchi; data given in text only
Heinrich et al. (1986)	Hamster, Syrian, M, F; Mouse, NMRI, F; Rat, Wistar, F	19 h/day 5 days/wk 120 wks	4.24	A	Inflammatory changes; thickened alveolar septa; bronchioloalveolar hyperplasia; alveolar lipo-proteinosis; emphysema (diagnostic methodology not described); hyperplasia; lung tumors
Barnhart et al. (1981, 1982); Vostal et al. (1981)	Guinea pig, Hartley, M	20 h/day 5.5 days/wk 104 wks	0.25 0.75 1.5 6.0	N A A A	Minimal response at 0.25 and ultrastructural changes at 0.75 mg/m^3; thickened alveolar membranes; cell proliferation; fibrosis at 6.0 mg/m^3; increase in PMN at 0.75 mg/m^3 and 1.5 mg/m^3
Plopper et al. (1983) Hyde et al. (1985)	Cat, inbred, M	8 h/day 7 days/wk 124 wks	6.0[e] 12.0[d]	A A	Inflammatory changes; AM aggregation; bronchiolar epithelial metaplasia; Type II cell hyperplasia; peribronchiolar fibrosis
Nikula et al. (1995)	Rat, F344, M	16 h/day 5 days/wk 23 mo	2.44 6.33	A, A $BMCL_{10}$	AM hyperplasia, epithelial hyperplasia, inflammation, septal fibrosis, bronchoalveolar metaplasia

[a]N= no-observed-adverse-effect level; A = adverse-effect level; $BMCL_{10}$ = benchmark concentration, lower limit, at a 10% response level (for incidence); see Appendix A for further specifics.
[b]AM = Alveolar macrophage; PMN = Polymorphonuclear leukocyte
[c]Light-duty engine.
[d]Heavy-duty engine.
[e]1 to 61 weeks exposure.
[d]62 to 124 weeks of exposure.
[e]See Appendix A.

6.3.2. Derivation of Human Continuous Equivalent Concentrations, HECs

Pharmacokinetic, or PK, models can be used to estimate across species the external concentrations of a toxicant that would result in equivalent internal doses. When used for these purposes, PK models may be termed comparative dosimetric models. Chapter 3 reviewed and evaluated a number of dosimetric models applicable to DPM. This analysis indicated that outputs from the human component of the model developed by Yu et al. (1991) specifically for DPM, such as deposition and estimated lung burden, were not substantially different from other available models. The analysis also demonstrated that the Yu model accounted for several diesel-specific phenomena, including particle overload lung clearance rates and interspecies kinetics of desorption of organics from the carbonaceous core of DPM, both slow- and fast-cleared. Of importance, the Yu model was parameterized for deposition and clearance in both animals and humans. Also, the animal component of the model was based on data from rats actually exposed to DPM, whereas other models analyzed used data based only on generic particles in the size range of DPM. It was concluded from this analysis that the Yu model could be used to estimate disposition of DPM both in animals and in humans and would therefore be an acceptable choice in performing animal-to-human extrapolation in deriving a continuous human-equivalent concentration. Note, however, that use of this or any other available PK model would address species differences in dose (i.e., pharmacokinetics, PK), and not necessarily pharmacodynamics (PD), the other component of uncertainty in animal-to-human or interspecies extrapolation (U.S. EPA, 1994).

Guidance on choosing measures of exposure for poorly soluble particles such as DPM (ILSI, 2000) states that some measures of external dose (e.g., the aerosol exposure parameters of MMAD, σ_g, particle surface area, and density) should be characterized. Likewise, some indication of internal dose resulting from the external exposure (e.g., lung burden) should be measured so that differences in dose metrics may be considered as new mechanistic insights are developed. The whole particle, as characterized in this assessment and used in the model of Yu et al. (1991), meets this recommended guidance, and DPM, in $\mu g/m^3$, is used as the measure of external exposure. Internal measures of exposure or dose were also considered in Chapter 3 (Section 3.3.1.1) with the conclusion that the dose metric of lung burden of DPM in terms of surface area (mg/cm^2) at the termination of the exposure period appears to be the most defensible and appropriate measure of internal dose, especially where clearance is involved. More detailed specifics are available in Chapter 3 and in Appendix A.

The logical and operational sequence of deriving a HEC using the Yu model and these metrics, i.e. external air concentration (in $\mu g/m^3$) and lung burden (in mg/cm^2), is demonstrated in Figure 6-1. First, the experimental animal exposures, including external concentration and

Figure 6-1. Flow diagram of procedure for calculating HECs.

daily and weekly duration, are entered into the animal component of the Yu model to estimate the animal lung burden, in mg DPM/cm^2, for the specific exposure scenario. The human component of the Yu model is then used by setting desired exposure conditions (continuous for 70 years) and running the model to find an external exposure DPM concentration that would result in this same lung burden. The human external DPM concentration matching this lung burden is the human-equivalent concentration. The step-by-step specifics and results of this procedure as applied to the various studies in Table 6-1 are shown in Table A-4 and fully explained in Appendix A.

The foregoing discussion does not address the variability in outcomes that may be estimated from the Yu et al. (1991) model from deposition of DPM. The model comparison exercises in Chapter 3 showed relatively minor differences among the various human models for one measure, deposition, and indicated that human lung burdens estimated by the human component of the Yu and ICRP66 models were nearly identical at low-exposure concentrations. Variability in output of their model (lung burden) was also examined by Yu and Yoon (1990), who studied dependency on tidal volume, respiration rate, and clearance (in terms of the overall particle transport rate from the alveolar region, λ_A). Analysis indicated that the model output is sensitive, but not overly so, for these determinative parameters. A ± 20% change in values for λ_A, for example, was estimated to result in a 16%–26% change in soot burden at a 0.1 mg/m^3 continuous diesel exposure for 10 years. For a ± 10% change in tidal volume, the model projected changes in soot burden ranging from 14% to 22% for this same exposure scenario. The fact that the changes in the model outcome were comparable to changes in the input parameters, such as tidal volume, indicates that the variability of the model when applied to the human population would reflect the variability of these physiological parameters across that population. In sum, at low concentrations of DPM (< 0.5 mg/m^3), relatively minor differences exist among the models currently available, and the input parameters in the human population may be a major source of variability. As discussed below, variability within the human population often is addressed by applying safety or uncertainty factors, usually in the range of 10 (Renwick and Lazarus, 1998; U.S. EPA, 1994).

6.3.3. Dose-Response Analysis—Choice of an Effect Level

HECs were obtained for the dose levels and exposure scenarios presented in the studies of Mauderly et al. (1987b), Ishinishi et al. (1986, 1988), Nikula et al. (1995), and Heinrich et al. (1995), the specifics of which are presented in Appendix A, specifically Table A-4. The HECs, along with the corresponding specific lung burdens in terms of $\mu g/cm^2$, were transcribed from Table A-4 and, along with the accompanying effect level (NOAEL, LOAEL or $BMCL_{10}$), are arrayed ordinally in Table 6-2. It is acknowledged that Table 6-2 is by no means a full portrayal of the dose-response relationship that may exist for DPM and health effects.

As indicated by the $BMCL_{10}$ values listed for the Nikula et al. (1995) study in Table 6-2, the BMC analysis was carried out on the DPM database and is documented in Appendix B. The chronic rat studies identified in this chapter were analyzed for information suitable for BMC analysis. Results yielded only a few datasets of pulmonary toxicity data from a single study, that of Nikula et al. (1995), that could be used for BMC analysis. These pulmonary data (histopathology incidence data) were extracted, HEC concentrations were calculated using the model of Yu, and the BMCs were generated. The results yielded a complex array of $BMCL_{10}$s from three different effects in two sexes (both separate and combined) with nine different models that were evaluated based on the nature of the dataset, on the goodness-of-fit parameters, and on visual inspection of the graphical outputs. From among all the benchmark data generated, the $BMCL_{10}$ of 0.37 mg/m^3 calculated from combined male and female rat pulmonary histopathology was judged as the most defensible choice. However, further characterization of this same benchmark value indicates that it is not a suitable candidate for use as a point of departure for development of a dose-response assessment such as the RfC. Limitations included the excessive extent of extrapolation from the observed experimental range (see Figure B-1 in Appendix B) and the paucity of data points (there were only two exposure groups) overall. Another serious limitation is that the high experimental concentrations used (and their $C \times t$ product) are well in the range where the problematic phenomenon of pulmonary overload in rats occurs (Section 5.1.3.3.4).

Inspection of Table 6-2 shows that calculating and ordering the HECs created a partial concentration-response continuum reflected in the estimated internal lung burden also given in this table. The continuum extends from HECs with no observed adverse effects at concentrations as low as 0.032 mg/m^3 to as high as 0.144 mg/m^3 to HECs with an adverse effect level that first appears definitively in the continuum probably at 0.33 mg/m^3 and extends out to 1.95 mg/m^3.

It should be noted that the relationship between HEC and lung burden is not consistently proportional. For example, at the lowest HEC listed, 0.032 mg/m^3, a lifetime (70 years) of continuous exposure to this concentration is estimated to result in a specific burden to the lung of 0.0587 $\mu g/cm^2$. At the other end of this spectrum, a lifetime of continuous exposure to 4.4

Table 6-2. Human equivalent continuous concentrations: 70-year HECs calculated with the model of Yu et al. (1991) from long-term studies of rats repeatedly exposed to DPM[a]

Study	Exposure concentration (mg/m^3)	Effect level[a]	Lung burden (modeled) (μg DPM $/cm^2$)[b]	HEC (mg/m^3)
Ishinishi et al. (1988) (LD[c])	0.11	NOAEL	0.0587	0.032
Mauderly et al. (1987a)	0.35	NOAEL	0.0685	0.038
Ishinishi et al. (1988) (LD[c])	0.41	NOAEL	0.245	0.128
Ishinishi et al. (1988) (HD[c])	0.46	NOAEL	0.281	0.144
Heinrich et al. (1995)	0.84	LOAEL	0.94	0.33
Nikula et al. (1995)	2.44 & 6.3[d]	$BMCL_{10}$ -inflam	1.34	0.37
Ishinishi et al. (1988) (HD[c])	0.96	LOAEL	3.16	0.883
Ishinishi et al. (1988) (LD[c])	1.18	LOAEL	4.50	1.25
Nikula et al. (1995)	2.44 & 6.3[d]	$BMCL_{10}$ - fibrosis	4.70	1.3
Mauderly et al. (1987a)	3.47	LOAEL	4.95	1.375
Nikula et al. (1995)	2.44	LOAEL	7.00	1.95
Ishinishi et al. (1988) (HD[c])	1.84	AEL	7.63	2.15
Heinrich et al. (1995)	2.5	AEL	8.40	2.35
Ishinishi et al. (1988) (LD[c])	2.32	AEL	9.75	2.75
Mauderly et al. (1987a)	7.08	AEL	10.9	3.05
Ishinishi et al. (1988) (HD[c])	3.72	AEL	15.8	4.4

[a]Effect levels are based on the critical effects of pulmonary histopathology and inflammation as reported in the individual studies. NOAEL: no-observed-adverse-effect level; LOAEL: lowest-observed-adverse-effect level; AEL: adverse-effect level; $BMCL_{10}$: lower 95% confidence estimate of the concentration of DPM associated with a 10% incidence of chronic pulmonary inflammation (inflam) or fibrosis (see Appendices A and B for more specifics).

[b]Lung burdens were derived from data generated from the animal portion of the Yu model using the concentration and duration scenario of each study. The human portion of the Yu model was then used to estimate the continuous, 70-year exposures that would result in this same lung burden, i.e., the HEC. See Table A-4 in Appendix A and accompanying text for further specifics on derivation.

[c]LD/HD = light-duty/heavy-duty diesel engine.

[d]These values are the actual exposure levels used in the Nikula study. These values were converted into HEC and entered into BMC equations to obtain the estimate of the $BMCL_{10}$ listed. The lung burdens for the two $BMCL_{10}$s listed here were derived by interpolation.

mg/m^3 is estimated to result in a specific lung burden of 15.8 μg/cm^2. This latter lung burden is disproportionally elevated compared with the burden estimated to result from exposure to the lowest concentration. Applying the absolute ratio of lung burden/HEC at the lowest HEC exposure (i.e., 0.0587/ 0.032 = 1.8) to the highest concentration would result in a lower lung burden, 4.4 × 1.8 = 7.9 μg/cm^2, which is much lower than the 15.8 μg/cm^2 indicated. This disproportionate increase in lung burden as a function of DPM concentration would be predicted from the assumption in the Yu model that the overload phenomena occurs in humans, as is demonstrated in Figure 3-9 in Chapter 3. Inspection of Table 6-2 shows that this disproportion between lung burden and HEC begins to be noticeable around 0.33 mg/m^3, at the HEC derived from the Heinrich et al. (1995) study. HECs below this value are not appreciably influenced by the overload/disproportionate lung burden phenomenon.

Inspection of the combined interstudy dose-response continuum in Table 6-2 to elucidate a point of departure for an RfC entails some interpretation. Exposures at the lower end of this table show that elevated chronic exposures to DPM consistently result in AELs. Conversely, entries in the upper portion of this table show that low-level chronic exposures to DPM have minimal, if any, effects within the capability of these studies to detect them. Intermediate chronic exposures, from 0.128 mg/m^3 to 0.9 mg/m^3, are, however, less clear and effect levels and exposures either have no or few observable effects, or effects that are minimally adverse.
In choosing from among levels (e.g., NOAELs, LOAELs, $BMCL_x$s) as a POD for derivation of an RfC, the methodology (U.S. EPA, 1994) provides guidance for choice of a highest no-effect level below an effect level; the interim guidance for the BMC suggests that for use as a point of departure, a benchmark (e.g., $BMCL_{10}$) should be within the range of the observable response data so as to avoid excessive extrapolation, and take the shape of the dose-response curve into consideration (Barnes et al., 1995; U.S. EPA, 1995). The highest no-effect HECs ($NOAEL_{HEC}$) in this table are 0.128 mg/m^3 and 0.144 mg/m^3 from the Ishinishi et al. (1988) study, nearly fivefold above other no-effect levels of 0.032 and 0.038 mg/m^3. The lower $BMCL_{10}$ (0.37 mg/m^3) is at nearly the same concentration as the lowest LOAEL of 0.33 mg/m^3 and thus may be too high an estimate for use as a POD based on these data. As discussed above, the limitations on this $BMCL_{10}$, including excessive extrapolation out of the observable range (see Appendix B for more specifics), make it a less than optimal candidate for consideration as a POD in the development of dose-response assessments and therefore was not used for this purpose in this assessment. However, this $BMCL_{10}$ (i.e., at a response rate of 0.1 or 10%) was generated directly from a modeled dose-response curve for chronic inflammation and lends credence to the other NOAELs in Table 6-2 as being associated with their respective dose-response curve at incidences of considerably less than 10%. Moreover, the HECs of less than 0.33 mg/m^3 are not appreciably influenced by the overload phenomenon (see above). Based on this analysis, the value of 0.144

mg/m^3 is chosen as the POD for development of the RfC, because it is the highest $NOAEL_{HEC}$ among those available.

6.3.4. Uncertainty Factors (UF) for the RfC—A Composite Factor of 30

Areas of uncertainty designated in the RfC that are relevant to the DPM assessment are interindividual variability and animal-to-human extrapolation. Each shall be addressed in this section.

Considerable qualitative but little, if any, quantitative information exists regarding subgroups that could be sensitive to any respiratory tract effects of DPM. It is acknowledged that exposure to DPM could be additive to many other daily or lifetime exposures to airborne organic compounds and nondiesel ambient PM. It is also likely that individuals who predispose their lungs to increased particle retention through smoking or other high particulate burdens, who have existing respiratory tract inflammation or infections, or who have chronic bronchitis, asthma, or fibrosis could be more susceptible to adverse impacts from DPM exposure (U.S. EPA, 1996a, Chapter 5 of this document). Also, infants and children could have a greater susceptibility to the acute/chronic toxicity of DPM because of their greater breathing frequency and consequent potential for greater particle deposition in the respiratory tract, which has not reached full development. Increased respiratory symptoms and decreased lung function in children versus ambient PM levels, of which DPM is a part, have been observed (U.S. EPA, 1996a). Thus, even though the limited evidence currently available (see Chapter 5) produces no clear evidence that children are especially sensitive to effects from breathing DPM, the possibility that they actually may be more susceptible because of their inherent physiology and anatomy should remain a consideration. Likewise, a number of factors may modify normal lung clearance, including, aging, gender, and disease. It should be noted that the results of Mauderly et al. (1989) discussed in Chapter 5 indicated that rats with diseased lungs (emphysematous) were no more susceptible than rats with normal lungs to the effects of DE exposure. Although the exact role of these factors is not resolved, all would influence the particle dose to the lung tissue from inhalation exposure. Activity patterns related to occupation and habitation in the proximity of major roadways are certain to be contributory for some subgroups in receiving higher DPM exposures (Chapter 2). In the absence of DE-specific data, this assessment relies on a default UF value of 10 to account for possible interindividual human variability (U.S. EPA, 1994; Renwick and Lazarus, 1998).

Application of an animal-to-human extrapolation or interspecies uncertainty factor to an assessment may be modified via a number of circumstances. When the assessment is based on human data, no such UF is necessary. When the assessment is based on animal data, as is the case with DPM, a default UF of 10 typically is applied to the animal effect level. This latter

action implies that the effect observed in the animal study would occur in humans at a 10-fold lower concentration, ostensibly from some combination of pharmacokinetic and pharmacodynamic factors that would reflect greater dose (PK consideration) to the human target or greater sensitivity (PK consideration) of the human tissue.

The circumstances with DPM warrant modification away from application of the default UF for animal-to-human extrapolation. The first circumstance is the extensive effort in this assessment to address the pharmacokinetic component of the UF. The point of employing state-of-the-art lung dosimetry models with specific parameterization for DPM in conversion of animal exposures to human-equivalent exposures is to derive an estimate of interspecies pharmacokinetics; to know this aspect of interspecies difference with some degree of certainty. Having made this informed effort addresses a major portion of the PK component. It is acknowledged, however, that uncertainties about the model employed here (or any other model) persist. Although the model comparison shown in Chapter 3 indicates relatively minor variability in output among the various human models examined (see Table 3-3 and Figure 3-9) other sources of uncertainty and variability remain. These include, but are not limited to, matters such as the estimates if the model were applied to the general population or variability from the animal portion of the model(s). A second circumstance involves the pharmacodynamic or PD component of the interspecies UF, especially the aspect as to whether the experimental animal species used in the assessment is more or less sensitive than humans. In the consensus report of ILSI (2000) a specific recommendation is made concerning the PD aspect of the interspecies uncertainty factor for poorly soluble particles such as DPM. Because the pulmonary responses from DPM in the principal experimental species, the rat, are present under exposure conditions that do not appear to elicit any response in humans, the experimental species is considered more sensitive than humans. Accordingly, the report suggested that no accommodation be made for uncertainty concerning the pharmacodynamic component of the interspecies UF for DPM and presumably for any other PSP, as the rat appeared to be a sensitive species, more so even than the human. However, other information currently available on DPM suggests that, at least with regard to inflammatory effects, humans may indeed be as sensitive or even more so than rats. Section 5.1.1.1.3 discusses several studies where humans were exposed to airborne DPM and either precursors (Salvi et al., 2000; Nordenhall et al., 2000) or markers (Nightingale et al., 2000; Salvi et al.,1999) of inflammation were detected. These indicators of inflammation were in response to DPM levels of only 200–300 $\mu g/m^3$ of 1–2h duration. Note that in Table 6-2, NOAEL concentrations to which rats actually were exposed were only 100–400 $\mu g/m^3$, clearly within the range of the aforementioned human exposure levels. Thus, adverse effects (inflammation) have been shown to occur in humans at equivalent or possibly even lower levels

of DPM than observed in rats, indicating that humans may indeed be at least as sensitive if not more so than rats.

The sum of these considerations on the animal-to-human UF is that, although major portions of uncertainty have been addressed, degrees of uncertainty persist in both the pharmacodynamic and pharmacokinetic components of the factor. In considering both this residual uncertainty and the information discussed above, it would be prudent to acknowledge partial degrees of uncertainty in both these areas with a partial uncertainty factor, i.e., $10^{0.5}$ vice 10^{1}, such that a factor of 3 would be applied for interspecies extrapolation.

In summary, the application of UFs for the two areas discussed above, interhuman and animal to human, would result in a composite uncertainty factor of 30, 10 for interhuman × 3 for animal to human. Use of other UFs, as discussed in the RfC methodology (U.S. EPA, 1994) for deficiencies in database or for duration extrapolation, is not considered necessary. It should be noted that, given the emerging research on DE-induced immunological effects, it may be necessary at a later date to reconsider the basis for selection of the critical effect and UFs and thus the entire derivation of the DE RfC.

6.3.5. Derivation of the RfC for Diesel Exhaust

On the basis of the above analysis, the value of 0.144 mg/m^3 DPM was selected as the point of departure for the RfC evaluation. This value was derived from concentrations in rat chronic studies that were modeled to obtain HECs. The pulmonary effects, histopathology and inflammation, were determined to be the critical noncancer effects. Response data on inflammation also were suggested by a specific scientific working group as a satisfactory surrogate for fibrogenic responses in assessing the pulmonary responses of poorly soluble particles such as DPM (ILSI, 2000). Sufficient documentation from other studies showed no effect in the portal-of-entry tissues, the extrathoracic (nasopharyngeal) region of the respiratory system, or in other organs at the lowest levels that produce pulmonary effects in chronic exposures. Application of the dosimetric model of Yu et al. (1991) to the exposure value from Ishinishi et al. (1988) of 0.46 mg/m^3 16 hr/day, 6 days/wk, a NOAEL, yielded a $NOAEL_{HEC}$ of 0.144 mg/m^3. Application of the composite UF yields the RfC:

$$NOAEL_{HEC} \div UF = RfC$$

$$0.144\ mg/m^3 \div 30 = 0.0048 mg/m^3 = 5\mu g/m^3.$$

6.4. EPIDEMIOLOGICAL EVIDENCE AND NAAQS FOR FINE PM

Historically, EPA has established primary NAAQS to protect sensitive human population groups against adverse health effects associated with ambient exposures to certain widespread air pollutants, including PM, ozone (O_3), carbon monoxide (CO), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and lead (Pb). The U.S. Clean Air Act (the Act) requires that EPA periodically review and revise as appropriate the criteria (scientific bases) and standards for each pollutant or class of pollutants (e.g., PM) for which NAAQS have been established. The primary, health-based NAAQS must be based on the latest scientific information useful in indicating the kind and extent of all effects on public health expected from the presence of the pollutant in the ambient air, which is evaluated in a "Criteria Document" (CD). The NAAQS are then set at levels that, in the judgment of the EPA Administrator, protect public health (as contrasted with the health of any individual) with an adequate margin of safety. In determining the degree of protection that will satisfy this mandate, EPA considers the nature and severity of the effects, the types of health evidence available, the kind and degree of scientific uncertainty that effects would in fact occur at any particular level of pollution, and the size and nature of sensitive populations at risk of experiencing exposures of concern. The EPA develops a staff paper to bridge the gap between the scientific criteria and the public health policy considerations the Administrator must take into account in reaching a final judgment. The EPA also must consider the recommendations of the Clean Air Scientific Advisory Committee (CASAC), an independent committee established by the Act specifically to advise the Administrator on air quality criteria and NAAQS. In contrast to an RfC, the NAAQS are not intended to identify a concentration that is protective against a hypothetical continuous lifetime exposure to a given level, but rather take into account expected actual exposure conditions of U.S. populations.

The original PM NAAQS were set in 1971 in terms of total suspended particulate matter (TSP) and included both inhalable and noninhalable particles, ranging in size up to 25–50 μm. A later periodic review of the PM criteria and NAAQS led to the setting in 1987 of PM_{10} NAAQS (150 μg/m^3, 24-h average; 50 μg/m^3, annual average) aimed at protecting against health effects associated with those inhalable particles capable of penetrating to lower (thoracic) regions of the human respiratory tract and depositing in tracheobronchial and alveolar tissue of the lung ($\leq$10.0 μm) (52 FR 24634, July 1, 1987). The most recently completed PM NAAQS review was based on an assessment of the latest available scientific information characterized in the EPA PM CD (U.S. EPA, 1996a) and additional staff assessments contained in an associated PM Staff Paper (U.S. EPA, 1996b). In 1997, on the basis of this information and taking into account CASAC recommendations and extensive public comments, EPA established new $PM_{2.5}$ NAAQS (15 μg/m^3, annual average; 65 μg/m^3, 24-h average) to protect against adverse health effects associated with exposures to fine PM. At the same time, EPA retained, in modified form, the

PM_{10} NAAQS originally set in 1987 to protect against effects associated with coarse fraction PM (62 FR 38652, July 18, 1997).[3]

The 1997 PM NAAQS decisions were based, in part, on important distinctions already highlighted by information present in the PM CD between the fine and coarse fractions of PM_{10} with regard to size, chemical composition, sources, and transport. Also of key importance were the assessment and interpretation of new epidemiological findings on health effects associated with ambient PM. The epidemiological evidence and basis for the NAAQS for fine PM are summarized below, followed by a discussion of the relevance of this information for noncancer assessment of DE.

6.4.1. Epidemiological Evidence for Fine PM

The PM CD (U.S. EPA, 1996a) and Staff Paper (U.S. EPA, 1996b) highlighted more than 80 newly published community epidemiologic studies, of which more than 60 found significant associations between increased mortality and/or morbidity risks and various ambient PM indicators. The main findings of concern were community epidemiology results showing ambient PM exposures to be statistically associated with increased mortality (especially among people over 65 years of age and those with preexisting cardiopulmonary conditions) and morbidity (indexed by increased hospital admissions, respiratory symptom rates, and decrements in lung function).

Time-series mortality studies reviewed in the 1996 PM CD (U.S. EPA, 1996a) provide strong evidence that ambient PM air pollution is associated with increases in daily human mortality and morbidity (e.g., increased hospital admissions and respiratory symptoms). These studies provided evidence that such effects occur at routine ambient PM levels, extending to 24-h concentrations below the 150 $\mu g/m^3$ level of the PM_{10} NAAQS set in 1987. Overall, as shown in Table 6-3, the PM_{10} effects estimates derived from the recent PM_{10} total mortality studies suggest that an increase of 50 $\mu g/m^3$ in 24-h average PM_{10} is significantly associated with an increase in total mortality, with an RR on the order of 1.025 to 1.05 in the general population. Table 6-3 also shows higher relative risks for increased hospital admissions for the elderly and for those with preexisting respiratory conditions, both of which represent subpopulations at special risk for mortality implications of acute exposures to air pollution, including PM; higher relative risks are also shown for increased respiratory symptoms and decreased lung function in children. Results are very similar over a range of statistical models used in the analyses, and are not artifacts of the methods by which the data were analyzed. Further, these studies suggest a possible linear,

[3]At present, the 1997 $PM_{2.5}$ standards are the subject of ongoing litigation, although they legally remain in effect, as do the 1987 PM_{10} standards.

Table 6-3. Effect estimates per 50 μg/m³ increase in 24-h PM_{10} concentrations from U.S. and Canadian studies

Study location	RR (± CI) only PM in model	RR (± CI) other pollutants in model	Reported PM_{10} levels mean (min/max)[†]
Increased total acute mortality			
Six Cities[a]		—	
Portage, WI	1.04 (0.98, 1.09)	—	18 (±11.7)
Boston, MA	1.06 (1.04, 1.09)	—	24 (±12.8)
Topeka, KS	0.98 (0.90, 1.05)	—	27 (±16.1)
St. Louis, MO	1.03 (1.00, 1.05)	—	31 (±16.2)
Kingston/Knoxville, TN	1.05 (1.00, 1.09)	—	32 (±14.5)
Steubenville, OH	1.05 (1.00, 1.08)	—	46 (±32.3)
St. Louis, MO[c]	1.08 (1.01, 1.12)	1.06 (0.98, 1.15)	28 (1/97)
Kingston, TN[c]	1.09 (0.94, 1.25)	1.09 (0.94, 1.26	30 (4/67)
Chicago, IL[h]	1.04 (1.00, 1.08)	—	37 (4/365)
Chicago, IL[g]	1.03 (1.02, 1.04)	1.02 (1.01, 1.04)	38 (NR/128)
Utah Valley, UT[b]	1.08 (1.05, 1.11)	1.19 (0.96, 1.47)	47 (11/297)
Birmingham, AL[d]	1.05 (1.01, 1.10)	—	48 (21, 80)
Los Angeles, CA[f]	1.03 (1.00, 1.055)	1.02 (0.99, 1.036)	58(15/177)
Increased hospital admissions (for elderly > 65 yrs.)			
Respiratory Disease			
Toronto, CAN[i]	1.23 (1.02, 1.43)[‡]	1.12 (0.88, 1.36)[‡]	30-39[*]
Tacoma, WA[j]	1.10 (1.03, 1.17)	1.11 (1.02, 1.20)	37 (14, 67)
New Haven, CT[j]	1.06 (1.00, 1.13)	1.07 (1.01, 1.14)	41 (19, 67)
Cleveland, OH[k]	1.06 (1.00, 1.11)	—	43 (19, 72)
Spokane, WA[l]	1.08 (1.04, 1.14)	—	46 (16, 83)
COPD			
Minneapolis, MN[n]	1.25 (1.10, 1.44)	—	36 (18, 58)
Birmingham, AL[m]	1.13 (1.04, 1.22)	—	45 (19, 77)
Spokane, WA[l]	1.17 (1.08, 1.27)	—	46 (16, 83)
Detroit, MI[o]	1.10 (1.02, 1.17)	—	48 (22, 82)
Pneumonia			
Minneapolis, MN[n]	1.08 (1.01, 1.15)	—	36 (18,58)
Birmingham, AL[m]	1.09 (1.03, 1.15)	—	45 (19, 77)

Table 6-3. Effect estimates per 50 μg/m³ increase in 24-h PM_{10} concentrations from U.S. and Canadian studies (continued)

Study location	RR (± CI) only PM in model	RR (± CI) other pollutants in model	Reported PM_{10} levels mean (min/max)[†]
Spokane, WA[l]	1.06 (0.98, 1.13)	—	46 (16, 83)
Detroit, MI[o]	—	1.06 (1.02, 1.10)	48 (22, 82)
Ischemic HD			
Detroit, MI[p]	1.02 (1.01, 1.03)	1.02 (1.00, 1.03)	48 (22, 82)
Increased respiratory symptoms			
Lower Respiratory			
Six Cities[q]	2.03 (1.36, 3.04)	Similar RR	30 (13,53)
Utah Valley, UT[r]	1.28 (1.06, 1.56)[ε]	—	46 (11/195)
	1.01 (0.81, 1.27)[π]		
Utah Valley, UT[s]	1.27 (1.08, 1.49)	—	76 (7/251)
Cough			
Denver, CO[x]	1.09 (0.57, 2.10)	—	22 (0.5/73)
Six Cities[q]	1.51 (1.12, 2.05)	Similar RR	30 (13, 53)
Utah Valley, UT[s]	1.29 (1.12, 1.48)	—	76 (7/251)
Decrease in Lung Function			
Utah Valley, UT[r]	55 (24, 86)**	—	46 (11/195)
Utah Valley, UT[s]	30 (10, 50)**	—	76 (7/251)
Utah Valley, UT[w]	29 (7,51)***	—	55 (1,181)

References:

[a]Schwartz et al. (1996a).
[b]Pope et al. (1992, 1994)/O_3.
[c]Dockery et al. (1992)/O_3.
[d]Schwartz (1993).
[e]Kinney et al. (1995)/O_3, CO.
[f]Ito and Thurston (1996)/O_3.
[g]Styer et al. (1995).
[h]Thurston et al. (1994)/O_3.
[i]Schwartz (1995)/SO_2.
[j]Schwartz et al. (1996b).
[l]Schwartz (1996).
[m]Schwartz (1994e).
[n]Schwartz (1994f).
[o]Schwartz (1994d).
[p]Schwartz and Morris (1995)/O_3, CO, SO_2.
[q]Schwartz et al. (1994).
[r]Pope et al. (1991).
[s]Pope and Dockery (1992).
[t]Schwartz (1994g)
[u]Pope and Kanner (1993).
[v]Ostro et al. (1991)
[†]Min/Max 24-h PM_{10} in parentheses unless noted otherwise as standard deviation (± S.D), 10 and 90 percentile (10, 90). NR = not reported.
[x]Children.
[π]Asthmatic children and adults.
[ε]Means of several cities.
**PEFR decrease in ml/sec.
***FEV_1 decrease.
‡RR refers to total population, not just>65 years.

Source: Adapted from U.S. EPA, 1996b, Tables V-3, V-6, and V-7. See U.S. EPA (1996a,b) for all reference citations.

non-threshold PM/mortality relationship, but the data do not rule out the existence of an underlying nonlinear, threshold relationship (U.S. EPA, 1996a, 12-310-311; 1996b, VI-16). Figure 6-2 illustrates the consistency and coherence of the PM_{10} epidemiology findings for increased total and cause-specific mortality and morbidity risks in adults and children. In addition, Table 6-4 summarizes results from a wide array of U.S. and Canadian studies that showed increased risks of mortality and morbidity to be related to changes in short-term (24-h) fine PM (indexed by $PM_{2.5}$ and other fine particle indicators).

As summarized below, long-term exposure studies reviewed in the 1996 PM CD (U.S. EPA, 1996a) also provide evidence of associations between indicators of PM, including fine particle indicators, and chronic mortality and morbidity. Table 6-5 shows the direct comparisons of two key prospective studies of long-term PM mortality: the Harvard Six Cities Study (Dockery et al., 1993) and the American Cancer Society (ACS) Study (Pope et al., 1995). These two studies agree in their findings of strong associations between fine particles and increased mortality. The RR estimates for total mortality are large and highly significant in the Six Cities study. With their 95% confidence intervals, the RR estimate for a 50 $\mu g/m^3$ increase in $PM_{15/10}$ is 1.42 (1.16, 2.01), the RR estimate for a 25 $\mu g/m^3$ increase in $PM_{2.5}$ is 1.31 (1.11, 1.68), and the RR estimate for a 15 $\mu g/m^3$ increase in SO_4 is 1.46 (1.16, 2.16). The ACS study estimates for total mortality are smaller, but also more precise: RR = 1.17 (1.09, 1.26) for a 25 $\mu g/m^3$ increase in $PM_{2.5}$, and RR = 1.10 (1.06, 1.16) for a 15 $\mu g/m^3$ increase in SO_4. Both studies used Cox regression models and were adjusted for similar sets of individual covariates. In each case, however, caution must be applied in use of the stated quantitative risk estimates, given that the lifelong cumulative exposures of the study cohorts (especially in the dirtiest cities) included distinctly higher past PM exposures than those indexed by the more current PM measurements used to estimate long-term PM exposures in the study. Thus, somewhat lower relative risk estimates than the published ones may well apply. A third study by Abbey et al. (1991, 1995) reported no association between long-term PM exposure (indexed by TSP and other estimated PM indices) after 10 years, although the PM CD (U.S. EPA, 1996a) noted TSP may have been an inadequate index for exposure to inhalable particles and that additional follow-up might still reveal chronic effects.

An additional line of evidence concerning long-term effects may be seen in comparing cause-specific deaths in the Six Cities and ACS studies. The relative risks for the most versus the least polluted cities in the two studies are very similar for mortality from cardiopulmonary causes (U.S. EPA, 1996b, V-17). These two long-term exposure studies, taken together, suggest that there may be increases in mortality for specific disease categories that are consistent with long-term exposure to ambient fine particles. Moreover, at least some fraction of these deaths is

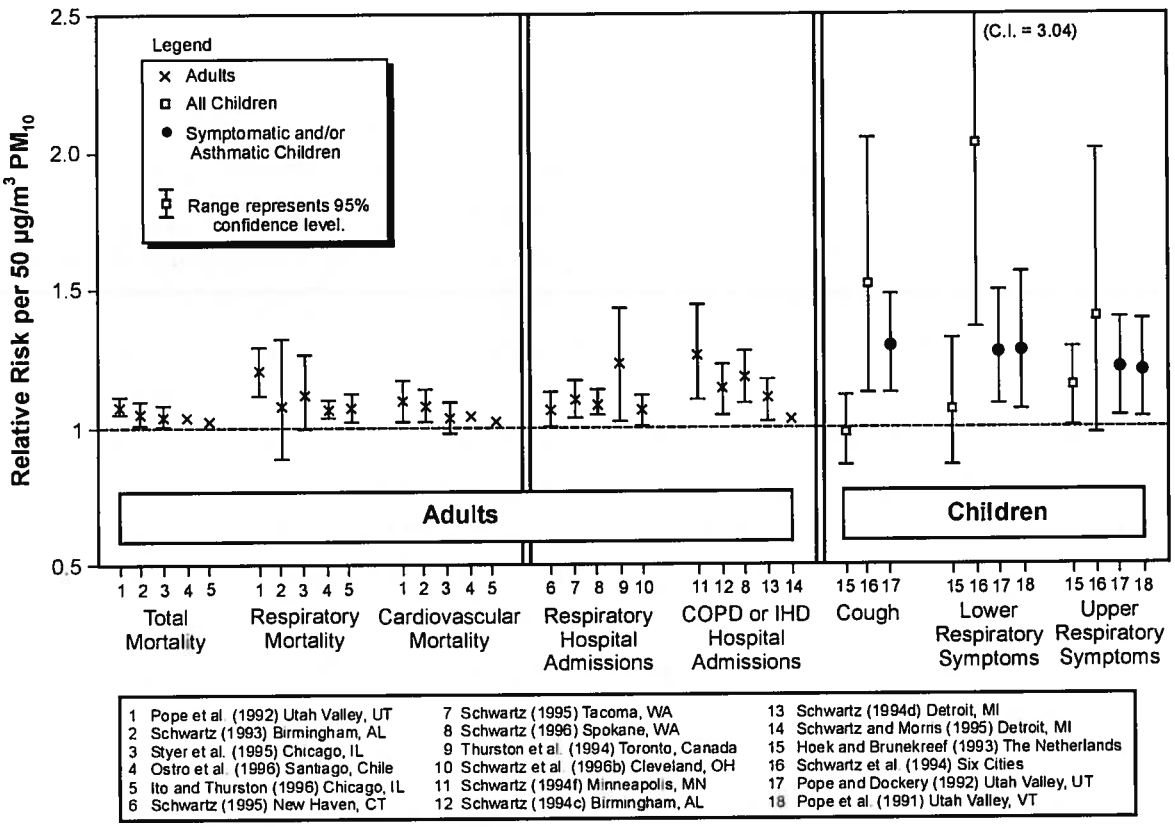

Figure 6-2. Relative risk (RR) estimates for increased mortality and morbidity endpoints associated with 50 µg/m³ increments in PM_{10} concentrations as derived from studies cited by numbers listed above each given type of health endpoint.

Note: Notice the consistency of RR elevations across studies for given endpoint and coherence of RR estimates across endpoints, e.g., higher RR values for symptoms versus hospital admissions and cause-specific mortality.

Source: PM Staff Paper (see U.S. EPA, 1996b for full reference citations for each study identified in figure.)

Table 6-4. Effect estimates per variable increments in 24-h concentrations of fine particle indicators ($PM_{2.5}$, $SO_4^=$, H^+) from U.S. and Canadian studies

Acute mortality	Indicator	RR (± CI) per 25 μg/m³ PM increase	Reported PM levels mean (min/max)†
Six Cities[a]			
Portage, WI	$PM_{2.5}$	1.030 (0.993, 1.071)	11.2 (±7.8)
Topeka, KS	$PM_{2.5}$	1.020 (0.951, 1.092)	12.2 (±7.4)
Boston, MA	$PM_{2.5}$	1.056 (1.038, 1.0711)	15.7 (±9.2)
St. Louis, MO	$PM_{2.5}$	1.028 (1.010, 1.043)	18.7 (±10.5)
Kingston/Knoxville, TN	$PM_{2.5}$	1.035 (1.005, 1.066)	20.8 (±9.6)
Steubenville, OH	$PM_{2.5}$	1.025 (0.998, 1.053)	29.6 (±21.9)
Increased hospitalization			
Ontario, CAN[b]	$SO_4^=$	1.03 (1.02, 1.04)	R = 3.1-8.2
Ontario, CAN[c]	$SO_4^=$ O_3	1.03 (1.02, 1.04) 1.03 (1.02, 1.05)	R = 2.0-7.7
NYC/Buffalo, NY[d]	$SO_4^=$	1.05 (1.01, 1.10)	NR
Toronto[d]	H^+ (Nmol/m³) $SO_4^=$ $PM_{2.5}$	1.16 (1.03, 1.30)* 1.12 (1.00, 1.24) 1.15 (1.02, 1.78)	28.8 (NR/391) 7.6 (NR, 48.7) 18.6 (NR, 66.0)
Increased respiratory symptoms			
Southern California[e]	$SO_4^=$	1.48 (1.14, 1.91)	R = 2-37
Six Cities[f] (Cough)	$PM_{2.5}$ $PM_{2.5}$ Sulfur H^+	1.19 (1.01, 1.42)** 1.23 (0.95, 1.59)** 1.06 (0.87, 1.29)**	18.0 (7.2, 37)*** 2.5 (3.1, 61)*** 18.1 (0.8, 5.9)***
Six Cities[f] (Lower Resp. Symp.)	$PM_{2.5}$ $PM_{2.5}$ Sulfur H^+	1.44 (1.15-1.82)** 1.82 (1.28-2.59)** 1.05 (0.25-1.30)**	18.0 (7.2, 37)*** 2.5 (0.8, 5.9)*** 18.1 (3.1, 61)***
Decreased lung function			
Uniontown, PA[g]	$PM_{2.5}$	PEFR 23.1 (-0.3, 36.9) (per 25 μg/m³)	25/88 (NR/88)

References:
[a]Schwartz et al. (1996a)
[b]Burnett et al. (1994)
[c]Burnett et al. (1995) O_3
[d]Thurston et al. (1992, 1994)
[e]Ostro et al (1993)
[f]Schwartz et al. (1994)
[g]Neas et al. (1995)

†Min/Max 24-h PM indicator level shown in parentheses unless otherwise noted as (± S.D.), 10 and 90 percentile (10,90) or R = range of values from min-max, no mean value reported.
*Change per 100 nmoles/m³.
**Change per 20 μg/m³ for $PM_{2.5}$; per 5 μg/m³ for $PM_{2.5}$ sulfur; per 25 nmoles/m³ for H^+.
***50th percentile value (10,90 percentile).

Source: Adapted from U.S. EPA, 1996b, Table V-12. See U.S. EPA (1996a,b) for all reference citations.

Table 6-5. Effect estimates per increments[a] in annual average levels of fine particle indicators from U.S. and Canadian studies

Type of health effect and location	Indicator	Change in health indicator per increment in PM[a]	Range of city PM levels mean ($\mu g/m^3$)
Increased total chronic mortality in adults		**Relative risk (95% CI)**	
Six City[b]	$PM_{15/10}$	1.42 (1.16-2.01)	18-47
	$PM_{2.5}$	1.31 (1.11-1.68)	11-30
	$SO_4^=$	1.46 (1.16-2.16)	5-13
ACS Study[c] (151 U.S. SMSA)	$PM_{2.5}$	1.17 (1.09-1.26)	9-34*
	$SO_4^=$	1.10 (1.06-1.16)	4-24
Increased bronchitis in children		**Odds ratio (95% CI)**	
Six City[d]	$PM_{15/10}$	3.26 (1.13, 10.28)	20-59
Six City[e]	TSP	2.80 (1.17, 7.03)	39-114
24 City[f]	H^+	2.65 (1.22, 5.74)	6.2-41.0
24 City[f]	$SO_4^=$	3.02 (1.28, 7.03)	18.1-67.3
24 City[f]	$PM_{2.1}$	1.97 (0.85, 4.51)	9.1-17.3
24 City[f]	PM_{10}	3.29 (0.81, 13.62)	22.0-28.6
Southern California[g]	$SO_4^=$	1.39 (0.99, 1.92)	—
Decreased lung function in children			
Six City[d,h]	$PM_{15/10}$	NS Changes	20-59
Six City[e]	TSP	NS Changes	39-114
24 City[i,j]	H^+ (52 nmoles/m^3)	-3.45% (-4.87, -2.01) FVC	—
24 City[i]	$PM_{2.1}$ (15 $\mu g/m^3$)	-3.21% (-4.98, -1.41) FVC	—
24 City[i]	$SO_4^=$ (7 $\mu g/m^3$)	-3.06% (-4.50, -1.60) FVC	—
24 City[i]	PM_{10} (17 $\mu g/m^3$)	-2.42% (-4.30, -.0.51) FVC	—

[a]Estimates calculated annual-average PM increments assume: a 100 $\mu g/m^3$ increase for TSP; a 50 $\mu g/m^3$ increase for PM_{10} and PM_{15}; a 25 $\mu g/m^3$ increase for $PM_{2.5}$; and a 15 $\mu g/m^3$ increase for $SO_4^=$, except where noted otherwise; a 100 nmole/m^3 increase for H^+.

[b]Dockery et al. (1993).
[c]Pope et al. (1995).
[d]Dockery et al. (1989).
[e]Ware et al. (1986).
[f]Dockery et al. (1996).
[g]Abbey et al. (1995a,b,c).
[h]NS Changes = No significant changes.
[i]Raizenne et al. (1996).
[j]Pollutant data same as for Dockery et al. (1996).
*Range of annual median values for subset of 50 cities.

Source: Adapted from U.S. EPA, 1996a, Table 12-6 and U.S. EPA, 1996b, Table V-8. See U.S. EPA (1996a,b) for all reference citations.

likely to be a consequence of cumulative, long-term exposure effects. These effects extend beyond the additive impacts of short-term exposure episodes, in terms of producing marked increases above the expected number of daily deaths among especially susceptible groups, such as the elderly and those with pulmonary disease.

The PM CD (U.S. EPA, 1996a) also highlighted a growing body of evidence directly comparing fine and coarse fraction PM effects that suggests that fine particles are more strongly related than coarse fraction particles to increased mortality and morbidity in both short- and long-term exposure studies. Such evidence notably includes the results of analyses of the type illustrated in Figure 6-3 through 6-5. More specifically, Figure 6-3 shows a stronger relationship between changes in short-term (24-h) concentrations of fine particles (indexed by $PM_{2.5}$) and increased mortality risks than for changes in short-term concentrations of coarse fraction particles (indexed by $PM_{15-2.5}$). Similarly, a stronger relationship is seen between chronic mortality and long-term exposure to fine particles (including both the sulfate and nonsulfate components) than exposure to coarse fraction particles (Figure 6-4), and a much stronger relationship between lung function decrements and long-term exposure to fine particles than to coarse fraction particles (Figure 6-5).

6.4.2. NAAQS for Fine PM

The health effects evidence discussed above is relevant to this current HAD, as both this document (Chapter 2) and the PM CD present information that clearly shows DPM to be a constituent of ambient fine particles. Therefore, it is reasonable to conclude that DPM is associated, but to an undetermined degree, with the health effects described above. Whereas broader public health factors are taken into account in setting NAAQS than are relevant for this noncancer assessment of lifetime exposure for DPM, the annual $PM_{2.5}$ NAAQS based primarily on this evidence is of interest in considering the extent to which the RfC for DE (as derived above in Section 6.3) is concordant with the information on fine particles.

As presented in the Federal Register final rule notice (62 FR 38652, July 18, 1997), EPA drew upon the quantitative epidemiology information concisely summarized above to derive a rationale for selection of an annual-average $PM_{2.5}$ standard.[4] First, to appropriately reflect the

[4]As an initial matter, EPA concluded that the existing PM_{10} standards were not adequate to protect public health, that fine and coarse fraction particles should be considered separately, that $PM_{2.5}$ was the appropriate indicator to use for fine particles, and that an annual $PM_{2.5}$ standard could provide the requisite reduction in risk associated with both annual and 24-h averaging times in most areas of the United States. This annual standard, together with a 24-h standard, could provide supplemental protection against extreme peak fine particle levels that

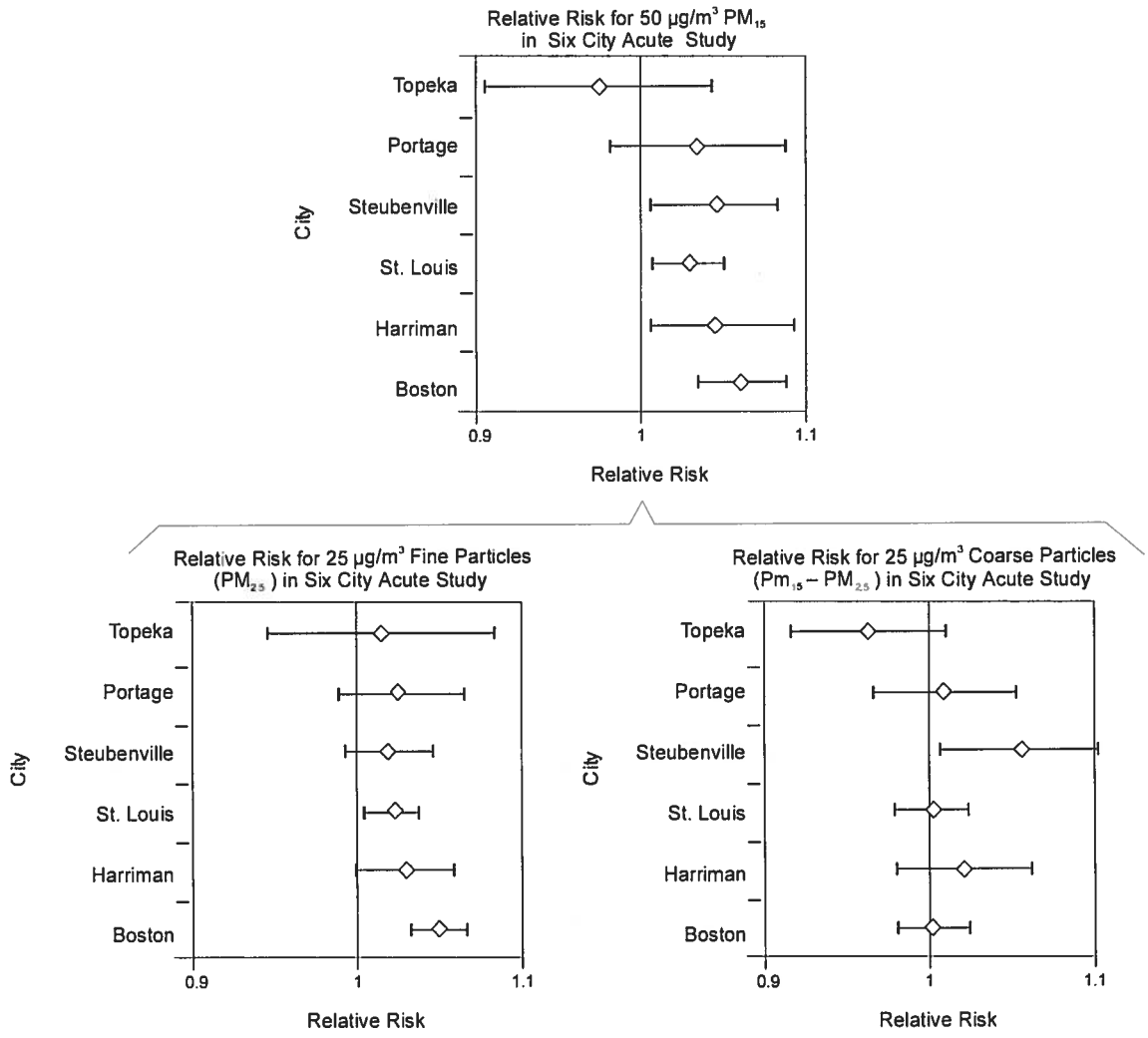

Figure 6-3. Relative risks of acute mortality in Harvard Six Cities Study, for inhalable thoracic particles (PM_{15}/PM_{10}), fine particles ($PM_{2.5}$), and coarse fraction particles (PM_{15}-$PM_{2.5}$).

Note: The coarse fraction effects are smaller and statistically nonsignificant (i.e., lower 95% confidence intervals do not exceed relative risk of 1.0), except in Steubenville where there is high correlation between fine and coarse particles ($R^2 = 0.69$).

Source: PM CD (U.S. EPA, 1996a) graphical depiction of results from Schwartz et al. (1996).

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might occur in some localized situations or in areas with distinct variations in seasonal fine particle levels (62 FR 38652).

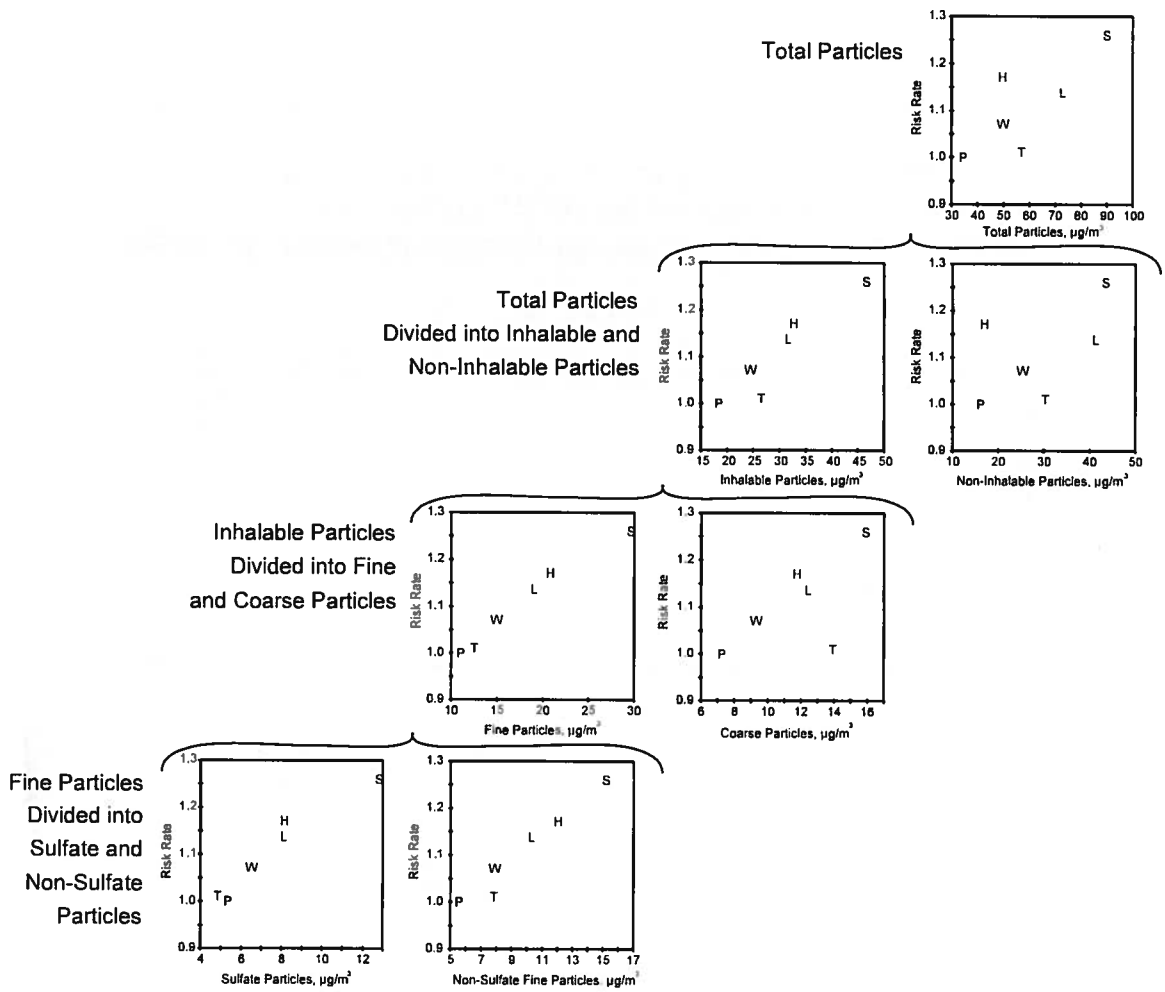

Figure 6-4. Adjusted relative risks for mortality are plotted against each of seven long-term average particle indices in the Harvard Six Cities Study, from largest range (total suspended particles, upper right) through sulfate and nonsulfate fine particle concentrations (lower left).

Note: A relatively strong linear relationship is seen for fine particles, and for sulfate and nonsulfate components. Topeka, which has a substantial coarse particle component of inhalable (thoracic) particle mass, stands apart from the linear relationship between relative risk and inhalable particle concentration.
Source: U.S. EPA (1996a) replotting of results from Dockery et al. (1993).

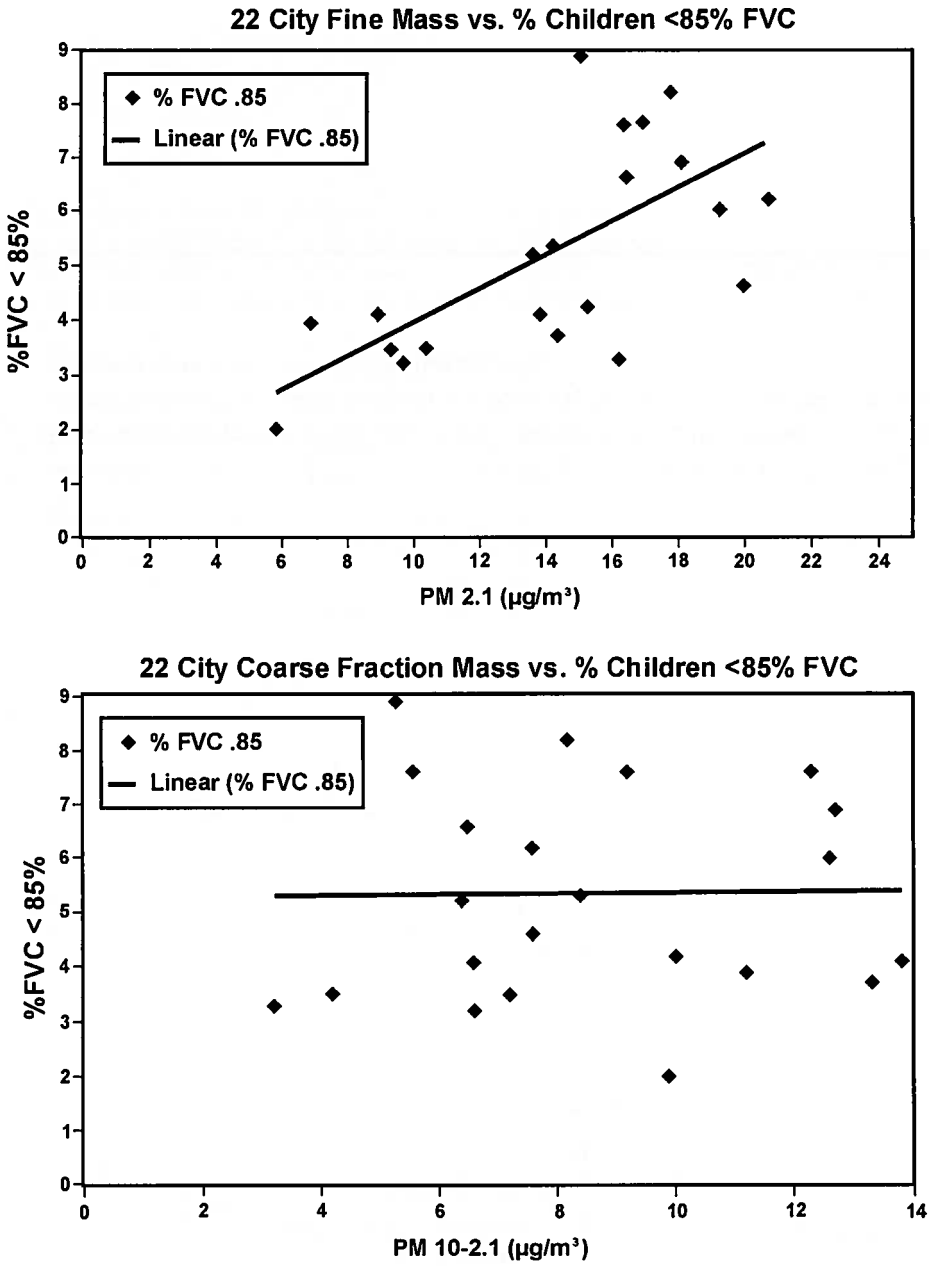

Figure 6-5. Percent of children with <85% normal FVC versus annual-average fine ($PM_{2.1}$) particle concentrations and coarse fraction ($PM_{10-2.1}$) levels for 22 North American cities.

Note: A much stronger connection appears between fine particles and lung function decrements (top panel) than for coarse fraction particles (bottom panel).
Source: PM Staff Paper (1996b) graphical depiction of results from Razienne et al. (1996).

weight of evidence as a whole, EPA concluded that it was appropriate to limit annual $PM_{2.5}$ concentrations to somewhat below those where the body of epidemiological evidence is most consistent and coherent, recognizing both the strengths and limitations of the full range of information on the health effects of PM, as well as associated uncertainties. In accordance with EPA staff and CASAC views on the relative strengths of the epidemiologic studies, major reliance was placed on several short-term (24-h) exposure studies showing significantly increased risks of daily mortality (Schwartz et al., 1996) and morbidity indexed by hospital admissions (Thurston et al., 1994) and respiratory symptoms/lung function decrements in children (Schwartz et al., 1994; Neas et al., 1995) in relationship to increased fine particle ($PM_{2.5}$) concentrations. Whereas it was recognized that health effects may occur over the full range of concentrations observed in these studies, it was concluded that the strongest evidence for short-term $PM_{2.5}$ effects occurs at concentrations near the long-term (e.g., annual) average. More specifically, the strength of the evidence of effects increases for concentrations of $PM_{2.5}$ that are at or above the long-term mean levels reported for these studies. Given the serious nature of the potential effects, EPA judged that it was both prudent and appropriate to select a level for an annual standard at or below such concentrations. More specifically, statistically significant increases in relative risks for daily mortality or morbidity were most clearly observed in these studies to be associated with 24-h fine particle concentrations in cities with long-term mean fine particle concentrations ranging from about 16 to about 21 $\mu g/m^3$, leading to the judgment that an annual standard level of 15 $\mu g/m^3$ would be appropriate.

Before reaching a final conclusion, the epidemiologic studies of long-term exposures to fine particles were also considered, which may reflect the accumulation of daily effects over time as well as potential effects uniquely associated with long-term exposures. Even subject to additional uncertainties, these studies were judged to provide important insights with respect to the overall protection afforded by an annual standard. In particular, the annual mean $PM_{2.5}$ concentrations for the multiple cities included in the two key long-term exposure mortality studies (Dockery et al., 1993; Pope et al., 1995) were 18 $\mu g/m^3$ and about 21–22 $\mu g/m^3$, respectively, with most of the 50 cities in the Pope, et al. (1995) having mean $PM_{2.5}$ concentrations above 15 $\mu g/m^3$. Taken together with other long-term exposure studies and considering other factors discussed in the final rule (62 FR 38676, July 18, 1997), EPA concluded that the concordance of evidence for PM effects and associated levels provides clear support for an annual standard set at 15 $\mu g/m^3$.

6.4.3. DPM as a Component of Fine PM

Chapter 2 of this document, as well as the PM CD (U.S. EPA, 1996a), report the extent to which DPM may contribute to ambient $PM_{2.5}$ concentrations. In some urban situations, the annual average fraction of $PM_{2.5}$ attributable to DPM (according to mass concentrations) is about 35% on the high end, although the proportion appears to be more typically in the range of about 10% (see Chapter 2, Table 2-23 and Section 2.4.2.1).

An approach to considering the relationship of toxicity between DPM and $PM_{2.5}$ would be simply to assume that, as DPM is contributory to the content of ambient $PM_{2.5}$, so too would it be contributory to toxicity of $PM_{2.5}$. This approach is qualitative only because no firm basis currently exists for apportioning toxicity among the various components of $PM_{2.5}$. Nevertheless, some qualitative information from laboratory animal studies does exist, showing that DPM is no more potent at eliciting pulmonary pathology than other poorly soluble particles such as talc, titanium dioxide, or carbon black in rats, or talc or titanium dioxide in mice. No data suggest that DPM is any more potent in eliciting pulmonary pathology than any other poorly soluble particle that typically may be present in ambient $PM_{2.5}$. It may be reasonable to suggest, then, that DPM is no more likely to be toxicologically potent than any other fine particle constituents that typically make up ambient $PM_{2.5}$.

Based on the foregoing aspects of such an approach, a conclusion could be drawn that as long as DPM constituted its current approximate proportion to $PM_{2.5}$, the annual $PM_{2.5}$ standard would also be expected to provide a measure of protection for DPM. Even if a basis did exist to apportion toxicity among the various components of ambient $PM_{2.5}$, such as DPM, use of such information in an approach to derive a safe air level for DPM would result in only a generalized, nonspecific estimate limited by a variety of factors including the accuracy of the apportionment of DPM from $PM_{2.5}$. The RfC derived in Section 6.3 was based on an approach that utilized toxicological information from actual DPM exposures, a more direct approach that would result in a more specific estimate not limited by any apportionment scheme.

6.5. CHARACTERIZATION OF THE NONCANCER ASSESSMENT FOR DIESEL EXHAUST

Adverse health effects from short-term acute (high-level) exposures to DE such as occupational reports of decreases in lung function, wheezing, chest tightness, increases in airway resistance, and reports in laboratory animals of inflammatory airway changes and lung function changes are acknowledged but are not assessed quantitatively. The focus of this dose-response assessment is on the adverse noncancer health consequences of a lifetime, low-level, continuous air exposure by humans to DE.

This assessment uses the whole particle, termed DPM, as the key index or measure of DE dose. DPM includes any and all adsorbed organics, among which are a large number of PAHs, heterocyclic compounds, and their derivatives (Chapter 2), as well as the carbon core. It is not possible to separate the carbon core of DPM from the adsorbed organics to compare the toxicity in exposures other than with limited in-vitro-type scenarios. The dosimetric model used in the derivation of the RfC (Yu et al., 1991) is consistent with this designation, as it considers DPM as well as the adsorbed organics as two types, slow-cleared and fast-cleared. Studies with diesel do occasionally report levels of accompanying gaseous components of DE (e.g., NO_x, CO), but nearly all report particle concentration and characteristics.

Adverse responses occurring in the rat lung have been used in this assessment as the basis for characterizing nonneoplastic human lung responses, yet use of these data in hazard evaluation for cancer is not considered relevant to humans. The basis for this use of these noncancer pulmonary effects in rats for derivation of an RfC includes the fact that humans and rats exhibit similar responses to other poorly soluble particles and also that similar noncancer effects are seen in other species (ILSI, 2000; Freedman and Robinson, 1988). Thus, when viewed across species (including humans), the nonneoplastic pulmonary effects of inflammation and fibrosis used in this assessment are dissociable from the cancer response and are of likely relevance to humans.

As a part of the RfC methodology (U.S. EPA, 1994), dose-response assessments are assigned levels of confidence that are intended to reflect the strengths and limitations of an assessment as well as to indicate the likelihood of the assessment changing with any additional information. Confidence levels of either low, medium, or high are assigned both to the study (or studies) used in the assessment to characterize the critical effects and to the overall toxicological database of the substance. An overall confidence level also is assigned to the entire assessment. Usually, it is the same, or in any case no higher than the level assigned to the database.

Compared with the databases of most other toxicants, the basic toxicological database for DE is substantial. The critical effects are characterized using not one but multiple long-term chronic studies conducted independently of one another (Tables 6-1 and 6-2). The exhaustive manner in which these studies were conducted and reported also imparts a high degree of confidence. Both developmental and reproductive areas are addressed. Also, ancillary studies that address mechanistic aspects of DE toxicity, either as the whole particle with adsorbed organics, or segregated as a poorly soluble particle and extracted organics, are available and used in this assessment. Although only limited human data are available, extensive consideration has been given to the relevancy of the animal studies to the human condition. On the other hand, data from related toxicants such as general ambient PM indicate effects in endpoints (e.g., cardiovascular measures) that have not been addressed in the DPM database. A major point to

consider in assigning confidence in this assessment, and a reason that the value of the RfC may change in the future, is the emerging issue of allergenicity caused or exacerbated by DE. Although information to evaluate allergenicity in parallel to the present effects (pulmonary inflammation and histopathology) is currently lacking, future efforts to elucidate and characterize this effect may well be a driver to make a reevaluation of the noncancer RfC derivation for DE appropriate. With respect to the current RfC for DE, the confidence level is medium, both for the database and overall. The level reflects the relevance of (and information lacking on) allergenicity effects associated with DE in humans, and the possibility that the current RfC could change as a consequence of this information becoming available from the scientific community.

In the introductory portion of this chapter, DPM is acknowledged as a constituent of ambient PM (U.S. EPA, 1996a,b). A discussion of the quantitative epidemiology, particularly regarding fine PM, indicated that public health effects, including premature mortality, increased hospital admissions, respiratory symptoms, and decreased lung function, were observed in populations living in areas with long-term mean $PM_{2.5}$ levels generally ranging above 15 $\mu g/m^3$. Application of the RfC method, which involved critical consideration of the entirety of the disparate DE database with many chronic studies from several different species, evaluation of a myriad of possible DE-specific toxicological endpoints, and use of extrapolation models, produced a value of 5 $\mu g/m^3$. As the accuracy of the RfC is stated in the definition (*"...within an order of magnitude ..."*), this dose-response estimate could be considered to be not different from the level of 15 $\mu g/m^3$, the lower end of the range identified for $PM_{2.5}$. It is acknowledged here again that the levels of the $PM_{2.5}$ NAAQS should not be considered as indicative of the same degree of health protection for DE as intended by the RfC. Nevertheless, the congruence of these estimates tends to enhance the overall confidence that this range of levels is near or inclusive of those that would be expected to be protective of the human population against the health effects of DE.

6.6. SUMMARY

Table 6-6 summarizes the key data and factors used in the dose-response analysis leading to the derivation of the RfC for DE. The DE RfC of 5 μg DPM/m^3 is a chronic exposure likely to be without an appreciable risk of adverse human health effects.

The link between ambient fine PM and DPM with respect to origin, content, and possible health effects has been presented and discussed in this chapter, and the general congruence between the DE RfC and the level of the annual NAAQS for fine particles has been noted. Although these values should not be compared directly, it is reasonable to observe that the annual $PM_{2.5}$ standard would be expected to provide a measure of protection for DPM, reflecting DPM's

Table 6-6. Decision summary for the quantitative noncancer RfC assessment for continuous exposure to diesel particulate matter (DPM)

Quantitative assessment for noncancer effects from lifetime exposure to DPM	5 μg/m³
Critical effect	Pulmonary inflammation and histopathology in rats
Principal study	Array of four chronic rat studies
Designated basis for quantitation (exposures in rats)	0.46 mg DPM /m³, 16 hr/day, 6 d/wk, 130 wks; a NOAEL
$NOAEL_{HEC}$ (HEC)	0.144 mg DPM / m³
Adjustments for uncertainty factors (interspecies variability and intraspecies extrapolation)	30
$NOAEL_{HEC}$/UF = RfC	0.144 mg/m³ / 30 = 5 μg/m³

current approximate proportion to $PM_{2.5}$.

The estimated air concentration of 5 μg/m³ (the RfC, a lifetime exposure to DE measured as DPM) is above the ambient air levels reported in most rural areas but could be below those levels reported under short-term conditions in some urban scenarios, such as at busy intersections or bus stops (see Chapter 2, Table 2-23). The RfC is intended to address lifetime chronic exposures and aspects of time-averaging for less than lifetime scenarios, such as, for example, acute exposures at busy intersections or bus stops, which are not addressed in this particular assessment.

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7. CARCINOGENICITY OF DIESEL EXHAUST

7.1. INTRODUCTION

Initial health hazard concerns regarding the potential carcinogenicity of diesel engine exhaust (DE) were based on the reported induction of skin papillomas by diesel particle extracts (Kotin et al., 1955), evidence for mutagenicity of extracts (Huisingh et al., 1978), evidence that components of diesel extract act as weak tumor promoters (Zamora et al., 1983), and the knowledge that diesel particles and their associated organics are respirable. During the 1980s, both human epidemiologic studies and long-term animal cancer bioassays were initiated. In 1981, Waller published the first epidemiologic investigation, a retrospective mortality study of London transport workers. Since then a large number of retrospective cohort and case-control studies have been carried out with railroad workers, dockworkers, truck drivers, construction workers, miners, and bus garage employees. During 1986 and 1987, several chronic animal cancer bioassays were published. These studies and numerous laboratory investigations carried out since then have been directed toward assessing the carcinogenic potential of whole exhaust, evaluating the importance of various exhaust components in the induction of cancer, and understanding the mode of action and implications of deposition, retention, and clearance of DE particles.

7.1.1. Overview

This chapter evaluates the carcinogenic potential of DE in both humans (Section 7.2) and animals (Section 7.3), discusses mode(s) of action (Section 7.4), and provides an overall weight-of-evidence evaluation (Section 7.5) for carcinogenicity in humans. This chapter also summarizes evaluations of DE conducted by other organizations (Section 7.6) and the final conclusions (Section 7.7) identify major uncertainties for which additional research is needed. This assessment focuses on DE, although it should be noted that diesel particles make up a portion of ambient particulate matter (PM) (Chapter 2, Section 2.2.3; Chapter 6, Section 6.4.3), and thus, the ambient PM data may have some relevance.

7.1.2. Ambient PM-Lung Cancer Relationships

A brief overview of the data regarding exposure to ambient PM and lung cancer is provided as background information and is based on analyses contained in the 1996 Air Quality Criteria for PM (PM CD) (U.S. EPA, 1996a).[1] With DE being part of ambient PM, the question

[1]As noted in Chapter 6, a new PM CD is now being prepared to reflect the latest scientific studies on ambient PM available since the last document was completed.

of what is seen in the ambient PM data is of interest, as epidemiologic evidence for an effect of ambient PM on lung cancer mortality or incidence could possibly contribute to evaluation of DE-specific epidemiologic data.

Chapters 2 and 5 noted that DPM, consisting mostly of fine particles (<1.0 mm diameter), represents a toxicologically important component of typical ambient fine particle mixes. As discussed in Chapter 6, several large-scale prospective studies (Harvard Six Cities Study; American Cancer Society (ACS) Study; Adventist Health Study of Smog (AHSMOG) provide important evidence regarding associations between chronic exposures to ambient fine particles and increased risks of noncancer mortality/morbidity effects (e.g., cardiorespiratory-related deaths or hospital admissions) (U.S. EPA, 1996a). As summarized below, these same studies also evaluated relationships between chronic PM exposures and lung cancer mortality and/or incidence.

As an initial matter, both the Harvard Six Cities Study (Dockery et al., 1993), of approximately 8,000 adults in six cities comprising a transect across the northcentral and northeastern United States, and the ACS Study (Pope et al., 1995), of 550,000 adults in 151 cities across all U.S. geographic regions, found markedly increased relative risks (RR) of lung cancer mortality associated with smoking. More specifically, the Six City Study reported increased risks of smoking for current (RR = 8.00, 95% CI = 2.97-21.6) and former (RR = 2.54, CI = 0.90-7.18) smokers, with the ACS Study reporting striking similar increased risks for current smokers (RR = 9.73, 95% CI = 5.96-15.9).

After controlling for smoking and other risk factors, both the Six Cities Study and the ACS Study (using a subset of 50 of the 151 cities) evaluated relationships between long-term exposure to fine PM (indexed by $PM_{2.5}$), from the least to the most polluted of the cities in each study, and lung cancer mortality. In both studies, lung cancer mortality risks were not statistically significantly associated with ambient $PM_{2.5}$ concentrations in combined analyses of data for both males and females (RR = 1.37, 95% CI = 0.81-2.31, in the Six Cities Study; RR = 1.03, 95% CI = 0.80-1.33, in the ACS Study). Also, lung cancer mortality risks were not statistically significantly associated with ambient $PM_{2.5}$ concentrations in the ACS Study for smaller sample size subgroups broken out by sex and smoking status. In addition, analyses of data from the AHSMOG series of studies, of 6,338 nonsmoking long-term California adult residents, found no statistically significant associations between $PM_{2.5}$ (estimated from visibility data) and lung cancer mortality or total mortality (Abbey et al., 1995); further, no such associations were reported for PM_{10} (estimated from total suspended particulate matter [TSP] data) in the same study. Earlier AHSMOG analyses (Abbey et al., 1991) reported no statistically significant associations between TSP (which includes not only fine PM but also larger coarse-

mode particles ranging up to 25-50 μm) and respiratory cancer for either sex (only respiratory symptoms and any-site female cancers were reported to be associated with TSP in this study).

The ACS Study and the later AHSMOG analyses (Abbey et al., 1995) also evaluated relationships between long-term exposures to sulfates (SO_4) (which are predominantly but not exclusively found in fine-mode particles, and can be considered an index for ambient fine particles) and lung cancer mortality. The ACS Study reported somewhat elevated and statistically significant lung cancer risk (RR = 1.36, 95% CI = 1.11-1.66) across 151 cities in combined analyses of data for both males and females. However, in further analyses of subgroups broken out by sex and smoking status (and thus having smaller sample sizes in each than for the above overall combined analyses), only the lung cancer mortality risks for male "ever-smokers" (RR = 1.44, 95% CI = 1.14-1.83) were statistically significant; no statistically significant relationships were reported for male "never-smokers" (RR = 1.36, 95% CI = 0.40 - 4.66), for female "ever-smokers" (RR = 1.10, 95% CI = 0.72-1.68), or for female "never-smokers" (RR = 1.61; 95% CI = 0.66 -3.92). In the later AHSMOG analyses, Abbey et al. (1995) found no statistically significant associations between sulfates and lung cancer or total mortality.

In summary, the three key prospective cohort studies summarized above, and discussed in more detail in the 1996 PM CD (U.S. EPA, 1996a), provide an equivocal array of results with regard to possible associations between chronic exposures to ambient PM and lung cancer mortality and/or incidence. None of the analyses of fine particles (as indexed by $PM_{2.5}$) in these three studies reported statistically significant relationships between long-term $PM_{2.5}$ concentrations and lung cancer mortality. Only the ACS Study found a statistically significant association of increased risk of lung cancer with one indicator of ambient fine particles (sulfates). Overall, then, these studies support a conclusion that there continues to be little epidemiologic evidence for an effect of ambient PM on lung cancer mortality or incidence. It is recognized, however, that subsequent AHSMOG analyses and other studies, published since completion of the 1996 PM CD, have further analyzed relationships between ambient PM and lung cancer. Results from these more recent studies are now being evaluated as part of the integrated assessment of ambient PM that will be part of the new PM CD targeted for completion in 2002.

7.2. EPIDEMIOLOGIC STUDIES OF THE CARCINOGENICITY OF EXPOSURE TO DIESEL EXHAUST

An increased risk from malignancies of the lung, bladder, and lymphatic tissue has been reported in populations potentially exposed to higher levels of DE than typically seen in the environment. A few authors have reported other malignancies, including testicular cancer

(Garland et al., 1988), gastrointestinal cancer (Balarajan and McDowall, 1988; Guberan et al., 1992), and prostate cancer (Aronsen et al., 1996). A detailed review of 22 lung cancer studies is presented in this section; a few more studies exist, but these 22 are judged to be the key ones. A detailed review of other health effect studies is not presented because findings are equivocal.

Excess risk of bladder cancer has been reported in several studies (Howe et al., 1980; Wynder et al., 1985; Hoar and Hoover et al., 1985; Silverman et al., 1983; Vineis and Magnani 1985; Silverman et al., 1986; Jensen et al., 1987; Steenland et al., 1987; Isocovich et al., 1987; Risch et al., 1988; Iyer et al., 1990; Steineck et al., 1990; Cordier et al., 1993; Notani et al., 1993). Very few studies found significant excesses after adjustment for cigarette smoking. Most studies failed to show any association between exposure to DE and occurrence of bladder cancer. Some authors have reported excess mortality from lymphohematopoietic system cancers in people potentially exposed to diesel fumes. Rushton and Alderson (1983) and Howe and Lindsay (1983) found increased mortality from lymphatic neoplasms. Balarajan and McDowall (1983) found raised mortality for malignant lymphomas. Flodin et al. (1987) observed increased risk for multiple myeloma, and Bender et al. (1989) reported excess mortality from leukemia. Because evidence for bladder cancer and lymphohematopoietic cancer was found to be equivocal, detailed reviews of these studies are not presented here.

The potential for elevated DE exposure in the occupational setting generally includes miners, railroad workers, truckers, bus and taxi drivers, heavy equipment operators, farm tractor drivers, and those involved with heavy duty marine engines. Regarding the mining industry some assert that excess lung cancer should be observed in the miners if exposure to DE is causally associated with the occurrence of lung cancer since DE is allegedly present in the mines. Our review of the mining industry data dose not support this assertion for the following reasons. In the United States, the introduction of diesel engines into metal mines dates from the early to the mid 1960s. Currently, there are approximately 265 underground metal/nonmetal mines in the United States. Virtually all of these mines use diesel powered equipment for various tasks, such as haulage, roof bolting etc. (Department of Labor, Mine Safety and Health Administration, 2001). Introduction of diesel equipment into coal mines was even later. Of 910 existing underground coal mines in the United States, only 145 currently use diesel-powered equipment. Of these 145 mines, 32 mines are currently using diesel equipment for face coal haulage. The remaining mines use diesel equipment for transportation, materials handling, and other support operations (Department of Labor, Mine Safety and Health Administration, 2001). It should be noted that there is a paucity of epidemiologic studies in miners where exposure to DE and health effects are explored. Furthermore, the majority of epidemiologic studies in miners do not mention exposure to diesel equipment use. Thus, it is impossible to know how many miners were exposed to DE and for how long and at what concentrations in a given study,

if any. Hence the studies in miners (coal, metal, and nonmetal with the exception of potash miners) are not reviewed in this chapter, because the available studies are uninformative relative to DE.

In this section, various mortality and morbidity studies of lung cancer from potential exposure to diesel engine emissions are reviewed. Although an attempt was made to cover all the relevant studies, a number of studies are not included for several reasons. In the United States the change from steam to diesel engines in locomotives began after World War II. By 1946 about 10% of the locomotives in service were diesel, by 1952 55% were diesel, and dieselization was about 95% complete by 1959 (Garshick et al., 1988). Therefore, exposure to DE was less common, and the follow-up period for studies conducted prior to 1960 (Raffle, 1957; Commins et al., 1957; Kaplan, 1959) was not long enough to cover the long latency period of lung cancer. The usefulness of these studies in evaluating the carcinogenicity of DE is greatly reduced; thus, they are not considered here.

On the other hand, the trucking industry changed to diesel trucks by the 1960s. In the 1960s sales of diesel-powered Class 8 trucks (long-haul trucks) were 48% of the market, and by the 1970s sales had risen to 85%. Thus, studies conducted among truck drivers prior to the 1970s may reflect exposures to gasoline exhaust as well as DE. Hence, studies with ambiguous exposures or studies that examined several occupational risk factors were excluded because they would have contributed little to the evaluation of the carcinogenicity of DE (Waxweiler et al., 1973; Williams et al., 1977; Ahlberg et al., 1981; Stern et al., 1981; Buiatti et al., 1985; Gustafsson et al., 1986; Siemiatycki et al., 1988). A study by Coggon et al. (1984) was excluded because occupational information abstracted from death certificates had not been validated; this would have resulted in limited information.

Several types of studies of the health effects of exposure to diesel engine emissions are reviewed in this chapter, such as cohort studies, case-control studies, and studies that conducted meta-analysis. In the cohort studies, cohorts of heavy construction equipment operators, railroad and locomotive workers, bus garage employees, and miners were studied retrospectively to determine increased mortality and morbidity resulting from exposures to varying levels of diesel emissions in the workplace. The evaluation of each study presents the study population, methodology used for the study, i.e., data collection and verification, analysis, results, and a critique of the study. There are some methodologic limitations that are common to studies with similar design. The total evidence, including limitations, is discussed at the end of the chapter in the summary and discussion section.

7.2.1. Cohort Studies

7.2.1.1. *Waller (1981): Trends in Lung Cancer in London in Relation to Exposure to Diesel Fumes*

A retrospective mortality study of a cohort of London transport workers was conducted to determine if there was an excess of deaths from lung cancer that could be attributed to DE exposure. From nearly 20,000 male employees in the early years, those aged 45 to 64 were followed for the 25-year period between 1950 and 1974 (the actual number of employees is not given in the paper), constituting a total of 420,700 man-years at risk. These workers were distributed among five job categories: drivers, garage engineers, conductors, motormen or guards, and engineers (works). Lung cancer were ascertained from death certificates of individuals who died while still employed, or if retired, following diagnosis. Expected death rates were calculated by applying greater London death rates to the population at risk within each job category. Data were calculated in 5-year periods and 5-year age ranges, and the results were combined to obtain the total expected deaths in the required age range for the calendar period. A total of 667 cases of lung cancer was reported, compared with 849 expected, to give a cancer mortality ratio of 79%. In each of the five job categories, the observed numbers were below those expected. Engineers in garages had the highest mortality ratio, 90%, motormen and guards had a mortality ratio of 87%, and both the bus drivers and conductors had mortality ratios of 75%. The engineers in the central works had a mortality ratio of 66%. These mortality ratios did not differ significantly from each other. Environmental sampling was done at one garage, on one day in 1979, for benzo[*a*]pyrene (B[*a*]P) concentrations and was compared with corresponding values recorded in 1957. Concentrations of B[*a*]P recorded in 1957 were at least 10 times greater than those measured in 1979.

This study failed to find any association between DE and occurrence of lung cancer, which may be due to several methodologic limitations. The lung cancer deaths were ascertained while the workers were employed (the worker either died of lung cancer or retired after lung cancer was diagnosed). Although man-years at risk were based on the entire cohort, no attempt was made to trace or evaluate the individuals who had resigned from the London transport company for any other reason. Hence, information on resignees who may have had significant exposure to DE, and on lung cancer deaths among them, was not available for analysis. This may have led to a dilution effect, resulting in underascertainment of observed lung cancer deaths and underestimation of mortality ratios. Eligibility criteria for inclusion in the cohort, such as starting date and length of service with the company, were not specified. Therefore, there may not have been sufficient latency for the development of lung cancer. Use of greater London population death rates to obtain expected number of deaths may have resulted in a deficit in mortality ratios reflecting the "healthy worker effect." Investigators did not categorize the five

job categories either by qualitative or quantitative levels of DE exposure; neither did they use an internal comparison group to derive risk estimates.

The age range considered for this study was limited (45 to 64 years of age) for the period between 1950 and 1974. It is not clear whether this age range was applied to calendar year 1950 or 1974, or at the midpoint of the 25-year follow-up period. No analyses were presented either by latency or by duration of employment (surrogate for exposure). The environmental survey based on B[*a*]P concentrations suggests that the cohort in its earlier years was exposed to much higher concentrations of environmental contaminants than currently exist. It is not clear when the reduction in B[*a*]P concentration occurred, because there are no environmental readings available between 1957 and 1979. It is also important to note that the concentrations of B[*a*]P inside the garage in 1957 were not very different from those outside the garage, thus indicating that exposure for garage workers was not much different from that of the general population. Thus, this study fails to provide either positive or negative association between the DE exposure and the occurrence of lung cancer.

7.2.1.2. *Howe et al. (1983): Cancer Mortality (1965 to 1977) in Relation to Diesel Fumes and Coal Exposure in a Cohort of Retired Railroad Workers*

This is a retrospective cohort study of the mortality experience of 43,826 male pensioners of the Canadian National Railroad (CNR) between 1965 and 1977. Members of this cohort consisted of male CNR pensioners who had retired before 1965 and who were known to be alive at the start of that year, as well as those who retired between 1965 and 1977. The records were obtained from a computer file that is regularly updated and used by the company for payment of pensions. To receive a pension, each pensioner must provide, on a yearly basis, evidence that he is alive. Specific cause of death among members of this cohort was ascertained by linking these records to the Canadian Mortality Data Base, which contains records of all deaths registered in Canada since 1950. Of the 17,838 deaths among members of the cohort between 1965 and 1977, 16,812 (94.4%) were successfully linked to a record in the mortality file. A random sample manual check on unlinked data revealed that failure to link was due mainly to some missing information on the death records.

Occupation at time of retirement was used by the Department of Industrial Relations to classify workers into three diesel fume and coal dust exposure categories: (1) nonexposed, (2) possibly exposed, and (3) probably exposed. Person-years of observation were calculated and classified by age at observation in 5-year age groups (35 to 39, 40 to 44, . . . , 80 to 84, and ≥85 years). The observed deaths were classified by age at death for different cancers, for all cancers combined, and for all causes of death combined. Standard mortality ratios (SMRs) were then calculated using rates of the Canadian population for the period between 1965 and 1977. The

relative risks were calculated using the three exposure categories: nonexposed, possibly exposed, and probably exposed.

Both total mortality (SMR = 95, $p<0.001$) and all cancer deaths (SMR = 99, $p>0.05$) were close to that expected for the entire cohort. Analysis by exposure to diesel fume levels in the three categories (nonexposed, possibly exposed, and probably exposed) revealed an increased relative risk for lung cancer among workers with increasing exposure to diesel fumes. The relative risk for nonexposed workers was presumed to be 1.0; for those possibly exposed, the relative risk was significantly elevated to 1.2 ($p=0.013$); and for those probably exposed, it was significantly elevated to 1.35 ($p=0.001$). The corresponding rates for exposure to varying levels of coal dust were very similar at 1.00, 1.21 ($p=0.012$), and 1.35 ($p=0.001$), respectively. The trend tests were highly significant for both exposures ($p<0.001$). Analysis performed after the exclusion of individuals who worked in the maintenance of steam engines, and hence were exposed to high levels of asbestos, yielded a risk of lung cancer of 1.00, 1.21, and 1.33 for those nonexposed, possibly exposed, and probably exposed to DE, respectively, with a highly significant trend ($p<0.001$).

An analysis done on individuals who retired prior to 1950 showed the relative risk of lung cancer among nonexposed, possibly exposed, and probably exposed to be 1.00, 0.70, and 0.44, respectively, based on fewer than 15 deaths in each category. A similar analysis of individuals who retired after 1950 found the results in the same categories to be 1.00, 1.23, and 1.40, respectively. Although retirement prior to 1950 indicated exposure to coal combustion fumes alone, retirement after 1950 shows the results of mixed exposure to coal combustion fumes and diesel fumes. As there was considerable overlap between occupations involving probable exposure to diesel fumes and probable exposure to coal, and as most members of the cohort were employed during the years in which the transition from coal to diesel occurred, it was difficult to distinguish whether lung cancer was associated with exposure to coal combustion fumes or diesel fumes or a mixture of both.

Although this study showed a highly significant dose-response relationship between diesel fumes and lung cancer, it has some methodological limitations. There were concurrent exposures to both diesel fumes and coal combustion fumes during the transition period; therefore, misclassification of exposure may have occurred, because only occupation at retirement was available for analysis. It is possible that the elevated response observed for lung cancer was due to the combined effects of exposure to both coal dust/coal combustion products and diesel fumes and not just one or the other. However, deaths due to lung cancer were not elevated among workers who retired prior to the 1950s and thus would have been primarily exposed to coal dust/coal combustion products. Furthermore, it should be noted that so far coal dust has not been demonstrated to be a pulmonary carcinogen in studies of coal miners. This

study was restricted to deaths among retired workers; therefore, it is unclear if a worker who developed lung cancer when actively employed and filed for a disability claim instead of retirement claim would be included in the study or not. Thus, it is possible that workers with heavy exposure might have been excluded from the study. Neither information on duration of employment in diesel work, nor coal dust-related jobs other than those held at retirement, nor details of how the exposure categories were created was provided. Therefore, it was not possible to evaluate whether this omission would have led to an under- or overestimate of the true relative risk. Although information on potential confounders such as smoking is lacking, the use of an internal comparison group to compute the relative risks minimizes the potential for confounding by smoking, as there is no reason to assume different smoking patterns among individuals exposed to DE versus those not exposed. Despite these limitations, this study provides suggestive evidence toward a causal association between exposure to DE and excess lung cancer.

7.2.1.3. *Rushton et al. (1983): Epidemiological Survey of Maintenance Workers in the London Transport Executive Bus Garages and Chiswick Works*

This is a retrospective mortality cohort study of male maintenance workers employed for at least 1 continuous year between January 1, 1967, and December 31, 1975, at 71 London transport bus (also known as rolling stock) garages and at Chiswick Works. The following information was obtained from computer listings: surname with initials, date of birth, date of joining company, last or present job, and location of work. For those individuals who left their job, date of and reason for leaving were also obtained. For those who died in service or after retirement, and for men who had resigned, full name and last known address were obtained from an alphabetical card index in the personnel department. Additional tracing of individuals who had left was carried out through social security records. The area of residence was assumed to be close to their work; therefore place of work was coded as residence. One hundred different job titles were coded into 20 broader groups. These 20 groups were not ranked for DE exposure, however. The reason for leaving was coded as died in service, retired, or other. The underlying cause of death was coded using the eighth revision of the International Classification of Diseases (ICD). Person-years were calculated from date of birth and dates of entry to and exit from the study using the man-years computer language program. The workers were then subdivided into 5-year age and calendar period groups. The expected number of deaths was calculated by applying the 5-year age and calendar period death rates of the comparison population with the person-years of corresponding groups. The mortality experience of the male population in England and Wales was used as the comparison population. Significance values were calculated for the difference between the observed and expected deaths, assuming a Poisson distribution.

The person-years of observation totaled 50,008 and were contributed by 8,490 individuals in the study, with a mean follow-up of 5.9 years. Only 2.2% (194) of the men were not traced. Observed deaths from all causes were significantly lower than expected (O = 495, $p<0.001$). Observed deaths from all neoplasms and cancer of the lung were approximately the same as those expected. The only significant excess observed, for cancer of the liver and gall bladder at Chiswick Works, was based on four deaths ($p<0.05$). A few job groups showed a significant excess of risks for various cancers. All the excess deaths observed for the various job groups, except for the general hand category, were based on very small numbers (usually fewer than five) and merited cautious interpretation. Only a notable excess in the general hand category for lung cancer was based on as many as 48 cases (SMR = 133, $p<0.03$).

This mortality study did not demonstrate any cancer excess. Details of work history were not obtained to permit any analysis by DE exposure. The study's limitations, including small sample size, short duration of follow-up (average of only 6 years), and lack of sufficient latency period, make it inadequate to draw any conclusions.

7.2.1.4. *Wong et al. (1985): Mortality Among Members of a Heavy Construction Equipment Operators Union With Potential Exposure to DE Emissions*

This retrospective mortality study was conducted on a cohort of 34,156 male members of a heavy construction equipment operators union with potential exposure to DE emissions. Study cohort members were identified from records maintained at Operating Engineers' Local Union No. 3-3A in San Francisco, CA. This union has maintained both work and death records on all its members since 1964. Individuals with at least 1 year of membership in this union between January 1, 1964, and December 31, 1978, were included in the study. Work histories of the cohort were obtained from job dispatch computer tapes. The study follow-up period was January 1964 to December 1978. Death information was obtained from a trust fund, which provided information on retirement dates, vital status, and date of death for those who were entitled to retirement and death benefits. Approximately 50% of the cohort had been union members for less than 15 years, whereas the other 50% had been union members for 15 years or more. The average duration of membership was 15 years. As of December 31, 1978, 29,046 (85%) cohort members were alive, 3,345 (9.8%) were dead, and 1,765 (5.2%) remained untraced. Vital status of 10,505 members who had left the union as of December 31, 1978, was ascertained from the Social Security Administration. Death certificates were obtained from appropriate State health departments. Altogether, 3,243 deaths (for whom death certificates were available) in the cohort were coded using the seventh revision of the ICD. For 102 individuals, death certificates could not be obtained, only the date of death; these individuals were included in the calculation of the SMR for all causes of death but were deleted from the

cause-specific SMR analyses. Expected deaths and SMRs were calculated using the U.S. national age-sex-race cause-specific mortality rates for 5-year time periods between 1964 and 1978. The entire cohort population contributed to 372,525.6 person-years in this 15-year study period.

A total of 3,345 deaths was observed, compared with 4,109 expected. The corresponding SMR for all causes was 81 (p=0.01), which is consistent with the "healthy worker effect." A total of 817 deaths was attributed to malignant neoplasms, slightly fewer than the 878 expected based on U.S. white male cancer mortality rates (SMR = 93, p=0.05). Mostly there were SMR deficits for cause-specific cancers, including lung cancer for the entire cohort (SMR = 99, O = 309). The only significant excess SMR was observed for cancer of the liver (SMR = 167, O = 23, p<0.05).

Analysis by length of union membership as a surrogate of duration for potential exposure showed statistically significant increases in SMRs of cancer of the liver (SMR = 424, p<0.01) in the 10- to 14-year membership group and of the stomach (SMR = 248, p<0.05) in the 5- to 9-year membership group. No cancer excesses were observed in the 15- to 19-year and 20+-year membership groups. Although the SMR for cancer of the lung had a statistically significant deficit in the less-than-5-year duration group, it showed a positive trend with increasing length of membership, which leveled off after 10 to 14 years.

Cause-specific mortality analysis by latency period showed a positive trend for SMRs of all causes of death, although all of them were statistically significant deficits, reflecting the diminishing "healthy worker effect." This analysis also demonstrated a statistically significant SMR excess for cancer of the liver (10- to 19-year group, SMR = 258). The SMR for cancer of the lung showed a statistically significant deficit for a <10-year latency but showed a definite positive trend with increasing latency.

In addition to these analyses of the entire cohort, similar analyses were carried out in various subcohorts. Analyses of retirees, 6,678 individuals contributing to 32,670 person-years, showed statistically significant increases (p<0.01) in SMRs for all cancers; all causes of death; cancers of the digestive system, large intestine, respiratory system, and lung; emphysema; and cirrhosis of the liver. The other two significant excesses (p<0.01) were for lymphosarcoma and reticulosarcoma and nonmalignant respiratory diseases. Further analysis of the 4,075 retirees (18,678 person-years) who retired at age 65 or who retired earlier but had reached the age of 65 revealed statistically significant SMR increases (p<0.05) for all cancers, cancer of the lung, and lymphosarcoma and reticulosarcoma.

To analyze cause-specific mortality by job held (potential exposure to DE emissions), 20 functional job titles were used, which were further grouped into three potential categories: high exposure, low exposure, and unknown exposure. A person was classified in a job title if he ever

worked on that job. Based on this classification system, if a person had ever worked in a high-exposure job title he was included in that group, even though he may have worked for a longer time in a low-exposure group or in an unknown exposure group. Information on length of work in any particular job, hence indirect information on potential length of exposure, was not available either.

For the high-exposure group a statistically significant excess was observed for cancer of the lung among bulldozer operators who had 15 to 19 years of membership and 20+ years of follow-up (SMR = 343, $p<0.05$). This excess was based on 5 out of 495 deaths observed in this group of 6,712 individuals, who contributed 80,328 person-years of observation.

The cause-specific mortality analysis in the low-exposure group revealed statistically significant SMR excesses in individuals who had ever worked as engineers. These excesses were for cancer of the large intestine (SMR = 807, O = 3, $p<0.05$) among those with 15 to 19 years of membership and length of follow-up of at least 20 years, and cancer of the liver (SMR = 872, O = 3, $p<0.05$) among those with 10 to 14 years of membership and length of follow-up of 10 to 19 years. There were 7,032 individuals who contributed to 78,403 person-years of observation in the low-exposure group.

For the unknown exposure group, a statistically significant SMR was observed for motor vehicle accidents only (SMR = 174, O = 21, $p<0.05$). There were 3,656 individuals who contributed to 33,388 person-years of observation in this category.

No work histories were available for those who started their jobs before 1967 and for those who held the same job prior to and after 1967. This group comprised 9,707 individuals (28% of the cohort) contributing to 104,448 person-years. Statistically significant SMR excesses were observed for all cancers (SMR = 112, O = 339, $p<0.05$) and cancer of the lung (SMR = 119, O = 141, $p<0.01$). A significant SMR elevation was also observed for cancer of the stomach (SMR = 199, O = 30, $p<0.01$).

This study demonstrates a statistically significant excess for cancer of the liver but also shows statistically significant deficits in cancers of the large intestine and rectum. It may be, as the authors suggested, that the liver cancer cases actually resulted from metastases from the large intestine and/or rectum, as tumors of these sites will frequently metastasize to the liver. The excess in liver cancer mortality and the deficits in mortality that are due to cancer of the large intestine and rectum could also, as the authors indicate, be due to misclassification. Both possibilities have been considered by the investigators in their discussion.

Cancer of the lung showed a positive trend with length of membership as well as with latency, although none of the SMRs were statistically significant except for workers without any work histories. The individuals without any work histories may have been the ones who were in their jobs for the longest period of time, because workers without job histories included those

who had the same job before and after 1967 and thus may have worked 12 to 14 years or longer. If they had belonged to the category in which heavy exposure to DE emissions was very common for this prolonged time, then the increase in lung cancer, as well as stomach cancer, might be linked to DE. Further information on those without work histories should be obtained if possible, because such information may be quite informative with regard to the evaluation of the carcinogenicity of DE.

The study design is adequate, covers about a 15-year observation period, has a large enough population, and is appropriately analyzed; however, it has too many limitations to permit any conclusions. First, no exposure histories are available; one has to make do with job histories, which provide limited information on exposure level. Any person who ever worked at the job, or any person working at the same job over any period of time, is included in the same category; this would have a dilution effect, because extremely variable exposures were considered in the study. Second, the length of time worked in any particular job is not available. Third, work histories were not available for 9,707 individuals, who contributed 104,448 person-years, a large proportion of the study cohort (28%). These individuals happen to show the most evidence of a carcinogenic effect. Confounding by alcohol consumption for cancer of the liver and smoking for emphysema and cancer of the lung was not ruled out. Fourth, 15 years' follow-up may not provide sufficient latency to observe excess lung cancer. Last, although 34,156 members were eligible for the study, the vital status of 1,765 individuals was unknown. Nevertheless, they were still considered in the denominator of all the analyses. The investigators fail to mention how the person-year calculation for these individuals was handled. Also, some of the person-years might have been overestimated, as people may have paid the dues for a particular year and then left work. These two causes of overestimation of the denominator may have resulted in some or all the SMRs being underestimated.

7.2.1.5. *Edling et al. (1987): Mortality Among Personnel Exposed to DE*

This retrospective cohort mortality study of bus company employees investigated a possible increased mortality of cardiovascular diseases and cancers from DE exposure. The cohort comprised all males employed at five different bus companies in southeastern Sweden between 1950 and 1959. Based on information from personnel registers, individuals were classified into one or more categories and could have contributed person-years at risk in more than one exposure category. The study period was from 1951 to 1983; information was collected from the National Death Registry, and copies of death certificates were obtained from the National Bureau of Statistics. Workers who died after age 79 were excluded from the study because diagnostic procedures were likely to be more uncertain at higher ages (according to investigators). The cause-, sex-, and age-specific national death rates in Sweden were applied to

the 5-year age categories of person-years of observation to determine expected deaths for all causes, malignant diseases, and cardiovascular diseases. A Poisson distribution was used to calculate *p*-values and confidence limits for the ratio of observed to expected deaths. The total cohort of 694 men (after loss of 5 men to follow-up) was divided into three exposure categories: (1) clerks with lowest exposure, (2) bus drivers with moderate exposure, and (3) bus garage workers with highest exposure.

The 694 men provided 20,304 person-years of observation, with 195 deaths compared with 237 expected. A deficit in cancer deaths largely accounted for this lower-than-expected mortality in the total cohort. Among subcohorts, no difference between observed and expected deaths for total mortality, total cancers, or cardiovascular causes was observed for clerks (lowest diesel exposure), bus drivers (moderate diesel exposure), and garage workers (high diesel exposure). The risk ratios for all three categories were less than 1 except for cardiovascular diseases among bus drivers, which was 1.1.

When the analysis was restricted to members who had at least a 10-year latency period and either any exposure or an exposure exceeding 10 years, similar results were obtained, with fewer neoplasms than expected, whereas cardiovascular diseases showed risk around or slightly above unity.

Five lung cancer deaths were observed among bus drivers who had moderate DE exposure, whereas seven were expected. The only other lung cancer death was observed among bus garage workers who had the highest DE exposure. This study's major limitations, including small size and poor data on DE exposure, make it inadequate to draw any conclusions.

7.2.1.6. *Boffetta and Stellman (1988): DE Exposure and Mortality Among Males in the American Cancer Society Prospective Study*

Boffetta and Stellman conducted a mortality analysis of 461,981 males with known smoking history and vital status at the end of the first 2 years of follow-up. The analysis was restricted to males aged 40 to 79 years in 1982 who enrolled in the American Cancer Society's prospective mortality study of cancer. Mortality was analyzed in relation to exposure to DE and to employment in selected occupations related to DE exposure. In 1982, more than 77,000 American Cancer Society volunteers enrolled more than 1.2 million men and women from all 50 States, the District of Columbia, and Puerto Rico in a long-term cohort study, the Cancer Prevention Study II (CPS-II). Enrollees were usually friends, neighbors, or relatives of the volunteers; enrollment was by family groups, with at least one person in the household 45 years of age or older. Subjects were asked to fill out a four-page confidential questionnaire and return it in a sealed envelope. The questionnaire included history of cancer and other diseases; use of medications and vitamins; menstrual and reproductive history; occupational history; and

information on diet, drinking, smoking, and other habits. The questionnaire also included three questions on occupation: (1) current occupation, (2) last occupation, if retired, and (3) job held for the longest period of time, if different from the other two. Occupations were coded to an ad hoc two-digit classification in 70 categories. Exposures at work or in daily life to any of the 12 groups of substances were also ascertained. These included diesel engine exhausts, asbestos, chemicals/acids/solvents, dyes, formaldehyde, coal or stone dusts, and gasoline exhausts. Volunteers checked whether their enrollees were alive or dead and recorded the date and place of all deaths every other year during the study. Death certificates were then obtained from State health departments and coded by a trained nosologist according to a system based on the ninth revision of the ICD.

The data were analyzed to determine the mortality for all causes and lung cancer in relation to DE exposure, mortality for all causes and lung cancer in relation to employment in selected occupations with high DE exposure, and mortality from other causes in relation to DE exposure. The incidence-density ratio was used as a measure of association, and test-based confidence limits were calculated by the Miettinen method. For stratified analysis, the Mantel-Haenszel method was used for testing linear trends. Although data on 476,648 subjects comprising 939,817 person-years of risk were available for analysis, 3% of the subjects (14,667) had not given any smoking history, and 20% (98,026) did not give information on DE exposure and were therefore excluded from the main DE analysis. Among individuals who had provided DE exposure history, 62,800 were exposed and 307,143 were not exposed. Comparison of the population with known information on DE exposure with the excluded population with no information on DE exposure showed that the mean ages were 54.7 and 57.7 years, the nonsmokers were 72.4% and 73.2%, and the total mortality rates per 1,000 per year were 23.0% and 28.8%, respectively.

All-cause mortality was elevated among railroad workers (relative risk [RR] = 1.43, 95% confidence interval [CI] = 1.2, 1.72), heavy equipment operators (RR = 1.7, 95% CI = 1.19, 2.44), miners (RR = 1.34, 95% CI = 1.06, 1.68), and truck drivers (RR = 1.19, 95% CI = 1.07, 1.31). The age-adjusted lung cancer relative risk was elevated significantly (RR = 1.41, 95% CI = 1.19,1.66), which was slightly decreased to 1.31 (95% CI = 1.10, 1.54). For lung cancer mortality the age- and smoking-adjusted risks were significantly elevated for miners (RR = 2.67, 95% CI = 1.63, 4.37) and heavy equipment operators (RR = 2.60, 95% CI = 1.12, 6.06). Risks were also elevated, but not significantly, for railroad workers (RR = 1.59, 95% CI = 0.94, 2.69) and truck drivers (RR = 1.24, 95% CI = 0.93, 1.66). These risks were calculated with the Mantel-Haenszel method, controlling for age and smoking. Although the relative risk was nonsignificant for truck drivers, a small dose-response effect was observed when duration of DE exposure was examined. For drivers who worked for 1 to 15 years, the relative risk was 0.87,

whereas for drivers who worked for more than 16 years, the relative risk was 1.33 (95% CI = 0.64, 2.75). Relative risks for lung cancer were not presented for other occupations. Mortality analysis for other causes and DE exposure showed a significant excess of deaths ($p<0.05$) in the following categories: cerebrovascular disease, arteriosclerosis, pneumonia, influenza, cirrhosis of the liver, and accidents.

The main strength of this study is detailed information on smoking. The two main methodologic concerns are the representativeness of the study population and the quality of information on exposure. The sample, though very large, was composed of volunteers. Thus, the cohort was healthier and less frequently exposed to important risk factors such as smoking and alcohol. Self-administered questionnaires were used to obtain data on occupation and DE exposure. None of this information was validated. Nearly 20% of the individuals had an unknown exposure status to DE, and they experienced a higher mortality for all causes and lung cancer than both the DE exposed and unexposed groups. This could have introduced a substantial bias in the estimate of the association. Given that all DE exposure occupations, such as heavy equipment operators, truck drivers, and railroad workers, showed elevated lung cancer risk, this study is suggestive of a causal association. It should be noted that after adjusting for smoking, the RR reduced slightly from 1.41 to 1.31 and remained significant, indicating that observed excess of lung cancer was associated mainly with DE exposure.

7.2.1.7. *Garshick et al. (1988): A Retrospective Cohort Study of Lung Cancer and DE Exposure in Railroad Workers*

An earlier case-control study of lung cancer and DE exposure in U.S. railroad workers by these investigators had demonstrated a relative odds of 1.41 (95% CI = 1.06, 1.88) for lung cancer with 20 years of work in jobs with DE exposure. To confirm these results, a large retrospective cohort mortality study was conducted by the same investigators. Data sources for the study were the work records of the U.S. Railroad Retirement Board (RRB). The cohort was selected based on job titles in 1959, which was the year by which 95% of the locomotives in the United States were diesel powered. DE exposure was considered to be a dichotomous variable depending on yearly job codes between 1959 and death or retirement through 1980. Industrial hygiene evaluations and descriptions of job activities were used to classify jobs as exposed or unexposed to diesel emissions. A questionnaire survey of 534 workers at one of the railroads where workers were asked to indicate the amount of time spent in railroad locations, either near or away from sources of DE, was used to validate this classification. Workers selected for this survey were actively employed at the time of the survey, 40 to 64 years of age, started work between 1939 and 1949 in the job codes sampled in 1959, and eligible for railroad benefits. To qualify for benefits, a worker must have had 10 years or more of service with the railroad and

should not have worked for more than 2 years in a nonrailroad job after leaving railroad work. Workers with recognized asbestos exposure, such as repair of asbestos-insulated steam locomotive boilers, passenger cars, and steam pipes, or railroad building construction and repairs, were excluded from the job categories selected for study. However, a few jobs with some potential for asbestos exposure were included in the cohort, and the analysis was done both ways, with and without them.

The death certificates for all subjects identified in 1959 and reported by the RRB to have died through 1980 were searched. Twenty-five percent of them were obtained from the RRB and the remainder from the appropriate State departments of health. Coding of cause of death was done without knowledge of exposure history, according to the eighth revision of the ICD. If the underlying cause of death was not lung cancer, but was mentioned on the death certificate, it was assigned as a secondary cause of death, so that the ascertainment of all cases was complete. Workers not reported by the RRB to have died by December 31, 1980, were considered to be alive. Deceased workers for whom death certificates had not been obtained or, if obtained, did not indicate cause of death, were assumed to have died of unknown causes.

Proportional hazard models were fitted that provided estimates of relative risk for death caused by lung cancer using the partial likelihood method described by Cox, using the time dimension being the time since first entry into the cohort. The model also controlled for the birth year and the calendar time. The 95% confidence intervals were constructed using the asymptotic normality of the estimated regression coefficients of the proportional hazards model. Exposure was analyzed by DE-exposed jobs in 1959 and by cumulative number of years of DE exposure through 1980. Directly standardized rate ratios for deaths from lung cancer were calculated for DE exposed compared with unexposed for each 5-year age group in 1959. The standardized rates were based on the overall 5-year person-year time distribution of individuals in each age group starting in 1959. The only exception to this was between 1979 and 1980, when a 2-year person-year distribution was used. The Mantel-Haenszel analogue for person-year data was used to calculate 95% confidence intervals for the standardized rate ratios.

The cohort consisted of 55,407 workers, 19,396 of whom had died by the end of 1980. Death certificates were not available for 11.7% of all deaths. Of the 17,120 deaths for whom death certificates were obtained, 48.4% were attributable to diseases of the circulatory system, whereas 21% were attributable to all neoplasms. Of all neoplasms, 8.7% (1,694 deaths) were due to lung cancer. A higher proportion of workers in the younger age groups, mainly brakemen and conductors, were exposed to DE, while a higher proportion of workers in the older age groups were potentially exposed to asbestos. In a proportional hazards model, analyses by age in 1959 found a relative risk of 1.45 (95% CI = 1.11, 1.89) among the age group 40 to 44 years and a relative risk of 1.33 (95% CI = 1.03, 1.73) for the age group 45 to 49 years. Risk estimates in

the older age groups 50 to 54, 55 to 59, and 60 to 64 years were 1.2, 1.18, and 0.99, respectively, and were not statistically significant. The two youngest age groups in 1959 had workers with the highest prevalence and longest duration of DE exposure and lowest exposure to asbestos. When potential asbestos exposure was considered as a confounding variable in a proportional hazards model, the estimates of relative risk for asbestos exposure were all near null value and not significant. Analysis of workers exposed to DE in 1959 (n = 42,535), excluding workers with potential past exposure to asbestos, yielded relative risks of 1.57 (95% CI = 1.19, 2.06) and 1.34 (95% CI = 1.02, 1.76) in the 1959 age groups 40 to 44 years and 45 to 49 years. Directly standardized rate ratios were also calculated for each 1959 age group based on DE exposure in 1959. The results confirmed those obtained by using the proportional hazards model.

Relative risk estimates were then obtained using duration of DE exposure as a surrogate for dose. In a model that used years of exposure up to and including exposure in the year of death, no exposure duration-response relationship was obtained. When analysis was done by disregarding exposure in the year of death and 4 years prior to death, the risk of dying from lung cancer increased with the number of years worked in a diesel-exhaust-exposed job. In this analysis, exposure to DE was analyzed by exposure duration groups and in a model entering age in 1959 as a continuous variable. The workers with greater than 15 years of exposure had a relative risk of lung cancer of 1.72 (95% CI = 1.27, 2.33). The risk for 1 to 4 years of cumulative exposure was 1.20 (95% CI = 1.01, 1.44); for 5 to 9 years of cumulative exposure, it was 1.24 (95% CI = 1.06, 1.44); and for 10 to 14 years of cumulative exposure, it was 1.32 (95% CI = 1.13, 1.56).

The results of this study, demonstrating a positive association between DE exposure and increased lung cancer, are consistent with the results of the case-control study conducted by the same investigators in railroad workers dying of lung cancer from March 1981 through February 1982. This cohort study has addressed many of the weaknesses of the other epidemiologic studies. The large sample size (55,400) allowed sufficient power to detect small risks and also permitted the exclusion of workers with potential past exposure to asbestos. The stability of job career paths in the cohort ensured that of the workers 40 to 44 years of age in 1959 classified as DE-exposed, 94% of the cases were still in DE-exposed jobs 20 years later.

The main limitation of the study is the lack of quantitative data on exposure to DE in either individual workers or overall job categories. This is one of the few studies in which industrial hygiene measurements of DE were done. These measurements were correlated with job titles to divide the cohort in dichotomous exposure groups of exposed and nonexposed. This may have led to an underestimation of the risk of lung cancer because exposed groups included individuals with low to high exposure. The number of years exposed to DE was used as a surrogate for dose. The dose, based on duration of employment, was inaccurate because

individuals were working on steam and diesel locomotives during the transition period. It should be noted that the investigators only included exposures after 1959; the duration of exposure prior to 1959 was not known. If the categories of exposure to DE had been set up as no, low, moderate, and high exposure, the results would have been more meaningful, as would the dose-response relationship. Another limitation of this study was its inability to examine the effect of years of exposure prior to 1959 and latency. No adjustment for smoking was made in this study. However, an earlier case-control study done in the same cohort (Garshick et al., 1987) showed no significant difference in the risk estimate after adjusting for smoking. Despite these limitations, the results of this study indicate that occupational exposure to DE is associated with a modest risk (1.5) of lung cancer.

The data of this study were used by Crump et al. (1991) to explore the development of dose-response-based quantitative estimates of lung cancer associated with DE exposure by using diesel exposure estimate data from the industrial hygiene (IH) studies conducted by Hammond (1998) and Woskie et al. (1988a,b). These studies were conducted in conjunction with the Garshick et al. (1988) study. The Woskie et al. (1988a,b) IH studies were conducted in four small northern railroads where the workers were exposed to DE in the early 1980s, prior to the Garshick et al. (1988) epidemiologic study. A total of 39 job titles were identified by Woskie et al. (1988a,b), which were subsequently combined into 13 job groups and finally merged into 5 career exposure job codes as follows: brakers, conductors, and hostlers; clerks; engineers and firers; signal maintainers; and shop workers. The average exposure estimates were assigned to the cohort members by Crump et al. (1991) based on the job codes in 1959. Cumulative exposures were calculated using these average exposures for each job code. The exposures in the IH study by Hammond (1998) were defined as the concentrations of respirable-sized particles (RSP), the adjusted respirable particles (ARP) concentrations, and the adjusted extractable mass (AEM). The concentrations of ARP were estimated in the IH study by removing the particle contribution of environmental tobacco smoke (ETS). Crump et al. (1991) also used another index called total extractable material (TEX), which was the extractable RSP including the particle contribution of ETS. Using these four exposure indices and the regional climates for the United States, Crump et al. (1991) constructed various exposure metrics. They conducted more than 50 analyses based on calendar year, age in 1959, attained age, and five job codes identified in 1959: brakers, conductors, and hostlers; clerks; engineers and firers; signal maintainers; and shop workers; using the exposure metrics. Crump et al. (1991) used the U.S. general population age- and year-specific death rates for comparison and found that the relative risk can be positively or negatively related to the duration of exposure depending on how age was controlled in a model. Their use of the U.S. general population rates instead of the internal unexposed group of railroad workers that was used by Garshick et al. (1988) identified that the

death ascertainment between 1977 and 1980 as incomplete. The Crump et al. (1991) analysis, limited to 1959 through 1976, found an excess lung cancer risk similar to the subsequent Garshick analysis (letter from Garshick, Harvard Medical School, to Chao Chen, U.S. EPA, dated August 15, 1991).

Garshick conducted some additional analyses after confirming the underascertainment of deaths by RRB identified by Crump et al. (1991). He reported that the relationship between years of exposure, when adjusted for attained age and calendar year, was flat to negative depending upon which model was used. He also found that in the years 1977-1980 the death ascertainment was incomplete; approximately 20% to 70% of deaths were missing depending upon the calendar year. Garshick's analysis, based on job titles in 1959 and limited to deaths occurring through 1976, showed that even though the relative risk for all exposure groups was elevated, the youngest workers still had the highest risk of dying of lung cancer.

Crump (1999), on the other hand, reported that the negative dose-response continued to be upheld in his latest analysis when age was controlled more carefully and years of exposure quantified more accurately. Crump (1999) asserted that the negative dose-response trends for lung cancer observed either with the cumulative exposure or with duration of exposure may be due to underascertainment of deaths in the last 4 years of follow-up of the Garshick et al. (1988) study as well as incomplete follow-up in earlier years.

California EPA's (Cal EPA, 1998) Office of Environmental Health Hazard Assessment (OEHHA) used the same railroad worker data for its quantitative risk assessment. The five job categories defined by Woskie et al. (1988a,b) and used by Crump et al. (1991) were combined into three exposure categories: exposed (engineers and firers; brakers, conductors, and hostlers; collectively known as "train workers"), unexposed (clerks and signalmen), and uncertain exposure (shop workers). In its analysis, OEHHA found a positive dose-response and a steadily increasing risk of lung cancer with increasing duration of exposure by using age in 1959 but allowing for an interaction term of age and calendar year in the model. This positive dose-response finding was contradictory to the negative to flat dose-response findings of both Crump et al. (1991) and Garshick (letter from Garshick, Harvard Medical School, to Chao Chen, U.S. EPA, dated August 15, 1991).

The Health Effects Institute (HEI, 1999) convened an expert panel specifically to evaluate strengths and limitations of two epidemiologic studies that had some exposure data, for quantitative risk estimation and to resolve the discrepancies in the dose-response results reported by Garshick et al. (1988), Crump et al. (1991), and OEHHA (Cal EPA, 1998). In their evaluation of the epidemiologic study of railroad worker data for quantitative risk assessment, the panel conducted their own analysis of the Garshick et al. (1988) data. They excluded the last 4 years of follow-up (1977-1980) because of underascertainment of deaths during these years.

The panel categorized the duration of exposure in 12 categories that were basically the duration of employment. The exposure was assumed to be linearly increasing for 15 years prior to 1959. Lags of 5 and 10 years were also considered in the analysis. The job categories based on job held in 1959 were classified as clerks, signalmen, engineers and firers, conductors and brakers, hostlers, and shop workers. For final analysis these were collapsed into three groups: clerks and signalmen, train workers (engineers and firers, conductors and brakers, and hostlers), and shop workers. Seven different models were used. The panel's analysis revealed consistently elevated lung cancer risk for train workers compared with clerks for each duration of employment (1-4, 5-9, 10-14, 15-17, 18+) in years and that shop workers had an intermediate risk of lung cancer. Their analysis also revealed decreasing risk of lung cancer with increasing duration of employment in all three job categories. These findings were similar to those of Garshick (letter from Garshick, Harvard Medical School, to Chao Chen, U.S. EPA, dated August 15, 1991) and Crump et al. (1991).

In addition to differences in adjusting the age (age in 1959 versus attained age) in their respective analyses, these three investigators made different assumptions in estimating exposure patterns in these railroad workers. Garshick et al. (1988) assumed that there was no exposure to DE prior to 1959 and that the exposure to DE was constant throughout the period of follow-up, i. e., 1959 to 1980 (block exposure pattern). Crump et al. (1991) assumed that the exposure to DE increased steadily from 1945 to 1959 to the same level as assumed in the block exposure pattern by Garshick et al. (1988) and then remained constant from 1959 through 1980 (ramp exposure pattern). OEHHA assumed that the exposure increased steeply from 1945 to 1959. The peak exposure attained in 1959 according to OEHHA was twice as high as assumed in the block and ramp exposure patterns by Garshick et al. (1988) and Crump et al. (1991), respectively. The exposures then declined steeply from 1959 to reach the levels assumed in the block and ramp exposure patterns in 1980 (roof exposure pattern). The roof exposure pattern was constructed on the assumption that diesel engines were "smokier" in the past. A detailed discussion of divergent results observed by Crump and Cal EPA can be found in Chapter 8.

The panel discussed various possibilities for the negative dose-response found among train workers and to a lesser extent among shop workers. They asserted that several types of biases could affect the data, alone or in combination, and mask a true positive association. The biases enumerated by the panel were: unmeasured confounding by smoking, exposure to other sources of pollution, previous occupational exposures, exposure misclassification, use of "duration of employment" as a surrogate measure for exposure, healthy worker survivor effect, and differential or incomplete ascertainment of lung cancer deaths (for detailed discussion of how an individual bias affects the results, please see HEI, 1999). The panel concluded, "However, despite the reason or reasons why the relative risks in these data decrease with

duration of employment, the lack of a positive exposure-response association in the railroad worker cohort substantially weakens that study's potential to provide a reliable quantitative estimate of risk of exposure to diesel engine emissions." Thus, the panel recommended against using the current railroad worker data as the basis for quantitative risk assessment in ambient settings.

The panel also reported that the Garshick et al. study (1987, 1988) had several strengths, such as a large number of study subjects (55,407 subjects, including 1,694 lung cancer deaths in the cohort study and 1,256 lung cancer cases for the case-control study). The workers were employed in an industry where many of them were exposed to DE. Confounding by asbestos was handled by either excluding certain job categories from the analyses or controlling for it in the analyses. Confounding by smoking was controlled in the analyses of case-control study. The panel concluded that the overall results of the Garshick studies were generally consistent with findings of a weak association between exposure to DE and occurrence of lung cancer.

Thus, it should be noted that although the railroad worker data are unsuitable for quantitative risk assessment, they provide qualitative support for a positive association between exposure to DE and occurrence of lung cancer.

7.2.1.8. *Gustavsson et al. (1990): Lung Cancer and Exposure to DE Among Bus Garage Workers*

A retrospective mortality study (from 1952 to 1986), cancer incidence study (from 1958 to 1984), and nested case-control study were conducted among a cohort of 708 male workers from five bus garages in Stockholm, Sweden, who had worked for at least 6 months between 1945 and 1970. Thirteen individuals were lost to follow-up, reducing the cohort to 695.

Information was available on location of workplace, job type, and beginning and ending of work periods. Workers were traced through a computerized register of the living population, death and burial books, and data from the Stockholm city archives.

For the cohort mortality analyses, death rates of the general population of greater Stockholm were used. Death rates of occupationally active individuals, a subset of the general population of greater Stockholm, were used as a second comparison group to reduce the bias from "healthy worker effect." Mortality analysis was conducted using the "occupational mortality analysis program" (OCMAP-PC). For cancer incidence analysis, the "epidemiology in Linköping" (EPILIN) program was used, with the incidence rates obtained from the cancer registry.

For the nested case-control study, both dead and incident primary lung cancers identified in the register of cause of deaths and the cancer register were selected. Six controls matched on age ± 2 years, selected from the noncases at the time of the diagnosis of cases, were drawn at

random without replacements. Matched analyses were done to calculate odds ratios using conditional logistic regression. The EGRET and Epilog programs were used for these analyses.

DE and asbestos exposure assessments were performed by industrial hygienists based on the intensity of exposure to DE and asbestos, specific for workplace, work task, and calendar time period. A DE exposure assessment was based on (1) amount of emission (number of buses, engine size, running time, and type of fuel), (2) ventilatory equipment and air volume of the garages, and (3) job types and work practices. Based on detailed historical data and very few actual measurements, relative exposures were estimated (these were not absolute exposure levels). The scale was set to 0 for unexposed and 1 for lowest exposure, with each additional unit increase corresponding to a 50% increase in successive intensity (i.e., 1.5, 2.25, 3.38, and 5.06).

Based on personal sampling of asbestos during 1987, exposures were estimated and time-weighted annual mean exposures were classified on a scale of three degrees (0, 1, and 2). Cumulative exposures for both DE and asbestos were calculated by multiplying the level of exposure by the duration of every work period. An exposure index was calculated by adding for every individual contribution from all work periods for both DE and asbestos. Four DE index classes were created: 0 to 10, 10 to 20, 20 to 30, and >30. The four asbestos index classes were 0 to 20, 20 to 40, 40 to 60, and >60. The cumulative exposure indices were used for the nested case-control study.

Excesses were observed for all cancers and some other site-specific cancers using both comparison populations for the cohort mortality study, but none of them was statistically significant. Based on 17 cases, SMRs for lung cancer were 122 and 115 using Stockholm occupationally active and general population, respectively. No dose-response was observed with increasing cumulative exposure in the mortality study. The cancer incidence study reportedly confirmed the mortality results (results not given).

The nested case-control study, on the other hand, showed increasing risk of lung cancer with increasing exposure. Using 0 to 10 DE exposure index as the comparison group yielded RRs of 1.34 (95% CI = 1.09 to 1.64), 1.81 (95% CI = 1.20 to 2.71), and 2.43 (95% CI = 1.32 to 4.47) for the DE indices 10 to 20, 20 to 30, and >30, respectively. The study was based on 17 cases and 6 controls for each case matched on age ± 2 years. Adjustment for asbestos exposure did not change the lung cancer risk for DE.

The main strength of this study is the detailed exposure matrices constructed for both DE and asbestos exposure, although they were based primarily on job tasks and very few actual measurements. There are a few methodological limitations to this study. The cohort is small and there were only 17 lung cancer deaths; thus the power is low. Exposure or outcome may be misclassified, although any resulting bias in the relative risk estimates is likely to be toward

unity, because exposure classification was done independently of the outcome. Although the analysis by dose indices was done, no latency analysis was performed. Although data on smoking were missing, it is unlikely to confound the results because this is a nested case-control study; therefore, smoking is not likely to be different among the individuals irrespective of their exposure status to DE. Overall, this study provides some support to the excess lung cancer results found earlier among populations exposed to DE.

7.2.1.9. *Hansen (1993): A Follow-up Study on the Mortality of Truck Drivers*

This is a retrospective cohort mortality study of unskilled male laborers, ages 15 to 74 years, in Denmark, identified from a nationwide census file of November 9, 1970. The exposed group included all truck drivers employed in the road delivery or long-haul business (14,225). The unexposed group included all laborers in certain selected occupational groups considered to be unexposed to fossil fuel combustion products and to resemble truck drivers in terms of work-related physical demands and various personal background characteristics (43,024).

Through automatic record linkage between the 1970 census register (the Central Population Register 1970 to 1980) and the Death Certificate Register (1970 to 1980), the population was followed for cause-specific mortality or emigration up to November 9, 1980. Expected number of deaths among truck drivers was calculated by using the 5-year age group and 5-year time period death rates of the unexposed group and applying them to the person-years accumulated by truck drivers. ICD Revision 8 was used to code the underlying cause of death. Test-based CIs were calculated using Miettinen's method. A Poisson distribution was assumed for the smaller numbers, and CI was calculated based on exact Poisson distribution (Ciba-Geigy). Total person-years accrued by truck drivers were 138,302, whereas for the unexposed population, they were 407,780. There were 627 deaths among truck drivers and 3,811 deaths in the unexposed group. Statistically significant excesses were observed for all cancer mortality (SMR = 121, 95% CI = 104 to 140); cancer of respiratory organs (SMR = 160, 95% CI = 128 to 198), which was due mainly to cancer of bronchus and lung (SMR = 160, 95% CI = 126 to 200); and multiple myeloma (SMR = 439, 95% CI = 142 to 1,024). When lung cancer mortality was further explored by age groups, excesses were observed in most age groups (30 to 39, 45 to 49, 50 to 54, 55 to 59, 60 to 64, and 65 to 74), but there were small numbers of deaths in each group when stratified by age, and the excesses were statistically significant for the 55 to 59 (SMR = 229, O = 19, 95% CI = 138 to 358) and 60 to 64 (SMR = 227, O = 22, 95% CI = 142 to 344) age groups only.

As acknowledged by the author, the study has quite a few methodologic limitations. The exposure to DE is assumed in truck drivers based on use of diesel-powered trucks, but no validation of qualitative or quantitative exposure is attempted. It is also not known whether any

of these truck drivers or any other laborers had changed jobs after the census of November 9, 1970, thus creating potential misclassification bias in exposure to DE. The truck drivers and the unexposed laborers were from the same socioeconomic class and may have the same smoking habits. Still, the lack of information on smoking data and a 36% rural population (usually consuming less tobacco) in the unexposed group may potentially confound the lung cancer results. However, a population survey carried out in 1988 showed very little difference in smoking habits of residents of rural areas and the total Danish male population. The investigator reports that diesel trucks were introduced in Denmark after World War II, and since the late 1940s the majority of the Danish fleet has been composed of diesel trucks. Consequently, even though the follow-up period is relatively short, the truck drivers may have had exposure to DE for 20 to 30 years. Therefore, the finding of excess lung cancer in this study is consistent with the findings of other truck driver studies.

7.2.1.10. ***Saverin et al. (1999): DE and Lung Cancer Mortality in Potash Mining***

This is a cohort mortality study conducted in male potash miners in Germany. The mines began using mobile diesel-powered vehicles in 1969 and 1970. Miners who had worked underground for at least 1 year after 1969 to 1991, when the mines were closed, were followed from 1970 to 1994. A total of 5,981 individuals were identified from the medical records by a team of medical personnel familiar with the mining technology. A total of 5,536 were eligible for follow-up after 5.5% were excluded due to implausible or incomplete work history and 1.9% were lost to follow-up. A subcohort of 3,258 miners who had worked for at least 10 years underground (80% had held a single job) was also identified. The miners' biannual medical examination records were used to extract the information about personal data, smoking data, and pre-mining occupation, and to reconstruct a chronology of workplaces occupied by the worker since hire for each person.

Exposure categories were defined as production, maintenance, and workshop, roughly corresponding to high, medium, and low. Concentrations of total carbon, including elemental and organics, were measured in the airborne fine dust in 1992. A total of 255 samples covering all workplaces was obtained. Most were personal dust samples; some were area dust samples. Cumulative exposure was calculated for each miner, for each year of observation, using the work chronology and the work category. For the workshop category years of employment were considered as exposure time; for production and maintenance years of employment was weighted by a factor of 5/8, since these workers for an 8-hour shift worked for only 5 hours underground. As neither the mining technology nor the type of machinery used had changed substantially from 1970 to 1992, the exposure measurements were considered to represent the exposures throughout the study period. Accrued person-years were classified into cumulative

exposures and were expressed in intervals of 0.5 ymg/m^3. Both the exposure data and the smoking data obtained from the medical files were validated by personal interviews with 1,702 cohort members. Death certificates were obtained from local health centers for 94.4% of deceased members. Autopsy data were available for 13% of the deceased. Internal comparison was done between production and workshop categories. Using East German general male population rates, SMRs were computed for the total cohort as well as the subcohort. Analyses were done using Poisson and Cox regression models.

The concentrations of total carbon for production, maintenance, and workshop categories were 0.39 mg/m^3, 0.23 mg/m^3, and 0.12 mg/m^3, respectively. The cumulative exposure ranged from 0.25 ymg/m^3 to 6.25 ymg/m^3. The regression analysis showed that the cohort's smoking habits were homogenous and that smoking had an even distribution over cumulative exposure.

A total of 424 deaths were observed for the entire cohort (SMR = 54). The all-cancer deaths were 133, of which 38 were from lung cancer (SMR = 78). Analysis for the subcohort using the internal comparison group of low exposure (workshop category, mean cumulative exposure = 2.12 ymg/m^3) RR of 2.17 (95% CI = 0.79, 5.99) was found for the production category (mean cumulative exposure = 4.38 ymg/m^3). The relative risks for lung cancer for 20 years of exposure in the production category (highest exposure = cumulative exposure of 4.9 ymg/m^3) were calculated using Poisson and Cox regression methods. RRs of 1.16 and 1.68 were observed for the total cohort, while RRs of 1.89 and 2.7 were observed for the subcohort by Poisson and Cox regression methods respectively.

The main strengths of the study are the information available on DE exposure and smoking. Although these potash miners were exposed to salt dust and nitric gases, exposures to other confounders such as heavy metals and radon were absent. Smoking does not seem to be a confounder in this study but cannot be completely ruled out. Unfortunately, the age distribution of the cohort is not available. Since there were only 424 deaths in 25 years of follow-up in this cohort of 5,536, it appears that the cohort is young. Although lung cancer risk was elevated by twofold in the production category of the subcohort of miners who had worked for at least 10 years underground at the same job for 80% of their time and did not have more than 3 jobs, it was not statistically significant. The follow-up period for this study was 25 years, but the cohort members could have entered the cohort any time between 1970 and 1990, as long as they worked underground for a year, i.e., they could have worked in the mines for 1 year to 21 years. Thus, the authors may not have had enough follow-up or latency to observe the lung cancer excess. Despite these limitations, the results of this study provide suggestive evidence for the causal association between DE and excess lung cancer.

Table 7-1 summarizes the above cohort studies.

Table 7-1. Epidemiologic studies of the health effects of exposure to DE: cohort mortality studies

Authors	Population studied	DE exposure assessment	Results	Limitations
Waller (1981)	Approximately 20,000 male London transportation workers Aged 45 to 64 years 25 years follow-up (1950-1974)	Five job categories used to define exposure Environmental B[*a*]P concentrations measured in 1957 and 1979	SMR = 79 for lung cancer for the total cohort SMRs for all five job categories were less than 100 for lung cancer	Exposure measurement of B[*a*]P showed very little difference between inside and outside the garage Incomplete information on cohort members No adjustment for confounding such as other exposures, cigarette smoking, etc. No latency analysis
Howe et al. (1983)	43,826 male pensioners of the Canadian National Railway Company Mortality between 1965 and 1977 among these pensioners was compared with mortality of general Canadian population	Exposure groups classified by a group of experts based on occupation at the time of retirement Three exposure groups: Nonexposed Possibly exposed Probably exposed	RR = 1.2 (p=0.013) and RR = 1.3 (p=0.001) for lung cancer for possible and probable exposure, respectively A highly significant dose-response relationship demonstrated by trend test (p<0.001)	Incomplete exposure assessment due to lack of lifetime occupational history Mixed exposures to coal dust/combustion products and DE No validation of method was used to categorize exposure Lack of data on smoking but use of internal comparison group to compute RRs minimizes the potential confounding by smoking No latency analysis

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Table 7-1. Epidemiologic studies of the health effects of exposure to DE: cohort mortality studies (continued)

Authors	Population studied	DE exposure assessment	Results	Limitations
Rushton et al. (1983)	8,490 male London transport maintenance workers Mortality of workers employed for 1 continuous year between January 1, 1967, and December 31, 1975, was compared with mortality of general population of England and Wales	100 different job titles were grouped in 20 broad categories The categories were not ranked for DE exposure	SMR = 133 (p<0.03) for lung cancer in the general hand job group Several other job categories showed SS increased SMRs for several other sites based on fewer than five cases	Ill-defined DE exposure without any ranking Average 6-year follow-up i.e., not enough time for lung cancer latency No adjustment for confounders
Wong et al. (1985)	34,156 male heavy construction equipment operators Members of the local union for at least 1 year between January 1, 1964, and December 1, 1978	20 functional job titles grouped into three job categories for potential exposure Exposure groups (high, low, and unknown) based on job description and proximity to source of DE emissions	SMR = 166 (p<0.05) for liver cancer for total cohort SMR = 343 (observed = 5, p<0.05) for lung cancer for high-exposure bulldozer operators with 15-19 years of membership, 20+ years of follow-up SMR = 119 (observed = 141, p<0.01) for workers with no work histories	No validation of exposure categories, which were based on surrogate information Incomplete employment records Employment history other than from the union not available 15 year follow-up may not provide sufficient time for lung cancer latency No data on confounders such as other exposures, alcohol, smoking, etc.
Edling et al. (1987)	694 male bus garage employees Follow-up from 1951 through 1983 Mortality of these men was compared with mortality of general population of Sweden	Three exposure groups based on job titles: High exposure, bus garage workers Intermediate exposure, bus drivers Low exposure, clerks	No SS differences were observed between observed and expected for any cancers by different exposure groups	Small sample size No validation of exposure No data on confounders such as other exposures, smoking, etc.

Table 7-1. Epidemiologic studies of the health effects of exposure to DE: cohort mortality studies (continued)

Authors	Population studied	DE exposure assessment	Results	Limitations
Boffetta and Stellman (1988)	46,981 male volunteers enrolled in the American Cancer Society's Prospective Mortality Study of Cancer in 1982 Aged 40 to 79 years at enrollment First 2-year follow-up	Self-reported occupations were coded into 70 job categories Employment in high DE exposure jobs were compared with nonexposed jobs	Total mortality (SS) elevated for railroad workers (RR=1.43), heavy equipment operators (RR=1.7), miners (RR=1.34), and truck drivers (RR=1.19) Lung cancer mortality (SS) adjusted for age & smoking, elevated for total cohort (RR=1.31), miners (RR=2.67), and heavy equipment operators (RR=2.6) Lung cancer mortality (SNS) elevated among railroad workers and truck drivers Truck drivers also showed a dose-response	Exposure information based on self-reported occupation for which no validation was done Volunteer population, probably healthy population

Table 7-1. Epidemiologic studies of the health effects of exposure to DE: cohort mortality studies (continued)

Authors	Population studied	DE exposure assessment	Results	Limitations
Garshick et al. (1988)	55,407 white male railroad workers Aged 40 to 64 years in 1959 Started work 10-20 years earlier than 1959	Industrial hygiene data correlated with job titles to dichotomize the jobs as "exposed" or "not exposed"	RR = 1.45 (40-44 year age group) RR = 1.33 (45-49 year age group) Both SS After exclusion of workers exposed to asbestos RR = 1.57 (40-44 year age group) RR = 1.34 (45-49 year age group) Both SS	Years of exposure used as surrogate for dose Not possible to separate the effect of time since first exposure and duration of exposure Lack of smoking data but case-control study showed very little difference between those exposed to DE versus those who were not
Garshick (ltr to Chao Chen, EPA, dtd 8/15/91			Dose response indicated by increasing lung cancer risk with increasing cumulative exposure Further analysis using attained age, limited through 1976 showed youngest workers still had the highest risk	
Crump et al. (1991)	Reanalysis of Garshick et al., 1988 data		Dose response found to be positive or negative depending upon how the age was controlled in the model	
Crump (1999)			Negative dose-response upheld in the latest analysis	
California EPA (1998)	Reanalysis of Garshick et al., 1988		Positive dose response using age at 1959 and interaction term of age & calendar year	

Table 7-1. Epidemiologic studies of the health effects of exposure to DE: cohort mortality studies (continued)

Authors	Population studied	DE exposure assessment	Results	Limitations
Gustavsson et al. (1990)	695 male workers from 5 bus garages in Stockholm, Sweden, who had worked for 6 months between 1945 and 1970 34 years follow-up (1952-1986) Nested case-control study 17 cases, six controls for each case matched on age ± 2 years	Four DE indices were created: 0 to 10, 10 to 20, 20-30, and >30 based on job tasks and duration of work	SNS SMRs of 122 and 115 (OA and GP), respectively Case-control study results showed dose response: RR = 1.34 (10 to 20) RR = 1.81 (20 to 30) RR = 2.43 (>30) All SS with 0-10 as comparison group	Exposure matrix based on job tasks (not on actual measurements) Small cohort, hence low power Lack of smoking data is unlikely to confound the results since it is a nested case-control study
Hansen (1993)	Cohort of 57,249 unskilled laborers, ages 15 to 74, in Denmark (nationwide census file) November 9, 1970 Follow-up through November 9, 1980	DE exposure assumed based on diesel-powered trucks	SS SMRs for lung cancer : SMR = 160 for total population SMR = 229 for age 55-59 years SMR = 227 for age 60-64 years	No actual exposure data available Lack of smoking data but population survey showed very little difference between rural and urban smoking habits Job changes may have occurred from laborer to driver Short follow-up period
Saverin et al. (1999)	Cohort of 5,536 potash miners who had worked underground for at least 1 year after 1969 Subcohort of 3,258 who had worked for at least 10 years underground Follow-up from 1970 to 1994	DE exposure categories defined as: production (high) maintenance (medium) workshop (low) 225 air samples obtained: for total carbon, organics, & fine dust in 1992	SNS increased RRs adjusted for smoking: 1.68 and 2.7 for total cohort & subcohort, respectively	Small, young cohort Few deaths No latency analysis

Abbreviations: RR = relative risk; SMR = standardized mortality ratio; SNS = statistically nonsignificant; SS = statistically significant; O = occupationally active; GP = general population.

7.2.2. Case-Control Studies of Lung Cancer

7.2.2.1. *Hall and Wynder (1984): A Case-Control Study of DE Exposure and Lung Cancer*

Hall and Wynder (1984) conducted a case-control study of 502 male lung cancer cases and 502 controls without tobacco-related diseases that examined an association between occupational DE exposure and lung cancer. Histologically confirmed primary lung cancer patients who were 20 to 80 years old were ascertained from 18 participating hospitals in 6 U.S. cities 12 months prior to the interview. Eligible controls, patients at the same hospitals without tobacco-related diseases, were matched to cases by age (± 5 years), race, hospital, and hospital room status. The number of male lung cancer cases interviewed totaled 502, which was 64% of those who met the study criteria for eligibility. Of the remaining 36%, 8% refused, 21% were too ill or had died, and 7% were unreliable. Seventy-five percent of eligible controls completed interviews. Of these interviewed controls, 49.9% were from the all-cancers category, whereas 50.1% were from the all-noncancers category. All interviews were obtained in hospitals to gather detailed information on smoking history, coffee consumption, artificial sweetener use, residential history, and abbreviated medical history as well as standard demographic variables. Occupational information was elicited by a question on the usual lifetime occupation and was coded by the abbreviated list of the U.S. Bureau of Census Codes. The odds ratios were calculated to evaluate the association between DE exposure and risk of lung cancer incidence. Summary odds ratios were computed by the Mantel-Haenszel method after adjusting for potential confounding by age, smoking, and socioeconomic class. Two-sided, 95% confidence intervals were computed by Woolf's method. Occupational exposure to DE was defined by two criteria. First, occupational titles were coded "probably high exposure" as defined by the industrial hygiene standards established for the various jobs. The job titles included under this category were warehousemen, bus and truck drivers, railroad workers, and heavy equipment operators and repairmen. The second method used the National Institute for Occupational Safety and Health (NIOSH) criteria to analyze occupations by diesel exposure. In this method, the estimated proportion of exposed workers was computed for each occupational category by using the NIOSH estimates of the exposed population as the numerator and the estimates of individuals employed in each occupational category from the 1970 census as the denominator. Occupations estimated to have at least 20% of their employees exposed to DE were defined as "high exposure," those with 10% to 19% of their employees exposed were defined as "moderate exposure," and those with less than 10% of their employees exposed were defined as "low exposure."

Cases and controls were compared with respect to exposure. The relative risk was 2.0 (95% CI = 1.2, 3.2) for those workers who were exposed to DE versus those who were not. The risk, however, decreased to a nonsignificant 1.4 when the data were adjusted for smoking.

Analysis by NIOSH criteria found a nonsignificant relative risk of 1.7 in the high- exposure group. There were no significantly increased cancer risks by occupation either by the first method or by the NIOSH method. To assess any possible synergism between DE exposure and smoking, the lung cancer risks were calculated for different smoking categories. The relative risks were 1.46 among nonsmokers and ex-smokers, 0.82 among current smokers of <20 cigarettes/day, and 1.3 among current smokers of 20+ cigarettes/day, indicating a lack of synergistic effects.

The major strength of this study is the availability of a detailed smoking history for all the study subjects. However, this is offset by lack of DE exposure measurements, use of a poor surrogate for exposure, and lack of consideration of latency period. Information was collected on only one major lifetime occupation, and it is likely that those workers who had more than one major job may not have reported the occupation with the heaviest DE exposures. Furthermore, the exposure categories based on job titles were broad, and thus would have made a true effect of DE difficult to detect.

7.2.2.2. *Damber and Larsson (1987): Occupation and Male Lung Cancer, a Case-Control Study in Northern Sweden*

A case-control study of lung cancer was conducted in northern Sweden to determine the occupational risk factors that could explain the large geographic variations of lung cancer incidence in that country. The study region comprised the three northernmost counties of Sweden, with a total male population of about 390,000. The rural municipalities, with 15% to 20% of the total population, have forestry and agriculture as dominating industries, and the urban areas have a variety of industrial activities (mines, smelters, steel factories, paper mills, and mechanical workshops). All male cases of lung cancer reported to the Swedish Cancer Registry during the 6-year period between 1972 and 1977 who had died before the start of the study were selected. Of 604 eligible cases, 5 did not have microscopic confirmation, and in another 5 the diagnosis was doubtful, but these cases were included nevertheless. Cases were classified as small-cell carcinomas, squamous cell carcinomas, adenocarcinomas, and other types. For each case a dead control was drawn from the National Death Registry matched by sex, year of death, age, and municipality. Deaths in controls classified as lung cancer and suicides were excluded. A living control matched to the case by sex, year of birth, and municipality was also drawn from the National Population Registry. Postal questionnaires were sent to close relatives of cases and dead controls, and to living controls themselves to collect data on occupation, employment, and smoking habits. Replies were received from 589 cases (98%), 582 surrogates of dead controls (96%), and 453 living controls (97%).

Occupational data were collected on occupations or employment held for at least 1 year and included type of industry, company name, task, and duration of employment. Supplementary telephone interviews were performed if occupational data were lacking for any period between age 20 and time of diagnosis. Data analysis involved calculation of the odds ratios by the exact method based on the hypergeometric distribution and the use of a linear logistic regression model to adjust for the potential confounding effects of smoking. Separate analyses were performed with dead and living controls, and on the whole there was good agreement between the two control groups. A person who had been active for at least 1 year in a specific occupation was in the analysis assigned to that occupation.

Using dead controls, the odds ratios adjusted for smoking were 1.0 (95% CI = 0.7, 1.5) and 2.7 (95% CI = 1.0, 8.1) for professional drivers (≥ 1 year of employment) and underground miners (≥ 1 year of employment), respectively. For 20 or more years of employment in those occupations, the odds ratios adjusted for smoking were 1.2 (95% CI = 0.9, 2.6) and 9.8 (95% CI = 1.5, 414). These were the only two occupations listed with potential DE exposure. An excess significant risk was detected for copper smelter workers, plumbers, electricians, and asbestos workers, as well as concrete and asphalt workers. All the odds ratios were calculated by adjusting for age, smoking, and municipality. A comparison with the live controls resulted in the odds ratios being lower than those observed with dead controls, and none were statistically significant in this comparison.

This study did not detect any excess risk of lung cancer for professional drivers, who, among all the occupations listed, had the most potential for exposure to motor vehicle exhaust. However, it is not known whether these drivers were exposed exclusively to gasoline exhaust, DE, or varying degrees of both. An excess risk was detected for underground miners, but it is not known if this was due to diesel emissions from engines or from radon daughters in poorly ventilated mines. Although a high response rate (98%) was obtained by the postal questionnaires, the use of surrogate respondents is known to lead to misclassification errors that can bias the results in either direction.

7.2.2.3. *Lerchen et al. (1987): Lung Cancer and Occupation in New Mexico*

This is a population-based case-control study conducted in New Mexico that examined the association between occupation and occurrence of lung cancer in Hispanic and non-Hispanic whites. Cases involved residents of New Mexico, 25 through 84 years of age, and diagnosed between January 1, 1980, and December 31, 1982, with primary lung cancer, excluding bronchioalveolar carcinoma. Cases were ascertained through the New Mexico Tumor Registry, which is a member of the Surveillance Epidemiology and End Results (SEER) Program of the National Cancer Institute. Controls were chosen by randomly selecting residential telephone

numbers and, for those over 65 years of age, from the Health Care Financing Administration's roster of Medicare participants. They were frequency-matched to cases for sex, ethnicity, and 10-year age category with a ratio of 1.5 controls per case. The 506 cases (333 males and 173 females) and 771 controls (499 males and 272 females) were interviewed, with a nonresponse rate of 11% for cases. Next of kin provided interviews for 50% and 43% of male and female cases, respectively. Among controls, only 2% of the interviews were provided by next of kin for each sex. Data were collected by personal interviews conducted by bilingual interviewers in the participants' homes. A lifetime occupational history and a self-reported history of exposure to specific agents were obtained for each job held for at least 6 months since age 12. Questions were asked about the title of the position, duties performed, location and nature of industry, and time at each job title. A detailed smoking history was also obtained. The variables on occupational exposures were coded according to the Standard Industrial Classification scheme by a single person and reviewed by another. To test the hypothesis about high-risk jobs for lung cancer, the principal investigator created an a priori listing of suspected occupations and industries by a two-step process involving a literature review for implicated industries and occupations. The principal investigator also determined the appropriate Standard Industrial Classification and Standard Occupational Codes associated with job titles. For four agents—asbestos, wood dust, DE, and formaldehyde—the industries and occupations determined to have exposure were identified, and linking of specific industries and occupations was based on literature review and consultation with local industrial hygienists.

The relative odds were calculated for suspect occupations and industries, classifying individuals as ever employed for at least 1 year in an industry or occupation and defining the reference group as those subjects never employed in that particular industry or occupation. Multiple logistic regression models were used to control simultaneously for age, ethnicity, and smoking status. For occupations with potential DE exposure, the analysis showed no excess risks for diesel engine mechanics and auto mechanics. Similarly, when analyzed by exposure to specific agents, the odds ratio (OR) adjusted for age, smoking, and ethnicity was not elevated for DE fumes (OR = 0.6, 95% CI = 0.2, 1.6). Significantly elevated ORs were found for uranium miners (OR = 2.8), underground miners (OR = 2.4), construction workers, and welders (OR = 4.3). No excess risks were detected for the following industries: shipbuilding, petroleum refining, printing, blast furnace, and steel mills. No excess risks were detected for the following occupations: construction workers, painters, plumbers, paving equipment operators, roofers, engineers and firemen, woodworkers, and shipyard workers. Females were excluded from detailed analysis because none of the Hispanic female controls had been employed in high-risk jobs; among the non-Hispanic white controls, employment in a high-risk job was recorded for at

least five controls for only two industries, construction and painting, for which the OR were not significantly elevated. Therefore, the analyses were presented for males only.

Among the many strengths of this study are its population-based design, high participation rate, detailed smoking history, and the separate analysis done for two ethnic groups, southwestern Hispanic and non-Hispanic white males. The major limitations pertain to the occupational exposure data. Job titles obtained from occupational histories were used as proxy for exposure status, but these were not validated. Further, for nearly half the cases, next of kin provided occupational histories. The authors acknowledge the above sources of bias but state without substantiation that these biases would not strongly affect their results. They also did not use a job exposure matrix to link occupations to exposures and did not provide details on the method they used to classify individuals as DE exposed based on reported occupations. The observed absence of an association for exposure to asbestos, a well-established lung carcinogen, may be explained by the misclassification errors in exposure status or by sample size constraints (not enough power). Likewise, the association for DE reported by only 7 cases and 17 controls also may have gone undetected because of low power. In conclusion, there is insufficient evidence from this study to confirm or refute an association between lung cancer and DE exposure.

7.2.2.4. *Garshick et al. (1987): A Case-Control Study of Lung Cancer and DE Exposure in Railroad Workers*

An earlier pilot study of the mortality of railroad workers by the same investigators (Schenker et al., 1984) found a moderately high risk of lung cancer among workers exposed to DE compared with those who were not. Based on these findings the investigators conducted a case-control study of lung cancer in the same population. The population base for this case-control study was approximately 650,000 active and retired male U.S. railroad workers with 10 years or more of railroad service who were born in 1900 or later. The U.S. Railroad Retirement Board (RRB), which operates the retirement system, is separate from the Social Security System, and to qualify for the retirement or survivor benefits the workers had to acquire 10 years or more of service. Information on deaths that occurred between March 1, 1981, and February 28, 1982, was obtained from the RRB. For 75% of the deceased population, death certificates were obtained from the RRB, and, for the remaining 25%, they were obtained from the appropriate State departments of health. Cause of death was coded according to the eighth revision of the ICD. The cases were selected from deaths with primary lung cancer, which was the underlying cause of death in most cases. Each case was matched to two deceased controls whose dates of birth were within 2.5 years of the date of birth of the case and whose dates of death were within 31 days of the date of death noted in the case. Controls were selected randomly from workers

who did not have cancer noted anywhere on their death certificates and who did not die of suicide or of accidental or unknown causes.

Each subject's work history was determined from a yearly job report filed by his employer with the RRB from 1959 until death or retirement. The year 1959 was chosen as the effective start of DE exposure for this study since by this time 95% of the locomotives in the United States were diesel powered. Investigators acknowledge that because the transition to diesel-powered engines took place in the early 1950s, some workers had additional exposure prior to 1959; however, if a worker had died or retired prior to 1959, he was considered unexposed. Exposure to DE was considered to be dichotomous for this study, which was assigned based on an industrial hygiene evaluation of jobs and work areas. Selected jobs with and without regular DE exposure were identified by a review of job title and duties. Personal exposure was assessed in 39 job categories representative of workers with and without DE exposure. Those jobs for which no personal sampling was done were considered exposed or unexposed based on similarities in job activities and work locations and by degree of contact with diesel equipment. Asbestos exposure was categorized based on jobs held in 1959, or on the last job held if the subject retired before 1959. Asbestos exposure in railroads occurred primarily during the steam engine era and was related mostly to the repair of locomotive steam boilers that were insulated with asbestos. Smoking history information was obtained from the next of kin.

Death certificates were obtained for approximately 87% of the 15,059 deaths reported by the RRB, from which 1,374 cases of lung cancer were identified. Fifty-five cases of lung cancer were excluded from the study for either incomplete data (20) or refusal by two States to use information on death certificates to contact the next of kin. Successful matching to at least one control with work histories was achieved for 335 (96%) cases ≤64 years of age at death and 921 (95%) cases ≥65 years of age at death. In both age groups, 90% of the cases were matched with two controls. There were 2,385 controls in the study; 98% were matched within ± 31 days of the date of death, whereas the remaining 2% were matched within 100 days. Deaths from diseases of the circulatory system predominated among controls. Among the younger workers, approximately 60% had exposure to DE, whereas among older workers, only 47% were exposed to DE.

Analysis by a regression model, in which years of DE exposure were the sum total of the number of years in diesel-exposed jobs, used as a continuous exposure variable, yielded an odds ratio of lung cancer of 1.39 (95% CI = 1.05, 1.83) for >20 years of DE exposure in the ≤64 years of age group. After adjustment for asbestos exposure and lifetime smoking (pack-years), the odds ratio was 1.41 (95% CI = 1.06, 1.88). Both crude odds ratio and asbestos exposure as well as lifetime smoking-adjusted odds ratio for the ≥65 years of age group were not significant.

Increasing years of DE exposure, categorized as ≥20 diesel years and 5 to 19 diesel years, with 0 to 4 years as the referent group, showed significantly increased risk in the ≤64 years of age group after adjusting for asbestos exposure and pack-year category of smoking. For individuals who had ≥20 years of DE exposure, the odds ratio was 1.64 (95% CI = 1.18, 2.29), whereas among individuals who had 5 to 19 years of DE exposure, the odds ratio was 1.02 (95% CI = 0.72, 1.45). In the ≥65 years of age group, only 3% of the workers were exposed to DE for more than 20 years. Relative odds for 5 to 19 years and ≥20 years of diesel exposure were less than 1 (p>0.01) after adjusting for smoking and asbestos exposure.

Alternative models to explain past asbestos exposure were tested. These were variables for regular and intermittent exposure groups and an estimate of years of exposure based on estimated years worked prior to 1959. No differences in results were seen. The interactions between DE exposure and the three pack-year categories (<50, >50, and missing pack-years) were explored. The cross-product terms were not significant. A model was also tested that excluded recent DE exposure occurring within the 5 years before death and gave an odds ratio of 1.43 (95% CI = 1.06, 1.94), adjusted for cigarette smoking and asbestos exposure, for workers with 15 years of cumulative exposure. For workers with 5 to 14 years of cumulative exposure, the OR were not significant.

The many strengths of the study are consideration of confounding factors such as asbestos exposure and smoking; classification of DE exposures by job titles and industrial hygiene sampling; exploration of interactions between smoking, asbestos exposure, and DE exposure; and good ascertainment (87%) of death certificates from the 15,059 deaths reported by the RRB.

The investigators also recognized and reported the following limitations: overestimation of cigarette consumption by surrogate respondents, which may have exaggerated the contribution of smoking to lung cancer risk, and use of the Interstate Commerce Commission (ICC) job classification as a surrogate for exposure, which may have led to misclassification of DE exposure jobs with low intensity and intermittent exposure, such as railroad police and bus drivers, as unexposed. These two limitations would result in underestimation of the lung cancer risk. This source of error could have been avoided if DE exposures were categorized by a specific dose range associated with a job title that could have been classified as heavy, medium, low, and zero exposure instead of a dichotomous variable. The use of death certificates to identify cases and controls may have resulted in misclassification. Controls may have had undiagnosed primary lung cancer, and lung cancer cases might have been secondary lesions misdiagnosed as primary lung cancer. However, the investigators quote a third National Cancer Survey report in which the death certificates for lung cancer were coded appropriately in 95% of the cases. Last, as in all previous studies, there is a lack of data on the contribution of unknown

occupational or environmental exposures and passive smoking. In conclusion, this study provides strong evidence that occupational DE emission exposure increases the risk of lung cancer.

7.2.2.5. *Benhamou et al. (1988): Occupational Risk Factors of Lung Cancer in a French Case-Control Study*

This is a case-control study of 1,625 histologically confirmed cases of lung cancer and 3,091 matched controls, conducted in France between 1976 and 1980. This study was part of an international study to investigate the role of smoking and lung cancer. Each case was matched with one or two controls, whose diseases were not related, to tobacco use, sex, age at diagnosis (± 5 years), hospital of admission, and interviewer. Information was obtained from both cases and controls on place of residence since birth, educational level, smoking, and drinking habits. A complete lifetime occupational history was obtained by asking participants to give their occupations from the most recent to the first. Women were excluded because most of them had listed no occupation. Men who smoked cigars and pipes were excluded because there were very few in this category. Thus, the study was restricted to nonsmokers and cigarette smokers. Cigarette smoking exposure was defined by age at the first cigarette (nonsmokers, ≤20 years, or >20 years), daily consumption of cigarettes (nonsmokers, <20 cigarettes a day, and ≥20 cigarettes a day), and duration of cigarette smoking (nonsmokers, <35 years, and ≥35 years). The data on occupations were coded by a panel of experts according to their own chemical or physical exposure determinations. Occupations were recorded blindly using the International Standard Classification of Occupations. Data on 1,260 cases and 2,084 controls were available for analysis. The remaining 365 cases and 1,007 controls were excluded because they did not satisfy the required smoking status criteria.

A matched logistic regression analysis was performed to estimate the effect of each occupational exposure after adjusting for cigarette status. Matched relative risk ratios were calculated for each occupation with the baseline category, which consisted of patients who had never been engaged in that particular occupation. The matched RR ratios, adjusted for cigarette smoking for the major groups of occupations, showed that the risks were significantly higher for production and related workers, transport equipment operators, and laborers (RR = 1.24, 95% CI = 1.04, 1.47). On further analysis of this group, for occupations with potential diesel emission exposure, significant excess risks were found for motor vehicle drivers (RR = 1.42, 95% CI = 1.07, 1.89) and transport equipment operators (RR = 1.35, 95% CI = 1.05, 1.75). No interaction with smoking status was found in any of the occupations. The only other significant excess was observed for miners and quarrymen (RR = 2.14, 95% CI = 1.07, 4.31). None of the significant associations showed a dose-response relationship with duration of exposure.

This study was designed primarily to investigate the relationship between smoking (not occupations or environmental exposures) and lung cancer. Although an attempt was made to obtain complete occupational histories, the authors did not clarify whether, in the logistic regression analysis, they used the subjects' first occupation, predominant occupation, last occupation, or ever worked in that occupation as the risk factor of interest. The most important limitation of this study is that the occupations were not coded into exposures for different chemical and physical agents, thus precluding the calculation of relative risks for diesel exposure. Using occupations as surrogate measures of diesel exposure, an excess significant risk was obtained for motor vehicle drivers and transport equipment operators, but not for motor mechanics. However, it is not known if subjects in these occupations worked with diesel engines or nondiesel engines.

7.2.2.6. *Hayes et al. (1989): Lung Cancer in Motor Exhaust-Related Occupations*

This study reports the findings from an analysis of pooled data from three lung cancer case-control studies that examine in detail the association between employment in motor exhaust-related (MER) occupations and lung cancer risk adjusted for confounding by smoking and other risk factors. The three studies were carried out by the National Cancer Institute in Florida (1976 to 1979), New Jersey (1980 to 1981), and Louisiana (1979 to 1983). These three studies were selected because the combined group would provide a sufficient sample to detect a risk of lung cancer in excess of 50% among workers in MER occupations. The analyses were restricted to males who had given occupational history. The Florida study was hospital based, with cases ascertained through death certificates. Controls were randomly selected from hospital records and death certificates, excluding psychiatric diseases, matched by age and county. The New Jersey study was population based, with cases ascertained through hospital records, cancer registry, and death certificates. Controls were selected from among the pool of New Jersey licensed drivers and death certificates. The Louisiana study was hospital based (it is not specified how the cases were ascertained), and controls were randomly selected from hospital patients, excluding those with lung diseases and tobacco-related cancers.

A total of 2,291 cases of male lung cancers and 2,570 controls were eligible, and the data on occupations were collected by next-of-kin interviews for all jobs held for 6 months or more, including the industry, occupation, and number of years employed. The proportion of next-of-kin interviews varied by site from 50% in Louisiana to 85% in Florida. The coding schemes were reviewed to identify MER occupations, which included truck drivers and heavy equipment operators (cranes, bulldozers, and graders); bus drivers, taxi drivers, chauffeurs, and other motor vehicle drivers; and automobile and truck mechanics. Truck drivers were classified as routemen and delivery men and other truck drivers. All jobs were also classified with respect to potential

exposure to known and suspected lung carcinogens. ORs were calculated by the maximum likelihood method, adjusting for age by birth year, usual amount smoked, and study area. Logistic regression models were used to examine the interrelationship of multiple variables.

A statistically significant excess risk was detected for employment of 10 years or more for all MER occupations (except truck drivers) adjusted for birth cohort, usual daily cigarette use, and study area. The odds ratio for lung cancer using data gathered by direct interviews was 1.4 (95% CI = 1.1, 2.0), allowing for multiple MER employment, and 2.0 (95% CI = 1.3, 3.0), excluding individuals with multiple MER employment. ORs for all MER employment, except truck drivers who were employed for less than 10 years, were 1.3 (95% CI = 1.0, 1.7) and 1.3 (95% CI = 0.9, 1.8) including and excluding multiple MER employment, respectively. ORs were then derived for specific MER occupations and, to avoid the confounding effects of multiple MER job classifications, analyses were also done excluding subjects with multiple MER job exposures. Truck drivers employed for more than 10 years had an odds ratio of 1.5 (95% CI = 1.1, 1.9). A similar figure was obtained excluding subjects with multiple MER employment. An excess risk was not detected for truck drivers employed less than 10 years. The only other job category that showed a statistically significant excess for lung cancer included taxi drivers and chauffeurs who worked multiple MER jobs for less than 10 years (OR = 2.5, 95% CI = 1.4, 4.8). For the same category, the risk for individuals working in that job for more than 10 years was 1.2 (95% CI = 0.5, 2.6). A statistically significant positive trend ($p<0.05$) with increasing employment of <2 years, 2 to 9 years, 10 to 19 years, and 20+ years was observed for truck drivers but not for other MER occupations. A statistically nonsignificant excess risk was also observed for heavy equipment operators, bus drivers, taxi drivers and chauffeurs, and mechanics employed for 10 years or more. All of the above-mentioned ORs were derived, adjusted for birth cohort, usual daily cigarette use, and State of residence. Exposure to other occupational suspect lung carcinogens did not account for the excess risks detected.

Results of this large study provide evidence that workers in MER jobs are at an excess risk of lung cancer that is not explained by their smoking habits or exposures to other lung carcinogens. Because no information on type of engine had been collected, it was not possible to determine if the excess risk was due to exposure to DE or gasoline exhaust or a mixture of the two. Among the study's other limitations are a possible bias due to misclassification of jobs reported by the large proportion of next-of-kin interviews. Such a bias would make the effect of DE harder to detect due to broad categorization of jobs and the problems in classifying individuals into uniform occupational groups based on the pooled data in the three studies that used different occupational classification schemes.

7.2.2.7. *Steenland et al. (1990): A Case-Control Study of Lung Cancer and Truck Driving in the Teamsters Union*

Steenland et al. conducted a case-control study of lung cancer deaths in the Teamsters Union to determine the risk of lung cancer among different occupations. Death certificates were obtained from the Teamsters Union files in the central States for 10,485 (98%) male decedents who had filed claims for pension benefits and who had died in 1982 and 1983. Individuals were required to have 20 years' tenure in the union to be eligible to claim benefits. Cases comprised all deaths (n = 1,288) from lung cancer, coded as ICD 162 or 163 for underlying or contributory cause on the death certificate. The 1,452 controls comprised every sixth death from the entire file, excluding deaths from lung cancer, bladder cancer, and motor vehicle accidents. Detailed information on work history and potential confounders such as smoking, diet, and asbestos exposure was obtained by questionnaire. Seventy-six percent of the interviews were provided by spouses and the remainder by some other next of kin. The response rate was 82% for cases and 80% for controls. Using these interview data and the 1980 census occupation and industry codes, subjects were classified either as nonexposed or as having held other jobs with potential DE exposure. Data on job categories were missing for 12% of the study subjects. A second work history file was also created based on the Teamsters Union pension application that lists occupation, employer, and dates of employment. A three-digit U.S. census code for occupation and industry was assigned to each job for each individual. This Teamsters Union work history file did not have information on whether men drove diesel or gasoline trucks, and the four principal occupations were long-haul drivers, short-haul or city drivers, truck mechanics, and dockworkers. Subjects were assigned the job category in which they had worked the longest.

The case-control analysis was done using unconditional logistic regression. Separate analyses were conducted for work histories from the Teamsters Union pension file and from next-of-kin interviews. Covariate data were obtained from next-of-kin interviews. Analyses were also performed for two time periods: employment after 1959 and employment after 1964. These two cut-off years reflect years of presumed dieselization: 1960 for most trucking companies and 1965 for independent driver and nontrucking firms. Data for analysis could be obtained for 994 cases and 1,085 controls using Teamsters Union work history and for 872 cases and 957 controls using next-of-kin work history. When exposure was considered as a dichotomous variable, for both Teamsters Union and next-of-kin work history, no single job category had an elevated risk. From the next-of-kin data, diesel truck drivers had an odds ratio of 1.42 (95% CI = 0.74, 2.47) and diesel truck mechanics had an odds ratio of 1.35 (95% CI = 0.74, 2.47). ORs by duration of employment as a categorical variable were then estimated. For the Teamsters Union work history data, when only employment after 1959 was considered, both long-haul ($p<0.04$) and short-haul drivers (not significant) showed an increase in risk with

increased years of exposure. The length-of-employment categories for which the trends were analyzed were 1 to 11 years, 12 to 17 years, and 18 years or more. Using 1964 as the cutoff date, long-haul drivers continued to show a significant positive trend (p=0.04), with an odds ratio of 1.64 (95% CI = 1.05, 2.57) for those who worked for 13+ years, the highest category. Short-haul drivers, however, did not show a positive trend when 1964 was used as the cutoff date. Similar trend analysis was done for most next-of-kin data. A marginal increase in risk with increasing duration of employment as a truck driver (p=0.12) was observed. For truck drivers who primarily drove diesel trucks for 35 years or longer, the odds ratio for lung cancer was 1.89 (95% CI = 1.04, 3.42). Similarly, the corresponding odds ratio was 1.34 (95% CI = 0.81, 2.22) for both gasoline truck drivers and drivers who drove both types of trucks, and 1.09 (95% CI = 0.44, 2.66) for truck mechanics.

No significant interactions between age and DE exposure or smoking and DE exposure were observed. All the ORs were adjusted for age, smoking, and asbestos in addition to various exposure categories.

This is a well-designed and analyzed study. The main strengths of the study are the availability of detailed records from the Teamsters Union, a relatively large sample size, availability of smoking data , and measurements of exposures. The authors acknowledge some limitations of this study, which include possible misclassifications of exposure and smoking habits, as information was provided by next of kin; lack of sufficient latency to observe lung cancer excess; and a small nonexposed group (n = 120). Also, they could not evaluate the concordance between Teamsters Union and next-of-kin job categories easily because job categories were defined differently in each data set. No data were available on levels of diesel exposure for the different job categories. Despite these limitations, the positive findings of this study, which are probably underestimated, provide a positive evidence toward causal association between DE exposure and excess lung cancer.

7.2.2.8. *Steenland et al. (1998): DE and Lung Cancer in the Trucking Industry: Exposure-Response Analyses and Risk Assessment*

Steenland et al. (1998) conducted an exposure-response analysis by supplementing the data from their earlier case-control study of lung cancer and truck drivers in the Teamsters Union (Steenland et al., 1990) with exposure estimates based on a 1990 industrial hygiene survey of elemental carbon exposure, a surrogate for DE in the trucking industry.

Study subjects were long-term Teamsters enrolled in the pension system who died during the period 1982-1983. Using death certificate information, the researchers identified 994 cases of lung cancer for the study period, and 1,085 non-lung-cancer deaths served as controls. Subjects were divided into job categories based on the job each held the longest. Most had held

only one type of job. The job categories were short-haul driver, long-haul driver, mechanic, dockworker, other jobs with potential diesel exposure, and jobs outside the trucking industry without occupational diesel exposure. Smoking histories were obtained from next of kin. ORs were calculated for work in an exposed job category at any time and after 1959 (an estimated date when the majority of heavy-duty trucks had converted to diesel) compared with work in nonexposed jobs. ORs were adjusted for age, smoking, and potential asbestos exposure. Trends in effect estimates for duration of work in an exposed job were also calculated.

An industrial hygiene survey by Zaebst et al. (1991) of elemental carbon exposures in the trucking industry provided exposure estimates for each job category in 1990. The elemental carbon measurements were generally consistent with the epidemiologic results, in that mechanics were found to have the highest exposures and relative risk, followed by long-haul and then short-haul drivers, although dockworkers had the highest exposures and the lowest relative risks.

Past exposures were estimated assuming that they were a function of (1) the number of heavy-duty trucks on the road, (2) the particulate emissions (grams/mile) of diesel engines over time, and (3) leaks from truck exhaust systems for long-haul drivers. Estimates of past exposure to elemental carbon, as a marker for DE exposure, for subjects in the case-control study were made by assuming that average 1990 levels for a job category could be assigned to all subjects in that category, and that levels prior to 1990 were directly proportional to vehicle miles traveled by heavy-duty trucks and the estimated emission levels of diesel engines. A 1975 exposure level of elemental carbon in terms of micrograms per cubic meter was estimated by the following equation: 1975 level = 1990 level*(vehicle miles 1975/vehicle miles 1990) (emissions 1975/emissions 1990). Once estimates of exposure for each year of work history were derived for each subject, analyses were conducted by cumulative level of estimated carbon exposure.

Estimates were made for long-haul drivers (n = 1,237), short-haul drivers (n = 297), dockworkers (n = 164), mechanics (n = 88), and those outside the trucking industry (n = 150). Logistic regression was used to estimate ORs adjusted for five categories of age, race, smoking (never, former-quitting before 1963, former-quitting in 1963 or later, current-with <1 pack per day, and current-with 1 or more packs per day), diet, and reported asbestos exposure. A variety of models for cumulative exposure were considered, including a log-linear model with cumulative exposure, a model adding a quadratic term for cumulative exposure, a log transform of cumulative exposure, dummy variables for quartile of cumulative exposure, and smoothing splines of cumulative exposure. The estimates of rate ratios from logistic regression for specific levels of exposure to elemental carbon were then used to derive excess risk estimates for lung cancer after lifetime exposure to elemental carbon.

The survey found that mechanics had the highest current levels of DE exposures and dockworkers who mainly used propane-powered forklifts had the lowest exposure. ORs of 1.69

and 0.93 were observed for the mechanics and dockworkers, respectively. The finding of the highest lung cancer risk for mechanics and lowest for dockworkers is indicative of causal association between the DE exposure and development of lung cancer. The log of cumulative exposure was found to be the best-fitting model and was a significant predictor ($p = 0.01$). However, the risk among mechanics did not increase with increasing duration of employment.

OR for quartile of cumulative exposure show a pattern of significantly increasing trends in risk with increasing exposure, ranging between 1.08 and 1.72, depending on the exposure level and lag structure used. The lifetime excess risk of lung cancer death (through age 75) for a male truck driver was estimated to be in the range of 1.4%-2.3% (95% confidence limits ranged from 0.3% to 4.6%) above the background risk, depending on the emissions scenarios assumed. The authors found that current exposures indicated that truck drivers are exposed to DE at levels about the same as ambient levels on the highways, which are about double the background levels in urban air. They conclude that the data suggest a positive and significant increase in lung cancer risk with increasing estimated cumulative exposure to DE among workers in the trucking industry. They assert that these estimates suggest that the lifetime excess risk for lung cancer is 10 times higher than the OSHA standards, but caution that the results should be viewed as exploratory.

The authors acknowledge that the increasing trend in risk with increasing estimates of cumulative exposure is partly due to the fact that a component of cumulative dose is simple duration of exposure, and that analyses by simple duration also exhibit a positive trend with duration. This analysis essentially weights the duration by contrived estimates of exposure intensity, and the authors acknowledge that this weighting depends on very broad assumptions.

This is not an analysis of new data that provides independent estimates of relative risk for DE and lung cancer incidence. Instead, it is an attempt to convert the data from Steenland's earlier study of lung cancer for the purpose of estimating a different risk metric, "lifetime excess risk of lung cancer," by augmenting these data with limited industrial hygiene data and rationalizations about plausible models for cumulative exposure.

The Health Effects Institute (HEI, 1999) and others have raised some concerns about the exposure estimations, selection of controls, and control for confounding variables, and hence, this study's usefulness for quantitative risk assessment. EPA and NIOSH will address these concerns in the year 2001. The HEI (1999) panel noted that some of the strengths of this study include the relevance of exposure levels to the general population and the use of an exposure marker for diesel engine emissions that was an improvement over the concentration of respirable-size particles (RSP). The number of study subjects (996 lung cancer cases) is large. Histories of exposures to asbestos and smoking were obtained, and confounding by these two variables was controlled in the analysis. Thus, it should be noted that these concerns are about

the use of these data for quantitative risk assessment, due to limitations of the exposure data. As far as qualitative risk assessment is concerned, this study is still considered to be positive and strong.

7.2.2.9. *Boffetta et al. (1990): Case-Control Study on Occupational Exposure to DE and Lung Cancer Risk*

This is an ongoing (since 1969) case-control study of tobacco-related diseases in 18 hospitals (six U.S. cities). Cases comprise 2,584 males with histologically confirmed primary lung cancers. Sixty-nine cases were matched to 1 control, whereas 2,515 were matched to 2 controls. Controls were individuals who were diagnosed with non-tobacco-related diseases. The matching was done for sex, age (±2 years), hospital, and year of interview. The interviews were conducted at the hospitals at the time of diagnosis. In 1985, the occupational section of the questionnaire was modified to include the usual occupation and up to five other jobs as well as duration (in years) worked in those jobs. After 1985, information was also obtained on exposure to 45 groups of chemicals, including DE at the workplace or during hobby activities. A priori aggregation of occupations was categorized into low probability of DE exposure (reference group), possible exposure (19 occupations), and probable exposure (13 occupations). Analysis was conducted based on "usual occupation" on all study subjects, and any occupation with sufficient cases was eligible for further analysis. In addition, cases enrolled after 1985 for which there were self-reported DE exposure and detailed work histories were also analyzed separately.

Both matched and unmatched analyses were done by calculating the adjusted (for smoking and education) relative odds using the Mantel-Haenzael method and calculating the test-based 95% confidence interval using the Miettinen method. Unconditional logistic regression was used to adjust for potential confounders (the PROC LOGIST of SAS). Linear trends for risk were also tested according to Mantel.

Adjusted relative odds for possible and probable exposure groups as well as the truck drivers were slightly below unity, none being statistically significant for the entire study population. Although slight excesses were observed for the self-reported DE exposure group and the subset of post-1985 enrollees for highest duration of exposure (for self-reported exposure, occupations with probable exposure, and truck drivers), none was statistically significant. Trend tests for the risk of lung cancer among self-reported DE exposure, probable exposure, and truck drivers with increasing exposure (duration of exposure used as surrogate for increasing dose) were nonsignificant too. Statistically significant lung cancer excesses were observed for cigarette smoking only.

The major strength of this study is availability of detailed smoking history. Even though detailed information was obtained for the usual and five other occupations (1985), because it

was difficult to estimate or verify the actual exposure to DE, duration of employment was used as a surrogate for dose instead. The numbers of cases and controls were large; however, the number of individuals exposed to DE was relatively few, thus reducing the power of the study. This study did not attempt latency analysis either. Due to these limitations, the findings of this study are unable to provide either positive or negative evidence for a causal association between DE and occurrence of lung cancer.

7.2.2.10. *Emmelin et al. (1993): DE Exposure and Smoking: A Case-Referent Study of Lung Cancer Among Swedish Dock Workers*

This case-control study of lung cancer was drawn from a cohort defined as all male workers who had been employed as dockworkers for at least 6 months between 1950 and 1974. In the population of 6,573 from 20 ports, there were 90 lung cancer deaths (cases), identified through Swedish death and cancer registers, during the period 1960 to 1982. Of these 90 deaths, the 54 who were workers at the 15 ports for which exposure surrogate information was available were chosen for the case-control study. Four controls, matched on port and age, were chosen for each case from the remaining cohort who had survived to the time of diagnosis of the case. Both live and deceased controls were included. The final analyses were done on 50 cases and 154 controls who had complete information on employment dates and smoking data. The smoking strata were created by classifying ex-smokers as nonsmokers if they had not smoked for at least 5 years prior to the date of diagnosis of the case; otherwise they were classified as smokers.

Relative odds and regression coefficients were calculated using conditional logistic regression models. Comparisons were made both with and without smoking included as a variable, and the possible interaction between smoking and DE was tested. Both the weighted linear regressions of the adjusted relative odds and the regression coefficients were used to test mortality trends with all three exposure variables.

Exposure to DE was assessed indirectly by initially measuring: (1) exposure intensity based on exhaust emission, (2) characteristics of the environment in terms of ventilation, and (3) measures of proportion of time in higher exposed jobs. For exhaust emissions, annual diesel fuel consumption at a port was used as the surrogate. For ventilation, the annual proportion of ships with closed or semiclosed holds was used as the surrogate. The proportion of time spent below decks was used as the surrogate for more exposed jobs. Although data were collected for all three measures, only the annual fuel consumption was used for analysis. Because every man was likely to rotate through the various jobs, the authors thought using annual consumption of diesel fuel was the appropriate measure of exposure. Consequently, in a second analysis, the annual fuel consumption was divided by the number of employees in the same port that year to come up with the fuel-per-person measure, which was further used to create a second measure,

"exposed time." The "annual fuel" and exposed-time data were entered in a calendar time-exposure matrix for each port, from which individual exposure measures were created. A third measure, "machine time" (years of employment from first exposure), was also used to compare the results with other studies. All exposure measures were accumulated from the first year of employment or first year of diesel machine use, whichever came later. The last year of exposure was fixed at 1979. All exposures up to 2 years before the date of lung cancer diagnosis were omitted from both cases and matched controls. A priori classification into three categories of low, medium, and high exposure was done for all three exposure variables: machine time, fuel, and exposed time.

Conditional logistic regression models, adjusting for smoking status and using low exposures and/or nonsmokers as a comparison group, yielded positive trends for all exposure measures, but no trend test results were reported, and only the relative odds for the exposed-time exposure measure in the high-exposure group (OR = 6.8, 90% CI = 1.3 to 34.9) was reported as statistically significant. For smokers, adjusting for DE exposure level, the relative odds were statistically significant and about equal for all three exposure variables: machine time, OR = 5.7 (90% CI = 2.4 to 13.3); fuel, OR = 5.5 (90% CI = 2.4 to 12.7); and exposed time, OR = 6.2 (90% CI = 2.6 to 14.6). Interaction between DE and smoking was tested by conditional logistic regression in the exposed-time variable. Although there were positive trends for both smokers and nonsmokers, the trend for smokers was much steeper: low, OR = 3.7 (90% CI = 0.9 to 14.6); medium, OR = 10.7 (90% CI = 1.5 to 78.4); and high, OR = 28.9 (90% CI = 3.5 to 240), indicating more than additive interaction between these two variables.

In the weighted linear regression model with the exposed-time variable, the results were similar to those using the logistic regression model. The authors also explored the smoking variable further in various analyses, some of which suggested a strong interaction between DE and smoking. However, with just six nonsmokers and no further categorization of smoking amount or duration, these results are of limited value.

The DE exposure matrices created using three different variables are intricate. Analyses by any of these variables yield essentially the same positive results and positive trends, providing consistent support for a real effect of DE exposure, at least in smokers. However, methodological limitations to this study prevent a more definitive conclusion. The numbers of cases and controls are small. There are very few nonsmokers; thus, testing the effects of DE exposure in them is futile. Lack of information on asbestos exposure, to which dockworkers are usually exposed, may also confound the results. Also, no latency analyses are presented. Overall, despite these limitations, this study supports the earlier findings of excess lung cancer mortality among individuals exposed to DE.

7.2.2.11. *Swanson et al. (1993): Diversity in the Association Between Occupation and Lung Cancer Among Black and White Men*

This population-based case-control study of lung cancer was conducted in metropolitan Detroit. The cases and controls for this study were identified from the Occupational Cancer Incidence Surveillance Study (OCISS). A total of 3,792 incident lung cancer cases and 1,966 colon and rectal cancer cases used as controls, diagnosed between 1984 and 1987 among white and black males aged 40 to 84 years, were selected for the study. Information was obtained by telephone interview either with the individual or a surrogate about lifetime work history and smoking history, as well as medical, demographic, and residential history. Occupation and industry data were coded using the 1980 U.S. Census Bureau classification codes. The investigators selected certain occupations and industries as having little or no exposure to carcinogens and defined them as an unexposed group. Analysis was done using logistic regression method and adjusting for age at diagnosis, pack-years of cigarette smoking, and race.

The results were presented by various occupations and industries; those with potential exposures to DE were drivers of heavy trucks and light trucks, farmers, and railroad workers, respectively. Among white males, increasing lung cancer risks were observed with increasing duration of employment for drivers of heavy trucks, drivers of light trucks, and farmers. Although none of the individual ORs were statistically significant, trend tests were significant for all three occupations ($p \leq 0.05$). On the other hand, among black males increasing lung cancer risks with increasing duration of employment were observed for farmers only, with an OR of 10.4 (95% CI = 1.4, 77.1) reaching significance for employment of 20+ years. As for the railroad industry, increasing lung cancer risks with increasing duration of employment were observed for both white and black males. The trend test was significant for white males only, with an OR of 2.4 (95% CI = 1.1, 5.1) reaching significance for employment of 10+ years.

The main strengths of the study are large sample size, availability of lifetime work history and smoking history, and the population-based study format, precluding selection bias. The major limitation, as in other studies, is lack of direct information on specific exposures. The interesting result of this study is lung cancer excesses observed in farmers, mainly among crop farmers, who have potential exposure to DE from their tractors in addition to pesticides, herbicides, and other PM_{10}. The authors point out that this is the first study to find excess lung cancer in this occupation.

7.2.2.12. *Hansen et al. (1998): Increased Risk of Lung Cancer Among Different Types of Professional Drivers in Denmark*

This is a population-based case-control study of lung cancer, conducted in professional drivers in Denmark. The cases first diagnosed as primary lung cancer between 1970 and 1989

among males born between 1897 and 1966 were identified from the Danish Cancer Registry. The registry provided the information on diagnosis from ICD-7, name, sex, and unique personal identification number (PIDN). Information about past employment was obtained by linkage with the nationwide pension fund. The fund keeps the records by name and PIDN about the date of start and end of each job and unique company number of the employer. The records are kept even after the employee has retired or died. Information about current employment was obtained from the Danish Central Population Registry (CPR) by linkage with the PIDN.

Of 37,597 cases identified from the Registry, 8,853 did not have any employment records. Controls (1:1) for 28,744 lung cancer cases with employment histories were selected randomly from CPR, matched with the case by year of birth and sex. Furthermore, these controls had to be alive, cancer free, and employed prior to the diagnosis of lung cancer in the corresponding case. Employment histories were obtained for the controls in the same fashion as cases from the pension fund. The employment record search resulted in a total of 1,640 lorry/bus drivers and 426 taxi drivers. They were further divided into subgroups by their duration of employment. Information about smoking in drivers was acquired from two national surveys conducted in 1970-72 and 1983. No direct information on smoking was available in either cases or controls. A separate case-control study of mesothelioma indirectly looked at asbestos exposure among professional drivers. OR, adjusting for socioeconomic status and 95% CI, were computed using conditional logistic regression (PECAN procedure in the statistical package EPICURE).

Significant ORs for lung cancer were found for lorry/bus drivers (OR = 1.31, 95% CI = 1.17, 1.46), taxi drivers (OR = 1.64, 95% CI = 1.22, 2.19), and unspecified drivers (OR = 1.39, 95% CI = 1.30, 1.51). Significant ORs were found for both lorry/bus drivers and taxi drivers by duration of employment in 1-5 years and >5 years categories, with no lag time and with a 10-year lag time. The ORs remained the same for lorry/bus drivers in these employment categories for no lag time and 10-year lag time. Among taxi drivers, on the other hand, the OR of 2.2 in >5 year employment in no-lag-time analysis increased to 3.0 in the 10-year lag time analysis. The authors asserted that the higher risk seen in the taxi drivers may be due to higher exposure attributable due to longer time spent in traffic congestion. The trend tests for increasing risk with increasing duration of employment (surrogate for exposure) were statistically significant ($p<0.001$) for both lorry/bus drivers and taxi drivers in no-lag-time and 10-year lag time analysis. All the ORs were adjusted for socioeconomic status.

The main strengths of the study are the large sample size, availability of information on socioeconomic status, and detailed employment records. The main limitation, however, is lack of information on what type of fuel these vehicles used. It is probably safe to assume that the lorry/buses were diesel powered, whereas the taxis could be either diesel or gasoline powered. A

personal communication with Dr. Johnni Hansen confirmed that dieselization in Denmark was completed in the late 1940s and lorries, buses, and taxis have been using diesel fuel since then. Although direct adjustments were not done for smoking and exposure to asbestos, indirect information on both these confounders indicates that they are unlikely to explain the observed excesses and the increasing risk with increasing duration of employment. Thus, the results of this study are strongly supportive of DE being associated with increased lung cancer.

7.2.2.13. *Brüske-Hohlfeld et al. (1999): Lung Cancer Risk in Male Workers Occupationally Exposed to Diesel Motor Emissions in Germany*

This paper presents a pooled analysis of two case-control studies of lung cancer. The first study, by Jöckel et al. (1995, 1998), was conducted between 1988 and 1993 and had 1,004 cases and 1,004 controls matched for sex, age, and region of residence, selected randomly from the compulsory municipal registries. The inclusion criteria for cases were: they should have been born in or after 1913, should have been of German nationality, and should have been diagnosed with lung cancer within 3 months prior to the interview. The second study, by Wichmann et al. (1998), was ongoing when it was included in this study. The study span covered the years 1990 to 1996. By 1994 a total of 3,180 cases and 3,249 controls, randomly selected from the compulsory population registries, were frequency matched on sex, age, and region. The cases were less than 76 years old, were residents of the region and living in Germany for more than 25 years, and had a diagnosis not more than 3 months old. Of 4,184 pooled cases and 4,253 pooled controls, the analysis was conducted on 3,498 male cases and 3,541 male controls. A personal interview was conducted with each study participant. Data were collected on basic demographic information, detailed smoking history, and lifelong occupational history about jobs held and industries worked in. The job titles and industries were classified into 33 and 21 categories, respectively, using the German Statistical Office codes.

Based on job codes with potential exposure to diesel motor emission (DME), four exposure groups were constituted. Group A comprised professional drivers of trucks, buses, taxis, etc. Group B comprised other traffic-related jobs such as switchmen, diesel locomotive drivers, and diesel forklift truck drivers. Group C comprised bulldozer operators, graders, and excavators. Group D comprised full-time farm tractor drivers. Validation of the jobs was done by written evaluation of the job task descriptions, which also avoided misclassification. The following information was acquired for the construction of job task descriptions: (1) What were your usual tasks at work and how often (in % of daily working hours) were they performed? (2) What did you produce, manufacture, or transport? (3) Which material was used? (4) What kind of machine did you operate? Some individuals had more than one job task

with DME exposure. The exposure assessment was done without knowing the status of the case/control.

For each individual, cumulative exposure was calculated for the complete work history by categorizing the duration of exposure as >0-3, >3-10, >10-20, >20-30, >30 years, and beginning and end of exposure. The first year of exposure was defined as ≤1945, 1946-1955, and ≥1956 while the last year of exposure was defined as ≤1965, 1966-1975, and ≥1976. For professional drivers, hours driven per day were accumulated and were classified as "driving hours."

A smoker was defined as any individual who had smoked regularly for at least 6 months. Smoking information was acquired in series with the starting time, type of tobacco, amount smoked, duration in years, and calender year of quitting. Asbestos exposure was estimated by certain job-specific supplementary questions.

The cases and controls were post-hoc stratified into 6 age and 17 region categories. ORs adjusted for smoking and asbestos exposure were calculated by conditional logistic regression, using "never exposed" workers as the reference group. The adjustment for cigarette smoking was done by using pack-years as a continuous variable; adjustment for other tobacco products was done by considering them as a binary variable. A total of 716 cases and 430 controls were found to be ever exposed to DME. The smoking- and asbestos-adjusted OR of 1.43 (95% CI = 1.23, 1.67) for all DME exposed was reduced from the crude OR of 1.91. For the entire group the various analyses yielded statistically significant ORs ranging from 1.25 to 2.31, adjusted for smoking and asbestos exposure (West Germany, >10-20 years and >20-30 years of exposure, first year of exposure in 1946-1955 and 1956+, end of exposure in 1966-1975 and 1976+, and for the job categories of Group A, B, and C). The risk increased with increasing years of exposure, and for both the first year of exposure (≤1945, 1946-1955, and ≥1956) and end year of exposure (≤1965, 1966-1975, and ≥1976).

Separate analyses by four job categories (all the ORs were adjusted for smoking and asbestos exposure) showed that for professional drivers (Group A) the overall OR was 1.25 (95% CI = 1.05, 1.47). Significant ORs were found for various factors in West Germany only. The factors were: >0-3 years and >10-20 years of exposure (OR = 1.69, 95% CI = 1.13, 2.53, and OR = 2.02, 95% CI = 1.32, 3.08, respectively), beginning of exposure in 1956+ and end of exposure in 1976+ (OR = 1.56, 95% CI = 1.21, 2.03, and OR = 1.5, 95% CI = 1.14, 1.98, respectively), and 1,000-49,999 driving hours (OR = 1.54, 95% CI = 1.15, 2.07). None of the ORs were significant in East Germany in this group.

For other traffic-related jobs (Group B) the overall OR was 1.53 (95% CI = 1.04, 2.24). The ORs for beginning of exposure in 1956+ and end of exposure in 1976+ were OR = 1.71, 95% CI = 1.05, 2.78, and OR = 2.68, 95% CI = 1.47, 4.90, respectively. The risk increased with

increasing duration of exposure and was statistically significant for >10-20 years (OR = 2.49) and more than 20 years (OR = 2.88). No separate analyses for West Germany and East Germany were presented in this category.

For heavy equipment operators (Group C) the overall OR of 2.31 (95% CI = 1.44, 3.7) was highest among all the job categories. Significant ORs were observed for beginning exposure in 1946-1955 (OR = 2.83, 95% CI = 1.10, 7.23) and end exposure in 1966-1975 (OR = 3.74, 95% CI = 1.20, 11.64). The risk increased with increasing duration of exposure and was statistically significant for more than 20 years of exposure (OR = 4.3). Although no separate analyses for West Germany and East Germany were presented, investigators mentioned that for this job group hardly any difference was seen between West Germany and East Germany.

For drivers of the farming tractors (Group D) the overall OR of 1.29 was not significant. Risk increased with increasing duration of exposure and was significant for exposure of more than 30 years (OR = 6.81, 95% CI = 1.17, 39.51). No separate analyses for West Germany and East Germany were presented in this category.

The professional drivers and the other traffic-related job categories probably have mixed exposures to gasoline exhaust in general traffic. On the other hand, it should be noted that exposure to DME among heavy equipment and farm tractor drivers is much higher and not as mixed as in professional drivers. The heavy equipment drivers usually drive repeatedly through their own equipment's exhaust. Therefore, the observed highest risk for lung cancer in this job category establishes a direct link with the DME. The only other study that found significantly higher risk for heavy equipment operators (RR = 2.6) was conducted by Boffeta et al. (1988). Although the only significant excess was observed for farming tractor operators among individuals with more than 30 years of exposure, a steady increase in risk was observed for this job category with increasing exposure. The investigators stated that the working conditions and the DME of tractors remained fairly constant over the years. This increase may be due mainly to exposure to DME and, in addition, PM_{10}.

This is a well-designed, well-conducted, and well-analyzed study. Its main strengths are large sample size, resulting in good statistical power; inclusion of incident cases that were diagnosed not more than 3 months prior to the interview; use of only personal interviews, reducing recall bias; diagnosis ascertained by cytology or histology; and availability of lifelong detailed occupational and smoking history. Exposure estimation for each individual was based on job codes and industry codes, which were validated by written job descriptions to avoid misclassification. The main limitation of the study is lack of data on actual exposure to DME. The cumulative quantitative exposures were calculated based on time spent in each job with potential exposure to DME and the type of equipment used. Thus, this study provides strong evidence for a causal association between exposure to DE and occurrence of lung cancer.

Table 7-2 summarizes the above lung cancer case-control studies.

Table 7-2. Epidemiologic studies of the health effects of exposure to DE: case-control studies of lung cancer

Authors	Population studied	DE exposure assessment	Results	Limitations
Hall and Wynder (1984)	502 histologically confirmed lung cancers Cases diagnosed 12 mo prior to interviews 502 matched hospital controls without tobacco-related diseases, matched for age, sex, race, and geographical area Population from 18 hospitals in controls	Based on previous Industrial Hygiene Standards for a particular occupation, usual lifetime occupation coded as "probably high exposure" and "no exposure" NIOSH standards used to classify exposures: High Moderate Low	SNS excess risk after adjustment for smoking for lung cancer: RR = 1.4 (1st criteria) and RR = 1.7 (NIOSH criteria)	Complete lifetime employment history not available Self-reported occupation history not validated No analysis by dose, latency, or duration of exposure No information on nonoccupational diesel exposure
Damber and Larsson (1987)	589 lung cancer cases who had died prior to 1979 reported to Swedish registry between 1972 and 1977 582 matched dead controls (sex, age, year of death, municipality) drawn from National Registry of Cause of Death 453 matched living controls (sex, year of birth, municipality) drawn from National Population Registry	Occupations held for at least 1 year or more A 5-digit code was used to classify the occupations according to Nordic Classification of Occupations	For underground miners: SS OR = 2.7 (≥1 year of employment) SS OR = 9.8 (≥20 years of employment) For professional drivers: SNS OR = 1.2 (≥20 years of employment) with dead controls All ORs adjusted for smoking	Uncertain DE exposure No validation of exposure done Underground miners data not adjusted for other confounders such as radon, etc.

Table 7-2. Epidemiologic studies of the health effects of exposure to DE: case-control studies of lung cancer (continued)

Authors	Population studied	DE exposure assessment	Results	Limitations
Lerchen et al. (1987)	506 lung cancer cases from New Mexico tumor registry (333 males and 173 females) Aged 25-84 years Diagnosed between January 1, 1980, and December 31, 1982 771 (499 males and 272 females) frequency matched with cases, selected from telephone directory	Lifetime occupational history and self-reported exposure history were obtained Coded according to Standard Industrial Classification Scheme	No excess of relative odds were observed for DE exposure	Exposure based on occupational history and self-report, which was not validated 50% occupational history provided by next of kin Absence of lung cancer association with asbestos suggests misclassification of exposure
Garshick et al. (1987)	1,319 lung cancer cases who died between March 1, 1981, and February 28, 1982 2,385 matched controls (two each, age and date of death) Both cases and controls drawn from railroad worker cohort who had worked for 10 or more years	Personal exposure assessed for 39 job categories This was corrected with job titles to dichotomize the exposure into: Exposed Not exposed Industrial hygiene sampling done	SS OR = 1.41 (≤64 year age group) SS OR = 1.64 (≤64 year age group) for ≥20 years DE exposure group when compared to 0- to 4-year exposure group All ORs adjusted for lifetime smoking and asbestos exposure	Probable misclassification of DE exposure jobs Years of exposure used as surrogate for dose 13% of death certificates not ascertained Overestimation of smoking history
Benhamou et al. (1988)	1,260 histologically confirmed lung cancer cases 2,084 non-tobacco-related disease matched controls (sex, age at diagnosis, hospital admission, and interviewer) Occurring between 1976 and 1980 in France	Based on exposures determined by panel of experts The occupations were recorded blindly using International Standard Classification of Occupations as chemical or physical exposures	Significant excess risks were found in motor vehicle drivers (RR = 1.42) and transport equipment operators (RR = 1.35) (smoking adjusted)	Exposure based on occupational histories not validated Exposures classified as chemical and physical exposures, not specific to DE

Table 7-2. Epidemiologic studies of the health effects of exposure to DE: case-control studies of lung cancer (continued)

Authors	Population studied	DE exposure assessment	Results	Limitations
Hayes et al. (1989)	Pooled data from three different studies consisting of 2,291 male lung cancer cases 2,570 controls	Occupational information from next of kin for all jobs held Jobs classified with respect to potential exposure to known and suspected pulmonary carcinogens	SS OR = 1.5 for truck drivers (>10 years of employment) SS positive trend with increasing employment as truck driver Adjusted for age, smoking, & study area	Exposure data based on job description given by next of kin, which was not validated Could have been mixed exposure to both diesel and gasoline exhausts Job description could have led to misclassification
Steenland et al. (1990)	1,058 male lung cancer deaths between 1982 and 1983 1,160, every sixth death from entire mortality file, sorted by Social Security number (excluding lung cancer, bladder cancer, and motor vehicle accidents) Cases and controls were from Central State Teamsters who had filed claims (requiring 20-year tenure)	Longest job held: diesel truck driver, gasoline truck driver, both types of trucks, truck mechanic, and dockworkers	As 1964 cut-off point: SS OR = 1.64 for long-haul drivers with 13+ years of employment Positive trend test for long-haul drivers (p=0.04) SS OR = 1.89 for diesel truck drivers of 35+ years of employment Adjusted for age, smoking, & asbestos	Exposure based on job titles not validated Possible misclassification of exposure and smoking, based on next-of-kin information Lack of sufficient latency
Steenland et al. (1998)	Exposure-response analyses of their 1990 case-control study	Industrial hygiene data of elemental carbon in trucking industry collected by Zaebst et al. (1991) used to estimate individual exposures Cumulative exposures calculated based on estimated lifetime exposures	For mechanics: OR = 1.69 (had the highest DE exposure) Lowest DE exposure and lowest OR = 0.93 observed for dockworkers Increasing risk of lung cancer with increasing exposure Adjusted for age & smoking	

Table 7-2. Epidemiologic studies of the health effects of exposure to DE: case-control studies of lung cancer (continued)

Authors	Population studied	DE exposure assessment	Results	Limitations
Boffetta et al. (1990)	From 18 hospitals (since 1969), 2,584 male lung cancer cases matched to either one control (69) or two controls (2,515) were drawn. Matched on age, hospital, and year of interview	A priori aggregation of occupations categorized into low probability, possible exposure (19 occupations), and probable exposure (13 occupations) to DE	OR slightly below unity SNS Adjusted for smoking	No verification of exposure Duration of employment used as surrogate for dose Number of individuals exposed to DE was small
Emmelin et al. (1993)	50 male lung cancer cases from 15 ports (worked for at least 6 months between 1950 and 1974), 154 controls matched on age and port	Indirect DE exposure assessment done based on (1) exposure intensity, (2) characteristics of ventilation, (3) measure of proportion of time in higher exposure jobs	SS OR for high-exposure group = 6.8 Positive trend for DE observed (trend much steeper for smokers than nonsmokers) Adjusted for smoking	Numbers of cases and controls are small Very few nonsmokers Lack of exposure information on asbestos No latency analysis
Swanson et al. (1993)	Population based case-control study in metropolitan Detroit 3,792 lung cancer cases and 1,966 colon cancer (cases) controls, diagnosed between 1984 and 1987 in white and black males (aged between 40-84)	Telephone interviews with the individual or surrogate about lifetime work history Occupation and industry data coded per 1980 U.S. Census Bureau classification codes Certain occupations and industries were selected as unexposed to carcinogens	SS excess ORs observed for - black farmers OR= 10.4 for 20+ years employment - white railroad industry workers OR= 2.4 for 10+ years employment Among white trend tests were SS for -drivers of heavy duty trucks - drivers of light duty trucks - farmers - railroad workers Among blacks trend test was SS for farmers only All the ORs were adjusted for age at diagnosis, pack-years of cigarette smoking and race	Lack of direct information on specific exposures No latency analysis

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Table 7-2. Epidemiologic studies of the health effects of exposure to DE: case-control studies of lung cancer (continued)

Authors	Population studied	DE exposure assessment	Results	Limitations
Hansen et al. (1998)	Population-based case-control study of professional drivers in Denmark Male lung cancer cases diagnosed between 1970-1989, controls matched by year of birth and sex	Information about past employment obtained by linkage with nationwide pension fund Employment as lorry/bus drivers (n=1,640) and taxi drivers (n=426) was used as surrogate for exposure to DE	For lorry/bus drivers: SS OR = 1.31 For taxi drivers: SS OR = 1.64, which increased to 2.2 in > 5-year employment with no lag time & 3.0 in > 5 year employment with 10- year lag time SS trend test for increasing risk with increasing employment for both lorry/bus drivers & taxi drivers ($p<0.001$) All ORs adjusted for socioeconomic status	Lack of information on the type of fuel (personal communication with the principal investigator confirmed that diesel fuel is used for the lorry/buses and taxis since early 1960s) Even though direct adjustment was not done for smoking/asbestos, indirect methods indicate that the results are not likely to be confounded by these factors

Table 7-2. Epidemiologic studies of the health effects of exposure to DE: case-control studies of lung cancer (continued)

Authors	Population studied	DE exposure assessment	Results	Limitations
Brüske-Hohlfeld et al. (1999)	Pooled analysis of two case-control studies (3,498 cases & 3,541 controls) Controls frequency matched on sex, age, & region, randomly selected from the compulsory population registry Inclusion criteria: (1) born in or after 1913/less than 75 years old, (2) German nationality/resident of the region - lived in Germany for more than 25 years, & (3) lung cancer diagnosis should be 3 months prior to the study Information obtained by personal interview on:	Lifetime detailed occupational & smoking histories obtained from each individual in a personal interview Based on job codes (33 job titles & 21 industries) potential DE exposure classified in 4 categories: A- professional drivers of trucks, buses, & taxis; B- other traffic related i.e., switchman, locomotive, & forklift drivers; C- bulldozer operators, graders,& excavators; D- farm tractor drivers Cumulative DE exposures and pack-years (smoking) calculated for each individual	SS higher risk adjusted for smoking observed for all 4 categories: A- ORs ranged from 1.25 to 2.53 B- ORs ranged from 1.53 to 2.88 C- ORs ranged from 2.31 to 4.3 D- 6.81 (exposure < 30 years) Risk increased with increasing exposure	Lack of data on actual exposure to diesel exaust

Abbreviations: OR = odds ratio; RR = relative risk; SNS = statistically nonsignificant; SS = statistically significant.

7.2.3. Summaries of Studies and Meta-Analyses of Lung Cancer

7.2.3.1. *Cohen and Higgins (1995): Health Effects of DE: Epidemiology*

The Health Effects Institute (HEI) reviewed all published epidemiologic studies on the health effects of exposure to DE available through June 1993, identified by a MEDLINE search and by reviewing the reference sections of published research and earlier reviews. HEI identified 35 reports of epidemiologic studies (16 cohort and 19 case-control) of the relation of occupational exposure to diesel emissions and lung cancer published between 1957 and 1993. HEI reviewed the 35 reports for epidemiologic evidence of health effects of exposure to DE for lung cancer, other cancers, and nonmalignant respiratory disease. They found that the data were strongest for lung cancer. The evidence suggested that occupational exposure to DE from diverse sources increases the rate of lung cancer by 20% to 40% in exposed workers generally, and to a greater extent among workers with prolonged exposure. They also found that the results are not explicable by confounding caused by cigarette smoking or other known sources of bias.

Control for smoking was identified in 15 studies. Six studies (17%) reported relative risk estimates less than 1; 29 studies (83%) reported at least one relative risk greater than one indicating positive association. Twelve studies indicating a relative risk greater than 1 had 95% confidence intervals, which excluded unity.

The authors conclude that epidemiologic data consistently show weak associations between exposure to DE and lung cancer. They find that the evidence suggests that long-term exposure to DE in a variety of occupational circumstances is associated with a 1.2- to 1.5-fold increase in the relative risk of lung cancer compared with workers classified as unexposed. Most of the studies that controlled for smoking found that the association between increased risk of lung cancer and exposure to DE persisted after such controls were applied, although in some cases the excess risk was lower. None of the studies measured exposure to diesel emissions or characterized the actual emissions from the source of exposure for the time period most relevant to the development of lung cancer. Most investigators classified exposure based on work histories reported by subjects or their next of kin, or by retirement records. Although these data provide relative rankings of exposure, the absence of concurrent exposure information is the key factor that limits interpretation of the epidemiologic findings and subsequently their utility in making quantitative estimates of cancer risks.

This is a comprehensive and thorough narrative review of studies of the health effects of DE. It does not undertake formal estimation of summary measures of effect or evaluation of heterogeneity in the results. The conclusion drawn about the consistency of the results is based on the author's assessment of the failure of potential biases and alternative explanations for the increase in risk to account for the observed consistency. In many if not most studies, the quality of the data used to control confounding was relatively crude. Although the studies do include qualitative assessment of whether control for smoking is taken into account, careful scrutiny of

the quality of the control or adjustment for smoking among the studies is absent. This leaves open the possibility that prevalent residual confounding by inadequate control for smoking in many studies may account for the consistent associations seen.

7.2.3.2. *Bhatia et al. (1998): DE Exposure and Lung Cancer*

Bhatia et al. (1998) report a meta-analysis of 29 published[2] cohort and case-control studies of the relation between occupational exposure to DE and lung cancer. A search of the epidemiologic literature was conducted for all studies concerning lung cancer and DE exposure. Occupational studies involving mining were excluded because of concern about the possible influence of radon and silica exposures. Studies in which the minimum interval from time of first exposure to end of follow-up was less than 10 years, and studies in which work with diesel equipment or engines could not be confirmed or reliably inferred, were excluded. When studies presented risk estimates for more than one specific occupational category of DE-exposed workers, the subgroup risk estimates were used in the meta-analysis. Smoking-adjusted effect measures were used when present.

Of 29 studies 23 met the criteria for inclusion in the meta-analysis. The observed relative risk estimates were greater than 1 in 21 of these studies; this result is unlikely to be due to chance. The pooled relative risk weighted by study precision was 1.33 (95% CI = 1.24, 1.44), indicating increased relative risk for lung cancer from occupational exposure to DE. Subanalyses by study design (case-control and cohort studies) and by control for smoking produced results that did not differ from those of the overall pooled analysis. Cohort studies using internal comparisons showed higher relative risks than those using external comparisons (see Figure 7-1).

Bhatia and colleagues conclude that the analysis shows a small but consistent increase in the risk for lung cancer among workers with exposure to DE. The authors evaluate the dependence of the relative risk estimate on the presence of control for smoking among studies, and provide a table that allows assessment of whether the quality of the data contributing to control for smoking is related to the relative risk estimates (albeit in a limited number of studies). Bhatia et al. assert that residual confounding is not affecting the summary estimates or conclusions for the following reasons: (1) the pooled relative risks for studies adjusted for smoking were the same as those for studies not adjusting for smoking; (2) in those studies giving risk estimates adjusted for smoking and risk estimates not adjusted for smoking, there was only a small reduction in the pooled relative risk from DE exposure; and (3) in studies with internal

[2]Of 35 studies identified in the literature search, 6 pairs of studies represented analyses of the same study population, reducing the number of studies to 29.

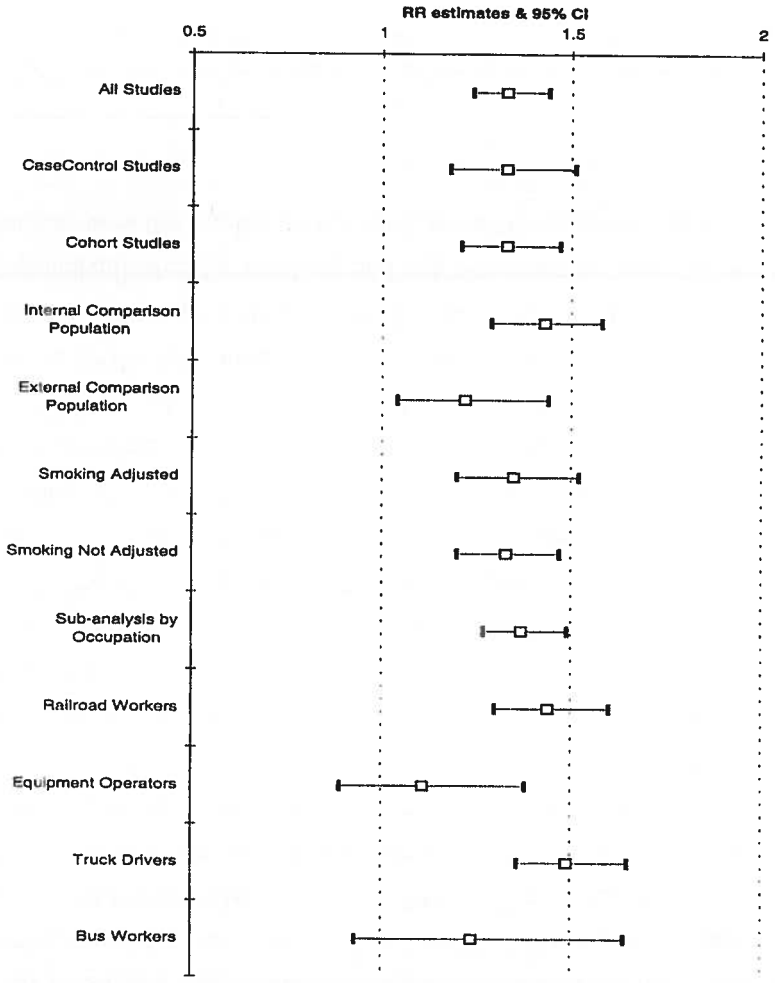


Figure 7-1. Pooled relative risk estimates and heterogeneity-adjusted 95% confidence intervals for all studies and subgroups of studies included in the meta-analysis.

Source: Bhatia et al., 1998.

comparison populations, in which confounding is less likely, the pooled relative risk estimate was 1.43.

The validity of this assessment depends on the adequacy of control for smoking in the individual studies. If inadequate adjustment for smoking is employed and residual confounding by cigarette smoking pertains in the result of the individual studies, then the comparisons and contrasts of the pooled estimates the authors cite as reasons for dismissing the effect of residual confounding by smoking will remain contaminated by residual confounding in the individual studies. In fact, Bhatia et al. erroneously identify the treatment of the smoking data in the main

analysis for the 1987 report by Garshick et al. as a continuous variable representing pack-years of smoking, whereas the analysis actually dichotomized the pack-years data into two crude dose categories (above and below the 50 pack-years level). This clearly reduced the quality of the adjustment for smoking, which already suffered from the fact that information on cumulative cigarette consumption was missing for more than 20% of the lung cancer cases. In this instance, the consistency between the adjusted and unadjusted estimates of the relative risk for DE exposure may be attributable to failure of adjustment rather than lack of confounding by cigarette smoking. A similar problem exists for the Bhatia et al. representation of the control for confounding in the study by Boffetta and Stellman (1988).

An evaluation of the potential for publication bias is presented that provides reassurance that the magnitude of published effects is not a function of the precision or study power; however, this assessment cannot rule out the possibility of publication bias.

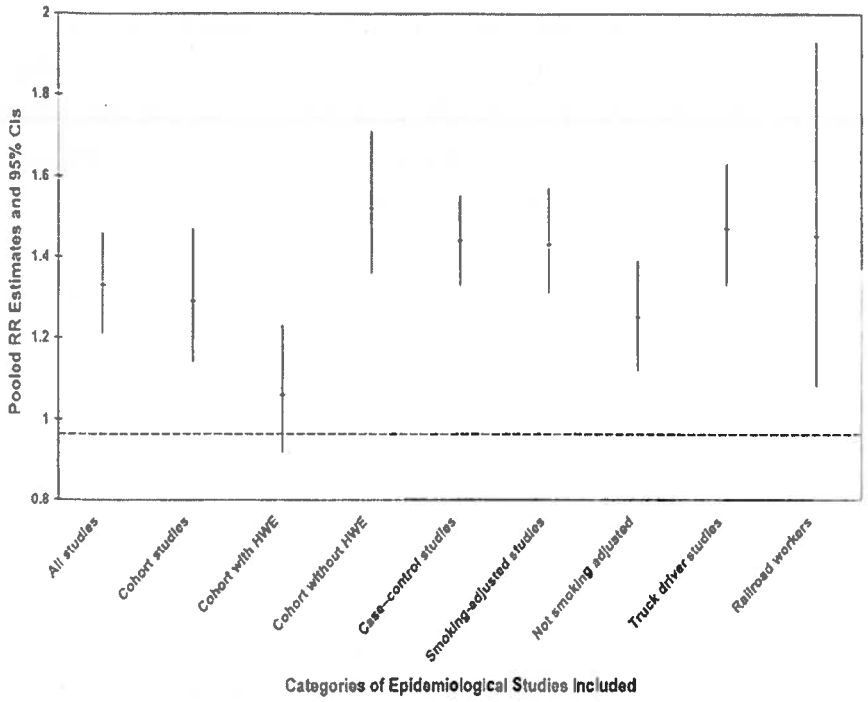
7.2.3.3. *Lipsett and Campleman (1999): Occupational Exposure to DE and Lung Cancer: A Meta-Analysis*

Lipsett and Campleman (1999) conducted electronic searches to identify epidemiologic studies published between 1975 and 1995 of the relationship of occupational exposure to DE and lung cancer. Studies were selected based on the following criteria: (1) Estimates of relative risks and their standard errors must be reported or derivable from the information presented. (2) Studies must have allowed for a latency period of 10 or more years for development of lung cancer after onset of exposure. (3) No obvious bias resulted from incomplete case ascertainment in follow-up studies. (4) Studies must be independent: that is, a single representative study selected from any set of multiple analyses of data from the same population. Studies focusing on occupations involving mining were excluded because of potential confounding by radon, arsenic, and silica, as well as possible interactions between cigarette smoking and exposure to these substances in lung cancer induction.

Thirty of the 47 studies initially identified as relevant met the specified inclusion criteria. Several risk estimates were extracted from six studies reporting results from multiple mutually exclusive diesel-related occupational subgroups. If a study reported effects associated with several levels or durations of exposure, the effect reported for the highest level or longest duration of exposure was used. If estimates for several occupational subsets were reported, the most diesel-specific occupation or exposure was selected. Adjusted risk estimates were used when available.

Thirty-nine independent estimates of relative risk and standard errors were extracted. Pooled estimates of relative risk were calculated using a random-effects model. Among study

populations most likely to have had substantial exposure to DE, the pooled smoking- adjusted relative risk was 1.47 (95% CI = 1.29, 1.67) (see Figure 7-2).



Note. CI = confidence interval; HWE = healthy worker effect.

Figure 7-2. Pooled estimates of relative risk of lung cancer in epidemiologic studies involving occupational exposure to DE (random-effects models).

Source: Lipsett and Campleman, 1999.

The between-study variance of the relative risks indicated the presence of significant heterogeneity in the individual estimates. The authors evaluated the potential sources of heterogeneity by subset analysis and linear meta-regressions. Major sources of heterogeneity included control for confounding by smoking, selection bias (a healthy worker effect), and exposure patterns characteristic of different occupational categories. A modestly higher, pooled relative risk was derived for the subset of case-control studies, which, unlike the cohort studies, showed little evidence of heterogeneity.

This meta-analysis also evaluated the potential for publication bias, which provides reassurance that the magnitude of published effects is not a function of the precision or study

power. Again, as stated in the Bhatia et al. (1998) review, this assessment cannot rule out the possibility of publication bias.

Although a relatively technical approach was used in deriving summary estimates of relative risk and the evaluation of possible sources of variation in the relative risks in this meta-analysis, this approach should not be confused with rigorous evaluation of the potential weaknesses among the studies included in the analysis. The heterogeneity attributable to statistical adjustment for smoking was evaluated based on a dichotomous assessment of whether control for smoking could be identified in the studies considered. This does not reflect the adequacy of the adjustment for smoking employed in the individual studies considered.

7.2.4. Summary and Discussion

Certain extracts of DE have been demonstrated as both mutagenic and carcinogenic in animals and in humans. Animal data suggest that DE is a pulmonary carcinogen among rodents exposed by inhalation to high doses over long periods of time. While rat lung cancer response to DE is not suitable for dose-response extrapolation to humans, the positive lung cancer response doses imply a hazard for humans. Because large working populations are currently exposed to DE and because nonoccupational ambient exposures currently are of concern as well, the possibility that exposure to this complex mixture may be carcinogenic to humans has become an important public health issue.

Because diesel emissions become diluted in the ambient air, it is difficult to study the health effects in the general population. Nonoccupational exposure to DE is worldwide in urban areas. Thus, "unexposed" reference populations used in occupational cohort studies are likely to contain a substantial number of individuals who are nonoccupationally exposed to DE. Furthermore, the "exposed" group in these studies is based on job titles, which in most instances are not verified or correlated with environmental hygiene measurement. The issue of health effect measurement is further complicated by the fact that occupational cohorts tend to be healthy and have below-average mortality, usually referred to as the "healthy worker effect." Hence, the usual standard mortality ratios observed in cohort mortality studies are likely to be underestimations of true risk.

A major difficulty with the occupational studies considered here was measurement of actual DE exposure. Because all the cohort mortality studies were retrospective, assessment of health effects from exposure to DE was naturally indirect. In these occupational settings, no systematic quantitative records of ambient air were available. Most studies compared men in job categories with presumably some exposure to DE with either standard populations (presumably no exposure to DE) or men in other job categories from industries with little or no potential for DE exposure. A few studies have included measurements of diesel fumes, but there is no

standard method for the measurement. No attempt is made to correlate these exposures with the cancers observed in any of these studies, nor is it clear exactly which extract should have been measured to assess the occupational exposure to DE. All studies have relied on the job categories or self-report of exposure to DE. Gustavsson et al. (1990), Emmelin et al. (1993), and Brüske-Hohlfeld et al. (1999) estimated exposure levels by getting detailed histories of job tasks/categories and computing cumulative exposures, which unfortunately were not verifiable due to of the lack of industrial hygiene data. In the studies by Garshick et al. (1987, 1988), the diesel-exhaust-exposed job categories were verified based on an industrial hygiene survey done by Woskie et al. (1988a,b). The investigators found that in most cases the job titles were good surrogates for DE exposure. Also, in the railroad industry, where only persons who had at least 10 years of work experience were included in the study, the workers tended not to change job categories over the years. Thus, a job known only at one point in time was a reasonable marker of past DE exposure. Unfortunately, the exposure was only qualitatively verified. Quantitative use of this information would have been much more meaningful. Zaebst et al. (1991) conducted an industrial hygiene survey of elemental carbon exposure in the trucking industry by job categories. Using these exposure measurements, Steenland et al. (1998) conducted an exposure-response analysis of their earlier lung cancer case-control study (Steenland et al., 1990). These exposure data are currently being verified and will be used for quantitative risk assessment in the near future.

Occupations involving potential exposure to DE are miners, truck drivers, transportation workers, railroad workers, and heavy equipment operators. No known studies in metal miners have assessed whether DE is associated with lung cancer. Currently, there are about 265 underground metal/nonmetal mines in the United States (Department of Labor, Mine Safety and Health Administration, 2001). Approximately 20,000 miners are employed, but not all of them are currently working in the mines. Diesel engines were introduced in metal mines in the United States in the early to mid-1960s. Although all these mines use diesel equipment, it is difficult to estimate how many of these miners were actually exposed to diesel fumes.

Diesel engines were introduced in coal mines at an even later date in the United States, and their use is still quite limited. There are 910 underground coal mines in the United States, of which only 145 currently use diesel powered equipment (Department of Labor, Mine Safety and Health Administration, 2001). Even if it were possible to estimate how many miners (metal and coal) were exposed to DE, it would be very difficult to separate out the confounding effects of other potential pulmonary carcinogens, such as radon decay products or heavy metals (e.g., arsenic, chromium). Furthermore, the relatively short latency period limits the usefulness of these cohorts of miners.

Both metal and coal mines in Europe and Australia, on the other hand, have been using diesel equipment for more than 50 years. The epidemiologic studies of coal miners conducted in these countries discuss only exposures to coal dust. In most of the coal miner studies, DE exposures are not even mentioned by the investigators as confounding exposures. Therefore, it is not known how many miners, if any, were exposed to DE, for how long, and at what concentrations. Although studies of coal miners reviewed by IARC (1997) generally found lower than expected lung cancer mortality (with some exceptions where some excess of lung cancer was observed), without knowing the concentrations, duration of exposure, and number of miners exposed to DE, it is inappropriate to conclude that the reported lung cancer mortality deficit in these studies provides a proof positive of absence of causal association between DE exposure and occurrence of lung cancer.

7.2.4.1. *Summary of the Cohort Mortality Studies*

The cohort studies mainly demonstrated an increase in lung cancer. Studies of bus company workers by Waller (1981), Rushton et al. (1983), and Edling et al. (1987) failed to demonstrate any statistically significant excess risk of lung cancer, but these studies have certain methodological problems, such as small sample sizes, short follow-up periods (just 6 years in the Rushton et al. study), lack of information on confounding variables, and lack of analysis by duration of exposure, duration of employment, or latency that preclude their use in determining the carcinogenicity of DE. Although the Waller (1981) study had a 25-year follow-up period, the cohort was restricted to employees (ages 45 to 64) currently in service. Employees who left the job earlier, as well as those who were still employed after age 64 and who may have died from cancer, were excluded.

Wong et al. (1985) conducted a mortality study of heavy equipment operators that demonstrated a nonsignificant positive trend for cancer of the lung with length of membership and latency. Analysis of deceased retirees showed a significant excess of lung cancer. Individuals without work histories who started work prior to 1967, when records were not kept, may have been in the same jobs for the longest period of time. Workers without job histories included those who had the same job before and after 1967 and thus may have worked about 12 to 14 years longer; these workers exhibited significant excess risks of lung cancer and stomach cancer. If this assumption about duration of jobs is correct, then these site-specific causes can be linked to DE exposure. One of the methodologic limitations of this study is that most of these men worked outdoors; thus, this cohort might have had relatively low exposure to DE. The authors did not present any environmental measurement data either. Because of the absence of detailed work histories for 30% of the cohort and the availability of only partial work histories for the remaining 70%, jobs were classified and ranked according to presumed diesel exposure.

Information is lacking regarding duration of employment in the job categories (used for surrogate of exposure) and other confounding factors (alcohol consumption, cigarette smoking, etc.). Thus, this study cannot be used to support or refute a causal association between exposure to DE and lung cancer.

A 2-year mortality analysis by Boffetta and Stellman (1988) of the American Cancer Society's prospective study, after controlling for age and smoking, demonstrated an excess risk of lung cancer in certain occupations with potential exposure to DE. These excesses were statistically significant among miners (RR = 2.67, 95% CI = 1.63, 4.37) and heavy equipment operators (RR = 2.6, 95% CI = 1.12, 6.06). Recently Brüske-Hohlfeld et al. (1999) also have observed significantly higher risk for lung cancer, in the range of 2.31 to 4.3, for heavy equipment operators. The elevated risks were nonsignificant in railroad workers (RR = 1.59) and truck drivers (RR = 1.24). A dose response was also observed for truck drivers. With the exception of miners, exposure to DE occurred in the three other occupations showing an increase in the risk of lung cancer. Despite methodologic limitations, such as the lack of representiveness of the study population (composed of volunteers only, who were probably healthier than the general population), leading to an underestimation of the risk, and the questionable reliability of exposure data based on self-administered questionnaires that were not validated, this study is suggestive of a causal association between exposure to DE and excess risk of lung cancer.

Two mortality studies were conducted by Gustavsson et al. (1990) and Hansen (1993) among bus garage workers (Stockholm, Sweden) and truck drivers, respectively. An SMR of 122 was found among bus garage workers, based on 17 cases. A nested case-control study was also conducted in this cohort. Detailed exposure matrices based on job tasks were assembled for both DE and asbestos exposures. Statistically significant increasing lung cancer relative risks of 1.34, 1.81, and 2.43 were observed for DE indices of 10 to 20, 20 to 30, and >30, respectively, using 0 to 10 as a comparison group. Adjustment for asbestos exposure did not change the results. The main strength of this study is the detailed exposure matrices; some of the limitations are low power (small cohort) and lack of smoking histories. But smoking is not likely to be different among study individuals irrespective of their exposure status to DE.

Hansen (1993), on the other hand, found statistically significant SMR of 160 from cancer of bronchus and lung. No dose response was observed, although the excesses were observed in most of the age groups (30 to 39, 45 to 49, 50 to 54, 55 to 59, 60 to 64, and 65 to 74). There are quite a few methodologic limitations to this study. Exposure to DE was assumed in truck drivers for diesel-powered trucks, but no validation of exposure was attempted. Follow-up period was short, no latency analysis was done, and smoking data were lacking. However, a population survey carried out in 1988 showed very little difference in smoking habits of residents of rural area and the total Danish male population, thus, smoking is unlikely to confound the finding of

excess lung cancer. The findings of both these studies are consistent with the findings of other truck driver studies and are supportive of causal association.

Two mortality studies of railroad workers were conducted by Howe et al. (1983) and Garshick et al. (1988). The Howe et al. study, which was conducted in Canada, found relative risks of 1.2 ($p<0.01$) and 1.35 ($p<0.001$) among "possibly" and "probably" exposed groups, respectively. The trend test showed a highly significant dose-response relationship with exposure to DE and the risk of lung cancer. The main limitation of the study was the inability to separate overlapping exposures of coal dust/combustion fumes and DE fumes. Information on jobs was available at retirement only. There also was insufficient detail on the classification of jobs by DE exposure. The exposures could have been nonconcurrent or concurrent, but because the data are lacking, it is possible that the observed excess could be due to the effect of both coal dust/combustion fumes and DE fumes and not just one or the other. It should be noted that, so far, coal dust has not been demonstrated to be a pulmonary carcinogen in studies of coal miners. However, lack of data on confounders such as asbestos and smoking (though use of the internal comparison group to compute relative risks minimizes confounding by smoking) makes interpretation of this study difficult. When three DE exposure categories were examined for smoking-related diseases such as emphysema, laryngeal cancer, esophageal cancer, and buccal cancer, positive trends were observed, raising a possibility that the dose response demonstrated for diesel exposure may have been due to smoking. The findings of this study are at best suggestive of DE being a lung carcinogen.

The strong evidence for linking DE exposure to lung cancer comes from the Garshick et al. (1988) railroad worker study conducted in the United States. Relative risks of 1.57 (95% CI = 1.19, 2.06) and 1.34 (95% CI = 1.02, 1.76) were found for ages 40 to 44 and 45 to 49, respectively, after the exclusion of workers exposed to asbestos. The investigators reported that the risk of lung cancer increased with increasing duration of employment. As this was a large cohort study with a lengthy follow-up and adequate analysis, including dose response (based on duration of employment as a surrogate) as well as adjustment for other confounding factors such as asbestos, the observed association between increased lung cancer and exposure to DE is more meaningful. Even though the reanalysis of these data by Crump et al. (1991) found that the relative risk could be positively or negatively related to duration of exposure depending on how age was controlled, additional analysis by Garshick et al. (letter from Garshick, Harvard Medical School, to Chao Chen, U.S. EPA, dated August 15, 1991) found that the relationship between years exposed when adjusted for the attained age and calendar years was flat to negative, depending on the choice of the model. They also found that deaths were underreported by approximately 20% to 70% between 1977 and 1980, and their analysis based on job titles, limited to 1959-1976, showed that the youngest workers still had the highest risk of dying of

lung cancer. On the other hand, an analysis of the same data by California EPA (CalEPA, 1998) yielded a positive dose response set using age at 1959 and adding an interaction term of age and calendar year in the model. However, Crump (1999) reported that the negative dose-response continued to be upheld in his latest analysis when age was controlled more carefully and years of exposure quantified more accurately. Crump (1999) asserted that the negative dose-response trends for lung cancer observed with either the cumulative exposure or duration of exposure may be due to underascertainment of deaths in the last 4 years of follow-up of the Garshick et al. (1988) study, as well as incomplete follow-up in earlier years. The HEI (1999) special panel conducted its own analyses using Garshick et al. (1988) data to evaluate their usefulness for quantitative risk assessment and found results similar to those of Crump et al. (1991) and Garshick (letter from Garshick, Harvard Medical School, to Chao Chen, U.S. EPA, dated August 15, 1991). The HEI panel reported consistently elevated risk of lung cancer for train workers compared with clerks for each duration of employment, and that shop workers had an intermediate risk of lung cancer. But they found decreasing risk of lung cancer with increasing duration of employment. The panel discussed various possibilities (different types of biases) for the negative dose-response and advised against using the Garshick et al. (1988) data for quantitative risk assessment. The panel also reported the strengths of the Garshick et al. (1988) study such as large population, control for asbestos, and smoking, and concluded that the study was generally consistent with findings of weak association between exposure to DE and occurrence of lung cancer. Hence, the divergent results of these recent analyses do not negate the positive evidence this study provides for the qualitative evaluation. The observance of dose-response would have strengthened the causal association, but an absence of a dose-response does not negate it.

Suggestive evidence is provided by a recent study of potash miners in Germany. The information on the exposure (including elemental carbon and organics), work chronology, and work category was used by the investigators to calculate cumulative exposures for each worker. Furthermore, information on smoking habits indicated homogeneity in the cohort.
A statistically nonsignificant twofold increase in lung cancer was observed in the production workers as compared to workshop workers. The lack of significance for this finding could be due to short follow-up, not enough latency, and relatively young age of the cohort.

7.2.4.2. *Summary of the Case-Control Studies of Lung Cancer*

Among the 11 lung cancer case-control studies reviewed in this chapter, only 2 studies did not find any increased risk of lung cancer. Lerchen et al. (1987) did not find any excess risk of lung cancer, after adjusting for age and smoking, for diesel fume exposure. The major limitation of this study was a lack of adequate exposure data derived from the job titles obtained

from occupational histories. Next of kin provided the occupational histories for 50% of the cases that were not validated. The power of the study was small (analysis done on males only, 333 cases). Similarly, Boffeta et al. (1990) did not find any excess of lung cancer after adjusting for smoking and education. This study had a few methodological limitations. The lung cancer cases and controls were drawn from the ongoing study of tobacco-related diseases. It is interesting to note that the leading risk factor for lung cancer is cigarette smoking. The exposure was not measured. Instead, occupations were used as surrogates for exposure. Furthermore, there were very few individuals in the study who were exposed to DE. On the other hand, statistically nonsignificant excess risks were observed for DE exposure by Hall and Wynder (1984) in workers who were exposed to DE versus those who were not (OR = 1.4 and 1.7 with two different criteria) and by Damber and Larsson (1987) in professional drivers (OR = 1.2). These rates were adjusted for age and smoking. Hall and Wynder (1984) had a high nonparticipation rate of 36%. Therefore, the positive results found in this study are underestimated at best. In addition, the self-reported exposures used in the study by Hall and Wynder (1984) were not validated. This study also had low power to detect excess risk of lung cancer for specific occupations.

The study by Benhamou et al. (1988), after adjusting for smoking, found significantly increased risks of lung cancer among French motor vehicle drivers (RR = 1.42) and transport equipment operators (RR = 1.35). The main limitation of the study was the inability to separate exposures to DE from those to gasoline exhaust because both motor vehicle drivers and transport equipment operators probably were exposed to the exhausts of both types of vehicles.

Hayes et al. (1989) combined data from three studies (conducted in three different states) to increase the power to detect an association between lung cancer and occupations with a high potential for exposure to DE. They found that truck drivers employed for more than 10 years had
a significantly increased risk of lung cancer (OR = 1.5, 95% CI = 1.1, 1.9). This study also found a significant trend of increasing risk of lung cancer with increasing duration of employment among truck drivers. The relative odds were computed by adjusting for birth cohort, smoking, and State of residence. The main limitation of this study is again the mixed exposures to diesel and gasoline exhausts, because information on type of engine was lacking. Also, potential bias may have been introduced because the way in which the cause of death was ascertained for the selection of cases varied in the three studies. Furthermore, the methods used in these studies to classify occupational categories were different, probably leading to incompatibility of occupational categories.

Emmelin et al. (1993), in their Swedish dockworkers from 15 ports, found increased relative odds of 6.8 (90% CI = 1.3 to 34.9). A strong interaction between smoking and DE was

observed in this study. Of 50 cases and 154 controls, only 6 individuals were nonsmokers. Although intricate exposure matrices were created using three different variables, no direct exposure measurement was done. Despite the limitations of small number of cases and controls; lack of data on asbestos exposure, which is fairly common in dockworkers; and very few nonsmokers; this study provides consistent support for a real effect of DE exposure and occurrence of lung cancer, at least in smokers.

The most convincing evidence comes from the case-control studies among railroad workers by Garshick et al. (1987); among truck drivers of the Teamsters Union by Steenland et al. (1990, 1998); among truck drivers, railroad workers, and farmers in a population-based study by Swanson et al. (1993); among different professional drivers in Denmark by Hansen et al. (1998); and among male workers occupationally exposed to diesel motor emissions in Germany by Brüske-Hohlfeld et al. (1999). Garshick et al. (1987) found that after adjustment for asbestos and smoking, the relative odds for continuous exposure were 1.39 (95% CI = 1.05, 1.83). Among the younger workers with longer DE exposure, the risk of lung cancer increased with duration of exposure after adjusting for asbestos and smoking. Even after the exclusion of recent DE exposure (5 years before death), the relative odds increased to 1.43 (95% CI = 1.06, 1.94). This appears to be a well-conducted and well-analyzed study with reasonably good power. Potential confounders were controlled adequately, and interactions between DE and other lung cancer risk factors were tested. Some of the limitations of this study are misclassification of exposure because ICC job classification was used as surrogate for exposure and use of death certificates for identification of cases and controls.

Steenland et al. (1990), on the other hand, created two separate work history files, one from Teamsters Union pension files and the other from next-of-kin interviews. Using duration of employment as a categorical variable and considering employment after 1959 (when presumed dieselization occurred) for long-haul drivers, the risk of lung cancer increased with increasing years of exposure. Using 1964 as the cutoff, a similar trend was observed for long-haul drivers. For short-haul drivers, the trend was positive with a 1959 cutoff, but not when 1964 was used as the cutoff. For truck drivers who primarily drove diesel trucks and worked for 35 years, the relative odds were 1.89. The main strengths of the study are availability of detailed records from the Teamsters Union, a relatively large sample size, availability of smoking data, and measurements of exposure. The limitations of this study include possible misclassifications of exposure and smoking, lack of levels of diesel exposure, a smaller nonexposed group, and an insufficient latency period. Recently Steenland et al. (1998) conducted an exposure-response analysis on these cases and controls, using the industrial hygiene survey results of Zaebst et al. (1991). The estimates were made for long-haul drivers, short-haul drivers, dockworkers, mechanics, and those outside the trucking industry. The survey found that mechanics had the

highest current levels of DE exposures and dockworkers who mainly used propane- powered forklifts had the lowest exposure. The finding of the highest lung cancer risk for mechanics and lowest for dock workers is indicative of a causal association between the DE exposure and development of lung cancer. However, the risk among mechanics did not increase with increasing duration of employment. The ORs for quartile cumulative exposures, computed by using logistic regression adjusted for age, race, smoking, diet, and asbestos exposure, showed a pattern of increasing trends in risk with increasing exposure, between 1.08 and 1.72 depending upon exposure level and lag structure used.

In a population-based lung cancer case-control study Swanson et al. (1993) found statistically significant excess risks adjusted for age at diagnosis, smoking, and race, among white male drivers of heavy trucks employed for ≥20 years and railroad workers employed for ≥10 years (OR = 2.5, 95% CI = 1.1, 4.4, and OR = 2.4, 95 % CI = 1.1, 5.1, respectively), and among black farmers employed for ≥20 years (OR = 10.4, 95% CI = 1.4, 77.1). Although individual ORs were not significant for various occupations with potential exposure to DE, statistically significant trends were observed for drivers of heavy trucks, light trucks, farmers, and railroad industry workers among whites, and among black farmers ($p \leq 0.05$). The main strengths of the study are availability of data on lifetime work history and smoking history; the main limitation is absence of actual specific exposure data. This is the first study that found increased lung cancer risk for farmers, who are exposed to DE of their farm tractors.

Hansen et al. (1998), in their study of professional drivers in Denmark, found statistically significant ORs (adjusted for socioeconomic status) of 1.31, 1.64, and 1.39 for lorry/bus drivers, taxi drivers, and unspecified drivers, respectively. The lag time analyses for duration of employment were unchanged for lorry/bus drivers but increased to OR = 3 from 2.2 in taxi drivers with a lag time of 10 years and duration of employment of > 5 years. The authors asserted that the higher risk seen in the taxi drivers may be due to higher exposure to these drivers because of longer time spent in traffic congestion. Furthermore, the trend tests for increasing risk of lung cancer with increasing duration of employment were statistically significant for both lorry/bus drivers and taxi drivers in both 10-year lag time and no lag time. The main strengths of the study are the large sample size, availability of detailed employment records, and information on socioeconomic status. The main limitations are absence of individual data on smoking habits and asbestos exposure, and information about the type of fuel used for the vehicles driven by these professional drivers. A personal communication with the main investigator revealed that the lorries/buses and taxis have been using diesel fuel since the late 1940s. Moreover, indirect information about smoking and asbestos exposure indicated that these two confounders are unlikely to explain the observed excesses or the trends, resulting in strong support of earlier positive studies.

Brüske-Hohlfeld et al. (1999) recently conducted a pooled analysis of two case-control studies among male workers occupationally exposed to DME in Germany. The investigators collected data on demographic information, detailed smoking, and occupational history. Job titles and industries were classified in 33 and 21 categories respectively. Job descriptions were written and verified to avoid misclassification of estimated exposure to diesel emissions. Individual cumulative DME exposures and smoking pack-years were calculated. Asbestos exposures were estimated by certain job-specific supplementary questions. Analysis of 3,498 lung cancer cases and 3,541 controls yielded statistically significant ORs ranging from 1.25 to 2.31 adjusted for smoking and asbestos exposure. The risk increased with increasing years of exposure for both the first year of exposure and the end year of exposure. These investigators presented analyses by various job categories, by years of exposure, first and end years of exposure and, when possible, separately for West and East Germany. Significantly higher risks were found among all four job categories. For professional drivers (of trucks, buses, and taxis) ORs ranged from 1.25 to 2.53. For other traffic-related jobs (switchmen, diesel locomotive drivers, diesel forklift truck drivers), ORs ranged from 1.53 to 2.88. For heavy equipment operators (bulldozers, graders, and excavators), ORs ranged from 2.31 to 4.3, and for drivers of farming equipment the only significant excess (OR = 6.81) was for exposure for <30 years.

This study shows increased risk for all the DME-exposed job categories. The professional drivers and the other traffic-related jobs also have some mixed exposures to gasoline exhaust in general traffic. On the other hand, it should be noted that exposure to DME among heavy equipment and farm tractor drivers is much higher and not as mixed as in professional drivers. The heavy equipment drivers usually drive repeatedly through their own equipment's exhaust. Therefore, the observed highest risk for lung cancer in this job category establishes a strong link with the DME. The only other study that found significantly higher risk for heavy equipment operators (RR = 2.6) was conducted by Boffeta et al. (1988). Although the only significant excess in the group was observed for farming tractor operators with more than 30 years of exposure, a steady increase in risk was observed for this job category with increasing exposure. The investigators stated that the working conditions and the DME of tractors remained fairly constant over the years. This increase may be due mainly to exposure to DME and PM_{10}.

The main strengths of the study are large sample size, resulting in good statistical power; inclusion of incident cases diagnosed not more than 3 months prior to the interview; use of only personal interviews, reducing recall bias; diagnoses ascertained by cytology or histology; and availability of lifelong detailed occupational and smoking history. Exposure estimation done for each individual was based on job codes and industry codes, which were validated by written job descriptions to avoid misclassification.

The main limitation of the study is lack of data on actual exposure to DME. The cumulative quantitative exposures were calculated based on time spent in each job with potential exposure to DME and the type of equipment used. Thus, this study provides strong evidence for causal association between exposure to DE and occurrence of lung cancer.

7.2.4.3. *Summary of the Reviews and Meta-Analyses of Lung Cancer*

Three summaries of studies concerned with the relationship of DE exposure and lung cancer risk are reviewed. The HEI report is a narrative study of 35 epidemiologic studies (16 cohort and 19 case-control) of occupational exposure to diesel emissions published between 1957 and 1993. Control for smoking was identified in 15 studies. Six of the studies (17%) reported relative risk estimates less than 1, whereas 29 (83%) reported at least 1 excess relative risk, indicating a positive association. Twelve studies indicating a relative risk greater than 1 had 95% confidence intervals that excluded unity. These studies found that the evidence suggests that occupational exposure to DE from diverse sources increases the rate of lung cancer by 20% to 40% in exposed workers generally, and to a greater extent among workers with prolonged exposure. They also found that the results are not explicable by confounding due to cigarette smoking or other known sources of bias.

Bhatia et al. (1998) identified 23 studies that met criteria for inclusion in the meta-analysis. The observed relative risk estimates were greater than 1 in 21 of these studies. The pooled relative risk weighted by study precision was 1.33 (95% CI= 1.24, 1.44), which indicated increased relative risk for lung cancer from occupational exposure to DE. Subanalyses by study design (case-control and cohort studies) and by control for smoking produced results that did not differ from those of the overall pooled analysis. Cohort studies using internal comparisons showed higher relative risks than those using external comparisons.

Lipsett and Campleman (1999) identify 39 independent estimates of relative risk among 30 eligible studies of DE and lung cancer published between 1975 and 1995. Pooled relative risks for all studies and for study subsets were estimated using a random effect model. Interstudy heterogeneity was also modeled and evaluated. A pooled smoking-adjusted relative risk was 1.47 (95% CI = 1.29, 1.67). Substantial heterogeneity was found in the pooled-risk estimates. Adjustment for confounding by smoking, having a lower likelihood of selection bias, and increased study power were all found to contribute to lower heterogeneity and increased pooled estimates of relative risk.

There is some variability in the conclusions of these summaries of the association of DE and lung cancer. The three analyses find that smoking is unlikely to account for the observed effects, and all conclude that the data support a causal association between lung cancer and DE exposure. On the other hand, Stöber and Abel (1996), Muscat and Wynder (1995), and Cox

(1997) call into question the assertions by Cohen and Higgins (1995), Bhatia et al. (1998), and Lipsett and Campleman (1999) that the associations seen for DE and lung cancer are unlikely to be due to bias. They argue that methodologic problems are prevalent among the studies, especially in evaluation of diesel engine exposure and control of confounding by cigarette smoking, and thus, the observed association between exposure to DE and excess risk of lung cancer is more likely to be due to bias. The conclusions of the two meta-analyses are based on magnitude of pooled relative risk estimates and evaluation of potential sources of heterogeneity in the estimates. Despite the statistical sophistication of the meta-analyses, the statistical models used cannot compensate for deficiencies in the original studies and will remain biased to the extent that bias exists in the original studies.

7.2.4.4. *Discussion of Relevant Methodologic Issues*

A persistent association of risk for lung cancer and DE exposure has been observed in more than 30 epidemiologic studies published in the literature over the past 40 years. Evaluation of whether this association can be attributed to a causal relation between DE exposure and lung cancer requires careful consideration of whether chance, bias, or confounding might be likely alternative explanations.

A total of 10 cohort and 12 case-control studies are reviewed in this chapter. An increased lung cancer risk was observed in 8 cohort and 10 case-control studies, even though the results were not always statistically significant. There is a consistent tendency for point estimates of relative risk to be greater than one in studies that adjusted (either directly or indirectly) for smoking, had a long enough follow-up, and sufficient statistical power among truck drivers, railroad workers, dock workers, and heavy equipment workers. If this elevated risk was due to chance one would expect almost equal distribution of these point estimates to be above and below one. Many of the studies provide confidence intervals for their estimates of excess risk or statistical tests, which indicate that it is unlikely that the individual study findings were due to random variation. The persistence of this association between DE and lung cancer risk in so many studies indicates that the possibility is remote that the observed association in aggregate is due to chance. It is unlikely that chance alone accounts for the observed relation between DE and lung cancer.

The excess risk is observed in both cohort and case-control designs, which contradicts the concern that a methodologic bias specifically characteristic of either design (e.g., recall bias) might account for the observed effect. Selection bias is certainly present in some of the occupational cohort studies that use external population data in estimating relative risks, but this form of selection bias (a healthy worker effect) would only obscure, rather than spuriously produce, an association between DE and lung cancer. Several occupational epidemiologic

studies that use more appropriate data for their estimates are available. Selection biases may be operating in some case-control studies, but it is not obvious how such a bias could be sufficiently uniform in effect, prevalent, and strong enough to lead to the consistent association seen in the aggregate data. Given the variety of designs used in studying the DE and lung cancer association and the number of studies in different populations, it is unlikely that routinely studying noncomparable groups is an explanation for the consistent association seen. Exposure information bias is certainly a problem for almost all of the studies concerned. Detailed and reliable individual-level data on DE exposure for the period of time relevant to the induction of lung cancer are not available and are difficult to obtain. Generally, the only information from which diesel exposure can be inferred is occupational data, which is a poor surrogate for the true underlying exposure distribution. The variability in actual lifetime exposure to DE in an occupational cohort may not be reflected in differences in job title, and there might be considerable variability in actual exposure despite similar job titles. Study endpoints are frequently mortality data taken from death certificate information, which is frequently inaccurate and often does not fully characterize the lung cancer incidence experience of the population in question. Using inaccurate surrogates for lung cancer incidence and for diesel exposure can lead to substantial bias, and these shortcomings are endemic in the field. In most cases these shortcomings will lead to misclassification of exposure and of outcome, which is nondifferential. Nondifferential misclassification of exposure and/or outcome can bias estimates of a DE–lung cancer association, if one exists, toward the null; but it is unlikely that such misclassification would produce a spurious estimate in any one study. It is even more unlikely that it would bias a sufficient number of studies in a uniform direction to account for the consistent aggregate association observed.

Moreover, throughout this chapter, various methodologic limitations of individual studies have been discussed, such as small sample size, short follow-up period, lack of data on confounding variables, use of death certificates to identify the lung cancer cases, and lack of latency analysis. The studies with small sample sizes (i.e., not enough power) and short follow-up periods (i.e., not enough latent period) have been difficult to interpret due to these limitations.

The most important confounding variable is smoking which is a strong risk factor for lung cancer. All the studies considered for this report are either cohort retrospective mortality or case-control studies where history of exposures in the past is elicited. Smoking history is usually difficult to obtain in such instances. The smoking histories obtained from surrogates (next of kin, either spouse or offspring) were found to be accurate by Lerchen and Samet (1986) and McLaughlin et al. (1987). Lerchen and Samet did not detect any consistent bias in the report of cigarette consumption. In contrast, overreporting of cigarette smoking by surrogates was observed by Rogot and Reid (1975), Kolonel et al. (1977), and Humble et al. (1984). Kolonel et

al. found that the age at which an individual started smoking was reported within 4 years of actual age 84% of the time. These studies indicate that surrogates were able to provide fairly credible information on the smoking habits of the study subjects. If the surrogates of the cases were more likely to overreport cigarette smoking compared with the controls, then it might be harder to find an effect of DE because most of the increase in lung cancer would be attributed to smoking rather than to exposure to DE.

Some studies do not adjust for tobacco smoke exposure. Even though smoking is a strong risk for lung cancer, it is only a confounder if there are differential smoking habits among individuals exposed to DE versus individuals who are not exposed. Most of the occupational cohorts include workers from the same socioeconomic background or used an internal comparison group; hence, it is unlikely that confounding by cigarette smoking is substantial in these studies. Some studies have adjusted for socioeconomic status and some studies have compared the cigarette smoking habits by conducting rural and urban general population surveys. Besides, in studies with long enough latency, adjustment for cigarette smoking did not alter substantially the observed higher risk.

Another methodologic concern in these studies is use of death certificates to determine cause of death. Death certificates were used by all of the cohort mortality studies and some of the case-control studies of lung cancer to determine cause of death. Use of death certificates could lead to misclassification bias because of overdiagnosis. Studies of autopsies done between 1960 and 1971 demonstrated that lung cancer was overdiagnosed when compared with hospital discharge, with no incidental cases found at autopsy (Rosenblatt et al., 1971). Schottenfeld et al. (1982) also found an overdiagnosis of lung cancer among autopsies conducted in 1977 and 1978. On the other hand, Percy et al. (1981) noted 95% concordance when comparing 10,000 lung cancer deaths observed in the Third National Cancer Survey from 1969 to 1971 (more than 90% were confirmed histologically) to death-certificate-coded cause of death. These more recent findings suggest that the diagnosis of lung cancer on death certificates is better than anticipated. In reality, lung cancer is one cause of death that has been found to be generally reliably reported on the death certificate. Thus, the misclassification bias probably is minimal in the studies described in this chapter.

Finally, several investigators have not conducted latency analysis in their studies. The latent period for lung cancer development is from 20 to 30 years or more. Considering the fact that dieselization was not complete till almost 1959 for locomotives and the 1970s for the trucking industry in the United States, most of the cohort studies conducted in the U.S. population do not have a long enough follow-up period to allow for latency of 20 to 30+ years. In addition, the study inclusion criteria for most of the studies are individuals who worked in the industry for at least 6 months /1 year from the beginning of the follow-up period to the end of

the follow-up period. Hence, the later the individual enters the cohort, the shorter the follow-up period; thus, the latent period is insufficient for the occurrence of lung cancer in these late entrants. Therefore, the observed slight to moderate increase in risk of lung cancer could be due to insufficient latency. On the other hand, in certain case-control studies the elapsed period between the identification of the lung cancer cases and exposure to DE is long enough to allow for the 30+ years latency needed for the development of lung cancer (Hansen et al., 1998; Brüske-Hohlfeld et al., 1999). These investigators identified lung cancer cases in the early to mid-1990s and found significant excess risks for lung cancer among the individuals exposed to DE. It should be noted that the use of diesel fuel for trucks, buses, and taxis had started in their countries (Denmark and Germany, respectively) in the late 1940s.

7.2.4.5. *Evaluation of Causal Association*

In most situations, epidemiologic data are used to delineate the causality of certain health effects. Several cancers have been causally associated with exposure to agents for which there is no direct biological evidence. Insufficient knowledge about the biological basis for diseases in humans makes it difficult to identify exposure to an agent as causal, particularly for malignant diseases when the exposure was in the distant past. Consequently, epidemiologists and biologists have used the original or modified version of a set of criteria provided by Hill (1965)[3] that define a causal relationship between exposure and the health outcome. A causal interpretation is enhanced for studies that meet these criteria. None of these criteria actually proves causality; actual proof is rarely attainable when dealing with environmental carcinogens. None of these criteria should be considered either necessary (except temporality of exposure) or sufficient in itself. The absence of any one or even several of these criteria does not prevent a causal interpretation. However, if more criteria apply, this provides more credible evidence for causality.

Thus, applying the Hill criteria (1965) of causal inference, as modified by Rothman (1986), to the studies reviewed here resulted in the following:

- *Strength of association.* This phrase refers to the magnitude of the ratio of incidence or mortality (RRs or ORs). Several studies found statistically significant RRs and ORs that ranged from 1.2 to 2.6 (Howe et al., 1983; Rushton

[3]Hill in his address to the Royal Society of Medicine in 1965 on "The environment and disease: association or causation" explored several aspects of association between exposure and occurrence of an event before deciding that the most likely interpretation of it is causation. He provided nine different aspects of association that he characterized as his viewpoints before interpreting the association being causal. The epidemiologic community universally adopted these (aspects/viewpoints) later as criteria for causality/causal association.

et al., 1983; Wong et al., 1985; Gustavsson et al., 1990; Emmlin et al., 1993; Hansen, 1993; Hansen et al., 1998) and, after adjustment for smoking and/or asbestos, RRs and ORs remained statistically significant and in the same range in certain studies (Dambar and Larson 1987; Garshick et al., 1987, 1988; Benhamou et al., 1988; Boffetta and Stellman, 1988; Hays et al., 1989; Steenland et al., 1990; Swanson et al., 1993; Brüsk-Hohlfeld et al., 1999). In addition, two meta-analyses demonstrated that not only did excess in lung cancer remain the same after stratification/adjustment for smoking and occupation, but in several instances the pooled RRs showed modest increases, with little evidence of heterogeneity. Overall, the studies in epidemiologic terms show relatively modest to weak association between DE and occurrence of lung cancer. Even though strong associations are more likely to be causal than modest-to-weak associations, the fact that association is relatively modest or weak does not rule out the causal link.

- *Consistency.* Increased lung cancer risk has been observed in several cohort and case-control studies, conducted in several industries and occupations in which workers were potentially exposed to DE. However, not all the excesses were statistically significant. Statistically significant lung cancer excesses adjusted for smoking were observed in truck drivers (Hayes et al., 1989; Hansen, 1993; Swanson et al., 1993; Brüske-Hohlfeld et al., 1999), professional drivers (Benhamou et al., 1988; Brüske-Hohlfeld et al., 1999), railroad workers (Garshick et al., 1987; Swanson et al., 1993), heavy equipment drivers (Boffetta and Stellman, 1988; Brüske-Hohlfeld et al., 1999), and farm tractor drivers (Swanson et al., 1993; Brüske-Hohlfeld et al., 1999). Furthermore, the two recent meta-analyses by Bhatia et al. (1998) and Lipsett and Campleman (1999) found that even though a substantial heterogeneity existed in their initial pooled estimates, stratification on several factors demonstrated a relationship between exposure to DE and excess lung cancer that remained positive throughout various analyses.

- *Specificity.* This criterion requires that a single cause lead to a single effect. With respect to exposure to DE, excess for lung cancer is the only effect that is found to be consistently elevated and statistically significant in several studies. Quite a few studies have examined DE for other effects such as bladder cancer, leukemia,

gastrointestinal cancers, prostate cancer etc. The evidence for these effects is inadequate.

- *Temporality.* The only necessary, but not sufficient, criterion described by Hill for causality inference is that exposure to a causal agent precedes the effect in time. This criterion is clearly satisfied in the studies reviewed here. Temporality can be explored further in addressing the latency issue. A certain period is necessary for development of an effect after exposure to a causal agent has occurred. For instance, in cancer-causing agents a latent period can vary from 5 years (childhood leukemia) to ≥30 years (mesothelioma). Most of the studies reviewed here did not conduct the latency analysis. Some studies had a short follow-up period that did not allow enough time for the latency period (Waller, 1981; Howe et al., 1983; Rushton et al., 1983; Wong et al., 1985, Hansen, 1993) while several studies clearly allowed for an adequate latency period (Garshick et al., 1987; Gustavsson et al., 1990; Steenland et al., 1990; Swanson et al., 1993; Brüske-Hohlfeld et al., 1999). Both type of studies showed mixed results.

- *Biological gradient.* This criterion refers to the dose-response curve. Due to the lack of quantitative data on DE exposure in most studies reviewed here, analyzing the dose-response curve directly was not possible. In very few studies, exposure to DE was addressed specifically. Most investigators have used job titles/categories and duration of employment as surrogates for exposure and thus have presented response in relation to duration of employment. Significant dose-response (using duration of employment as a surrogate) was observed in various studies for railroad workers (Howe et al., 1983; Garshick et al., 1987; Garshick et al., 1988; Swanson et al., 1993; Cal EPA, 1998), truck drivers (Boffetta and Stellman, 1988; Hayes et al., 1989; Steenland et al., 1990; Swanson et al., 1993; Hansen et al., 1998; Brüske-Hohlfeld et al., 1999), transportation/heavy equipment operators (Wong et al., 1985; Gustavsson et al., 1990; Brüske-Hohlfeld et al., 1999), farmers/farm tractor users (Swanson et al., 1993; Brüske-Hohlfeld et al., 1999), and dockworkers (Emmelin et al., 1993).

- *Biological plausibility.* This criterion refers to the biologic plausibility of the hypothesis, an important concern that may be difficult to judge. The hypothesis considered for this review is that occupational exposure to DE is causally associated with the occurrence of lung cancer and is supported by the following:

First, DE has been shown to cause lung and other cancers in animals (Heinrich et al., 1986b; Iwai et al., 1986b; Mauderly et al., 1987; Pott et al., 1990; Mauderly, 1994). Second, it contains highly mutagenic substances such as polycyclic aromatic hydrocarbons as well as nitroaromatic compounds (Claxton, 1983; Ball et al., 1990; Gallagher et al., 1993; Sera et al., 1994; Nielsen et al., 1996a) that are recognized human pulmonary carcinogens (IARC, 1989). Third, DE consists of carbon core particles with surface layers of organics and gases; the tumorigenic activity may reside in one, some, or all of these components. As explained in Chapter 4, there is clear evidence that the mixture of organic constituents, both in particles and vapor phases, have the capacity to interact with DNA and give rise to mutations, chromosomal aberrations, and cell transformations, all well-established steps in the process of carcinogenesis. Further, increased levels of peripheral blood cell DNA adducts associated with occupational exposure to DE have been observed in humans (Nielsen et al., 1996a,b). Thus, the above evidence makes a convincing case that occupational exposures to DE are causally associated with the occurrence of lung cancer is highly plausible biologically.

In conclusion, the epidemiologic studies of exposure to DE and occurrence of lung cancer furnish evidence that is consistent with a causal association. This association observed in several studies is unlikely to be due to chance or bias. Although many studies did not have information on smoking, significant confounding by smoking is unlikely in these studies because the comparison population was from the same socioeconomic class. The strength of association (i.e., RRs/ORs between 1.2 and 2.6) was weak to modest by epidemiologic standards, with dose-response relationships observed in several studies. Last, but not least, there is highly plausible biological evidence that exposure to DE could result in excess risk of lung cancer in humans.

7.3. CARCINOGENICITY OF DIESEL EXHAUST IN LABORATORY ANIMALS

This chapter summarizes studies that assess the carcinogenic potential of DE in laboratory animals. The first portion of this chapter summarizes results of inhalation studies. Experimental protocols for the inhalation studies typically consisted of exposure (usually chronic) to diluted exhaust in whole-body exposure chambers using rats, mice, and hamsters as model species. Some of these studies used both filtered (free of particulate matter) DE and unfiltered (whole) DE to differentiate gaseous-phase effects from effects induced by diesel PM (DPM) and its adsorbed components. Other studies were designed to evaluate the relative importance of the carbon core of the diesel particle versus that of particle-adsorbed compounds.

Finally, a number of exposures were carried out to determine the combined effect of inhaled DE and tumor initiators, tumor promoters, or cocarcinogens.

Particulate matter concentrations in the DE used in these studies ranged from 0.1 to 12 mg DPM /m^3. In this chapter, any mention of statistical significance implies that $p \leq 0.05$ was reported in the reviewed publications. A summary of the animal inhalation carcinogenicity studies and their results is presented in Table 7-3.

Results of lung implantation and intratracheal instillation studies of whole diesel particles, extracted diesel particles, and particle extracts are reported in Section 7.3.3 and in Tables 7-4 and 7-5. Studies destined to assess the carcinogenic effects of DPM as well as solvent extracts of DPM following subcutaneous (s.c.) injection, intraperitoneal (i.p.) injection, or intratracheal (itr.) instillation in rodents are summarized in Section 7.3.5. Individual chemicals present in the gaseous phase or adsorbed to the particle surface were not included in this review because assessments of those of likely concern (i.e., formaldehyde, acetaldehyde, benzene, polycyclic aromatic hydrocarbons [PAHs]) have been published elsewhere (U.S. EPA, 1993).

7.3.1. Inhalation Studies (Whole Diesel Exhaust)

7.3.1.1. *Rat Studies*

The potential carcinogenicity of inhaled DE was first evaluated by Karagianes et al. (1981). Male Wistar rats (40 per group) were exposed to room air or diesel engine exhaust diluted to a DPM concentration of 8.3 (± 2.0) mg/m^3, 6 hr/day, 5 days/week for up to 20 months. The animals were exposed in 3,000 L plexiglass chambers. Airflow was equal to 50 liters per minute. Chamber temperatures were maintained between 25 °C and 26.5 °C. Relative humidity ranged from 45% to 80%. Exposures were carried out during the daytime. The connected to an electric generator and operated at varying loads and speeds to simulate operating conditions in an occupational situation. To control the CO concentration at 50 ppm, the exhaust was diluted 35:1 with clean air. Six rats per group were sacrificed after 4, 8, 16, and 20 months exposure for gross necropsy and histopathological examination.

The only tumor detected was a bronchiolar adenoma in the group exposed over 16 months to DE. No lung tumors were reported in controls. The equivocal response may have been caused by the relatively short exposure durations (20 months) and small numbers of animals examined. In more recent studies, for example, Mauderly et al. (1987), most of the tumors were detected in rats exposed for more than 24 months.

Table 7-3. Summary of animal inhalation carcinogenicity studies

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m^3)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]				Comments
								Adenomas				
Karagianes et al. (1981)	Rat/Wistar	M, 40 M, 40	Clean air Whole exhaust	8.3	None None	6 hr/day, 5 days/ week, for up to 20 mo	NA	0/6 (0) 1/6 (16.6)				
								Bronchoalveolar carcinoma				
Kaplan et al. (1983) White et al. (1983)	Rat/F344	M, 30 M, 30 M, 30 M, 30	Clean air Whole exhaust Whole exhaust Whole exhaust	0 0.25 0.75 1.5	None None None None	20 hr/day, 7 days/ week, for up to 15 mo	8 mo 8 mo 8 mo 8 mo	0/30 (0) 1/30 (3.3) 3/30 (10.0) 1/30 (3.3)				
								Adenomas	Carcinomas	Squamous cell tumors	All tumors	
Heinrich et al. (1986a,b) Mohr et al. (1986)	Rat/ Wistar	F, 96 F, 92 F, 95	Clean air Filtered exhaust Whole exhaust	4	None None None	19 hr/day, 5 days/ week for up to 35 mo	NA	0/96 (0) 0/92 (0) 8/95 (8.4)	0/96 (0) 0/92 (0) 0/95 (0)	0/96 (0) 0/92 (0) 9/95 (9.4)	0/96 (0) 0/92 (0) 17/95 (17.8)[c]	
								Adenomas	Adenocarcinoma and adenosquamous carcinoma	Large cell and squamous cell carcinomas	All tumors	
Iwai et al. (1986a,b)	Rat/F344	F, 24 F, 24 F, 24	Clean air Filtered exhaust Whole exhaust	4.9	None None None	8 hr/day, 7 days/ week, for 24 mo	NA	1/22 (4.5) 0/16 (0) 3/19 (0)	0/22 (0) 0/16 (0) 3/19 (15.8)	0/22 (0) 0/16 (0) 2/19 (10.5)	1/22 (4.5)[f] 0/16 (0) 8/19 (42.1)[c,g]	

Table 7-3. Summary of animal inhalation carcinogenicity studies (continued)

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m^3)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]				Comments
								Adenoma	Carcinoma			
Takemoto et al. (1986)	Rat/F344	F, 12	Clean air	0	None	4 hr/day,	NA	0/12 (0)	0/12 (0)			
		F, 21	Clean air	0	DIPN[h]	4 days/		10/21 (47.6)	4/21 (19)			
		F, 15	Whole	2-4	None	week,		0/15 (0)	0/15 (0)			
		F, 18	exhaust	2-4	DIPN[h]	18-24 mo		12/18 (66.7)	7/18 (38.9)			
			Whole exhaust									
								Adenomas	Adenocarcinoma + squamous cell carcinoma	Squamous cysts	All tumors	
Mauderly et al. (1987)	Rat/F344	M + F, 230[b]	Clean air	0	None	7 hr/day,	NA	(0)	(0.9)	(0)	(0.9)	
		M + F, 223	Whole	0.35	None	5 days/		(0)	(1.3)	(0)	(1.3)	
		M + F, 221	exhaust	3.5	None	week up to		(2.3)	(0.5)	(0.9)	(3.6)[c]	
		M + F, 227	Whole	7.1	None	30 mo		(0.4)	(7.5)	(4.9)	(12.8)[c]	
			exhaust									
			Whole exhaust									
								Adenomas	Adenosquamous carcinomas	Squamous cell carcinomas	All tumors	
Ishinishi et al. (1988a)	Rat/F344	M + F, 123	Clean air	0	None	16 hr/day,	NA	0/123 (0)	1/123 (0.8)	0/123 (0)	1/123 (0.8)	
		M + F, 123	Whole	0.5	None	6 days/		0/123 (0)	0/123 (0)	1/123 (0.8)	1/123 (0.8)	
		M + F, 125	exhaust	1.0	None	week,		0/125 (0)	0/125 (0)	0/125 (0)	0/125 (0)	
Heavy-duty engine		M + F, 123	Whole	1.8	None	for up to		0/123 (0)	4/123 (3.3)	0/123 (0)	4/123 (3.3)	
		M + F, 124	exhaust	3.7	None	30 mo		0/124 (0)	6/124 (4.8)	2/124 (1.6)	8/124 (6.5)[c]	
			Whole exhaust									
			Whole exhaust									

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Table 7-3. Summary of animal inhalation carcinogenicity studies (continued)

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m^3)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]			Comments
								Adenomas	Carcinomas	All tumors	
Ishinishi et al. (1988a)	Rat/F344	NS, 5	Whole	0.1	None	16 hr/day,	6 mo	0/5 (0)	0/5 (0)	0/5 (0)	
		NS, 8	exhaust	0.1	None	6 days/	12 mo	0/8 (0)	0/8 (0)	0/8 (0)	
		NS, 11	Whole	0.1	None	week,	18 mo	0/11 (0)	0/11 (0)	0/11 (0)	
		NS, 5	exhaust	1.1	None	for 12 mo	6 mo	0/5 (0)	0/5 (0)	0/5 (0)	
Light duty		NS, 9	Whole	1.1	None		12 mo	0/9 (0)	0/9 (0)	0/9 (0)	
		NS, 11	exhaust	1.1	None		18 mo	0/11 (0)	0/11 (0)	0/11 (0)	
			Whole exhaust								
			Whole exhaust								
			Whole exhaust								
Heavy duty		NS, 5	Whole	0.5	None	16 hr/day,	6 mo	0/5 (0)	0/5 (0)	0/5 (0)	
		NS, 9	exhaust	0.5	None	6 days/	12 mo	0/9 (0)	0/9 (0)	0/9 (0)	
		NS 11	Whole	0.5	None	week,	18 mo	0/11 (0)	0/11 (0)	0/11 (0)	
		NS, 5	exhaust	1.8	None	for 12 mo	6 mo	0/5 (0)	0/5 (0)	0/11 (0)	
		NS, 6	Whole	1.8	None		12 mo	0/6 (0)	0/6 (0)	0/6 (0)	
		NS, 13	exhaust	1.8	None		18 mo	0/13 (0)	1/13 (0)	1/13 (0)	
			Whole exhaust								
			Whole exhaust								
			Whole exhaust								

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Table 7-3. Summary of animal inhalation carcinogenicity studies (continued)

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m³)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]			Comments
								Primary lung tumors			
Brightwell et al. (1989)	Rat/344	M + F, 260	Clean air	0	None	16 hr/day, 5 days/ week, for 24 mo	NA	3/260 (1.2)			Tumor incidence for all rats dying or sacrificed
		M + F, 144	Filtered exhaust (medium exposure)	0	None			0/144 (0)			
		M + F, 143	Filtered exhaust (high exposure)	0	None			0/143 (0)			
		M + F, 143	Whole exhaust	0.7	None			1/143 (0.7)			♀ 24/25 (96%) after 24 mo
		M + F, 144	Whole exhaust	2.2	None			14/144 (9.7)[c]			♂ 12/27 (44%) after 24 mo
		M + F, 143	Whole exhaust	6.6	None			55/143 (38.5)[c]			
								Squamous cell carcinoma	All lung tumors		
Henrich et al. (1989a)	Rat/Wistar	F, NS	Clean air	0	DPN[d]	19 hr/day, 5 days/ week for 24 to 30 mo	NA	(4.4)	(84.8)		
		F, NS	Whole exhaust	4.2	DPN[d]			(46.8)[c]	(83.0)		
		F, NS	Filtered exhaust	0	DPN[d]			(4.4)	(67.4)		
		F, NS	Clean air	0	DPN[e]			(16.7)	(93.8)		
		F, NS	Whole exhaust	4.2	DPN[e]			(31.3)[c]	(89.6)		
		F, NS	Filtered exhaust	0	DPN[e]			(14.6)	(89.6)		
Lewis et al. (1989)	Rat/F344	M + F, 288[n]	Clean air	2	None	7 hr/day, 5 days/ week, 24 mo	NA	No tumors	0/192 (0)		
			Whole exhaust		None				0/192 (0)		

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Table 7-3. Summary of animal inhalation carcinogenicity studies (continued)

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m^3)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]				Comments
								Adeno-squamous carcinomas	Squamous cell carcinomas	All tumors		
Takaki et al. (1989) Light-duty engine	Rat/F344	M + F, 123 M + F, 123 M + F, 125 M + F, 123 M + F, 124	Clean air Whole exhaust Whole exhaust Whole exhaust Whole exhaust	0 0.1 0.4 1.1 2.3	None None None None None	16 hr/day, 6 days/ week, for up to 30 mo	NA	1/23 (0.8) 1/23 (0.8) 1/25 (0.8) 0/23 (0) 1/24 (8.1)	2/123 (1.6) 1/23 (0.8) 0/125 (0) 5/123 (4.1) 2/124 (1.6)	1/23 (0.8) 1/23 (0.8) 0/125 (0) 0/123 (0) 0/124 (0)	4/123 (3.3) 3/123 (2.4) 1/125 (0.8) 5/123 (4.1) 3/124 (2.4)	
								Adenomas	Adenocarcinomas	Squamous cell carcinomas	Benign squamous cell tumors	
Heinrich et al. (1995)	Rat/Wistar	F, 220 F, 200 F, 200 F, 100 F, 100 F, 100	Clean air Whole exhaust Whole exhaust Whole exhaust Carbon black TiO_2	0 0.8 2.5 7.0 11.6 10.0	None None None None None None	18 hr/day, 5 days/ week, for up to 24 mo	6 mo	0/217 (0) 0/198 (0) 2/200 (1) 4/100 (4) 13/100 (13) 4/100 (4)	1/217 (<1) 0/198 (0) 1/200 (<1) 4/100 (4) 13/100 (13) 13/100 (13)	0/217 (0) 0/198 (0) 0/200 (0) 2/100 (2) 4/100 (4) 3/100 (3)	0/217 (0) 0/198 (0) 7/200 (3.5) 14/100 (14) 20/100 (20) 20/100 (20)	Tumor incidences after 30 mo
								Adenomas	Adenocarcinomas	Squamous cell carcinoma	Adeno-squamous carcinoma	Other neoplasms
Nikula et al. (1995)	Rat/F344	M + F, 214[b] M + F, 210 M + F, 212 M + F, 213 M + F, 211	Clean air Whole exhaust Whole exhaust Carbon black Carbon black	0 2.5 6.5 2.5 6.5	None None None None None	16 hr/day, 5 days/ week for up to 24 mo	6 weeks	1/214 (<1) 7/210 (3) 23/212 (11) 3/213 (1) 13/211 (6)	1/214 (<1) 4/210 (2) 22/212 (10) 7/213 (3) 21/211 (10)	1/214 (<1) 3/210 (1) 3/212 (1) 0/213 (0) 3/211 (1)	0/214 (0) 0/210 (0) 1/212 (<1) 0/213 (0) 2/211 (<1)	0/214 (0) 0/210 (0) 0/212 (0) 1/213 (<1) 0/211 (0)

Table 7-3. Summary of animal inhalation carcinogenicity studies (continued)

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m^3)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]	Comments
Iwai et al. (1997)	F/344	121, F 108, F 153, F	Clean air Filtered air Whole exhaust	0 0 3.2-9.4	None None None	NA 48-56 hr/day 48-56 hr/day	NA 6 mo 6 mo	5/121(4%) type not stated 2/108(4%) type not stated 53/153(35%) 61.3% adenoma, 25.8% adenocarcinoma, 2.2% benign squamous cell tumor, 7.5% squamous cell carcinoma, 3.2% adenosquamous carcinoma	Cumulative exposure dose ranged from 154-274 mg/m^3
Orthoefer et al. (1981) (Pepelko and Peirano, 1983)	Mouse/ Strong A	M, 25	Clean air	0	None	20 hr/day, 7 days/ week, for 7 weeks		3/22 (13.6)	0.13 tumors/ mouse
			Whole exhaust	6.4	None		26 weeks	7/19 (36.8)	0.63 tumors/ mouse
			Whole exhaust	6.4	UV irradiated		26 weeks	6/22 (27.3)	0.27 tumors/ mouse

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Table 7-3. Summary of animal inhalation carcinogenicity studies (continued)

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m^3)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]	Comments
								Lung tumors	
	Mouse/ Jackson A	M + F, 40	Clean air	0	None	20 hr/day, 7 days/ week,	8 weeks	16/36 (44.4)	0.5 tumors/ mouse
		M + F, 40	Whole exhaust	6.4	None	for 8 weeks	8 weeks	11/34 (32.3)	0.4 tumors/ mouse
	Mouse/ Jackson A	F, 60	Clean air	0	None			4/58 (6.9)	0.09 tumors/ mouse
		F, 60	Clean air	0	Urethan[l]	20 hr/day, 7 days/ week,		9/52 (17.3)	0.25 tumors/ mouse
		F, 60	Whole exhaust	6.4	None	for approx. 7 mo.		14/56 (25.0)	0.32 tumors/ mouse
		F, 60		6.4	Urethan[k]			22/59 (37.3)	0.39 tumors/ mouse
		M, 429	Whole exhaust	0	None			73/403 (18.0)	0.23 tumors/ mouse
		M, 430	Clean air	6.4	None			66/368 (17.9)	0.20 tumors/ mouse
Kaplan et al. (1982)	Mouse A/J	M, 458 M, 18 M, 485	Clean air Clean air Whole exhaust	1.5	None Urethan[k] None	20 hr/day, 7 days/ week, for 3 mo	6 mo	Pulmonary adenomas 144/458 (31.4) 18/18 (100) 165/485 (34.2)	
								Pulmonary adenoma	
Kaplan et al. (1983) White et al. (1983)	Mouse/ A/J	M, 388 M, 388 M, 399 M, 396	Clean air Whole exhaust Whole exhaust Whole exhaust	0 0.25 0.75 1.5	None None None None	20 hr/day, 7 days/ week, for up to 8 mo	NA	130/388 (33.5) 131/388 (33.8) 109/399 (27.3) 99/396 (25.0)	

Table 7-3. Summary of animal inhalation carcinogenicity studies (continued)

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m^3)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]			Comments
								Adenomas	Carcinomas	All tumors	
Pepelko and Peirano (1983)	Mouse/ Sencar	M + F, 260	Clean air	121212	None	Continuous for 15 mo	NA	(5.1)	(0.5)	(5.6)	
			Clean air		BHT[l]			(12.2)	(1.7)	(2.8)	
			Clean air		Urethan[k]			(8.1)	(0.9)	(9.0)	
			Whole exhaust		None			(10.2)[c]	(1.0)	(11.2)[c]	
			Whole exhaust		BHT[l]			(5.4)	(2.7)	(8.1)	
			Whole exhaust		Urethan[l]			(8.7)	(2.6)	(11.2)	

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Table 7-3. Summary of animal inhalation carcinogenicity studies (continued)

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m³)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]				Comments
								All tumors				
Pepelko and Peirano (1983)	Mouse/ Strain A	M + F, 90	Clean air	1212012	None		NA	21/87 (24)				0.29 tumors/ mouse
			Clean air		Exposure (darkness)			59/237 (24.9)				0.27 tumors/ mouse
			Whole exhaust		Exposure (darkness)			10/80 (12.5)				0.14
			Whole exhaust					22/250 (0.10)				0.10
					Urethan[m]			66/75 (88)				2.80
					Urethan[m]			42/75 (0.95)				0.95
			Clean air									
			Whole exhaust									
								Adenomas	Adenocarcinoma	Squamous cell tumors	All tumors	
Heinrich et al. (1986a,b)	Mouse/ NMRI	M + F, 84	Clean air	4	None	19 hr/day, 5 days/ week for up to 30 mo	NA	9/84 (11)	2/84 (2)	—	11/84 (13)	
		M + F, 93	Filtered exhaust		None			11/93 (12)	18/93 (19)[c]	—	29/93 (31)[c]	
		M + F, 76	Whole exhaust		None			11/76 (15)	13/76 (17)[c]	—	24/76 (32)[c]	
Takemoto et al. (1986)	Mouse/ IRC	M + F, 45	Clean air	0	None	4 hr/day, 4 days/ week, for 19-28 mo	NA					
		M + F, 69	Whole exhaust	2-4	None							
									Adenoma	Adenocarcinoma		
	Mouse/ C57BL	M + F, 12	Clean air	0	None	4 hr/day, 4 days/ week for 19-28 mo	NA		3/45 (6.7)	1/45 (2.2)		
		M + F, 38	Whole exhaust	2-4	None				6/69 (8.7)	3/69 (4.3)		

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Table 7-3. Summary of animal inhalation carcinogenicity studies (continued)

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m^3)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]					Comments
Heinrich et al. (1995)	Mouse/ C57BL/6N	F, 120	Clean air	4.5	None	18 hr/day, 5 days/ week, for up to 21 mo	6 mo	1/12 (8.3)	0/12 (0)				5.1% tumor rate
		F, 120	Whole exhaust		None			8/38 (21.1)	3/38 (7.9)				8.5% tumor rate
		F, 120	Particle-free exhaust		None								3.5% tumor rate
	Mouse/ NMRI	F, 120	Clean air	0	None	18 hr/day, 5 days/ week for up to 13.5 mo	9.5 mo	Adenomas	Adenocarcinomas				
		F, 120	Whole exhaust	4.5	None			(25)	(15.4)				
				11.6	None			(21.8)	(15.4)				
			Carbon black	10	None			(11.3)	(10)				
			TiO_2					(11.3)	(2.5)				
	Mouse/ NMRI	F, 120	Clean air	4.5	None	18 hr/day, 5 days/ week, 23 mo	None	(25)	(8.8)				
		F, 120	Whole exhaust		None			(18.3)	(5.0)				
		F, 120	Particle-free exhaust		None			(31.7)	(15)				
Mauderly et al. (1996)	Mouse/ CD-1	M + F, 157[b]	Clean air	0	None	7 hr/day, 5 days/week, for up to 24 mo	None	Multiple adenomas	Multiple carcinomas	Adenomas/ carcinoma	Alveolar/ bronchiolar adenoma	Alveolar/ bronchiolar carcinoma	
		M + F, 171	Whole exhaust	0.35	None			1/157 (0.6)	2/157 (1.3)	1/157 (0.6)	10/157 (6.4)	7/157 (4.5)	
		M + F, 155	Whole exhaust	3.5	None			2/171 (1.2)	1/171 (0.6)	1/171 (0.6)	16/171 (9.4)	5/171 (2.9)	
		M + F, 186	Whole exhaust	7.1	None			0/155 (0)	1/155 (0.6)	0/155 (0)	8/155 (5.2)	6/155 (3.9)	
								0/186 (0)	0/186 (0)	0/186 (0)	10/186 (5.4)	4/186 (2.2)	
Heinrich et al. (1986a,b)	Hamster/ Syrian	M + F, 96	Clean air		None	19 hr/day 5 days/week for up to 30 mo		Adenomas	Adenocarcinoma	Squamous cell tumors	All tumors		
		M + F, 96	Filtered exhaust		None			0/96(0)	0/96(0)	0/96	0/96(0)		
		M + F, 96	Whole exhaust	4	None		NA	0/96(0)	0/96(0)	0/96	0/96(0)		

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Table 7-3. Summary of animal inhalation carcinogenicity studies (continued)

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m^3)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]	Comments
								Primary lung tumors	
Brightwell et al. (1989)	Hamster/ Syrian Golden	M + F,	Clean air	0	None	16 hr/day, 5 days/ week, for 24 mo	NA	7/202 (3.5)	Respiratory tract tumors not related to exhaust exposure for any of the groups
		M + F, 202	Clean air	0	DEN[j]			4/104 (3.8)	
		M + F, 104	Filtered exhaust (medium dose)	0	DEN[j]			9/104 (8.7)	
		M + F, 104	Filtered exhaust (high dose)	0	DEN[j]			2/101 (2.0)	
		M + F, 101	Whole exhaust	0.7	DEN[j]			6/102 (5.9)	
		M + F, 102		2.2	DEN[j]			4/101 (3.9)	
		M + F, 101	Whole exhaust	6.6	DEN[j]			1/204 (0.5)	
		M + F, 204	Whole exhaust	0	None			0/203 (0)	
		M + F, 203	Filtered exhaust (high dose)	6.6	None				
			Whole exhaust						

[a]Table values indicate number with tumors/number examined (% animals with tumors).
[b]Number of animals examined for tumors.
[c]Significantly different from clean air controls.
[d]Dipentylnitrosamine; 6.25 mg/kg/week s.c. during first 25 weeks of exposure.
[e]Dipentylnitrasamine; 12.5 mg/kg/week s.c. during first 25 weeks of exposure.
[f]Splenic lymphomas also detected in controls (8.3%), filtered exhaust group (37.5%) and whole exhaust group (25%).
[g]5.3% incidence of large cell carcinomas.
[h]1 g/kg, i.p. 1/week for 3 weeks starting 1 mo into exposure.
[i]Includes adenomas, squamous cell carcinomas, adenocarcinomas, adenosquamous cell carcinoma, and mesotheliomas.
[j]4.5 mg/diethylnitrosamine (DEN)/kg, s.c., 3 days prior to start of inhalation exposure.
[k]Single i.p. dose 1 mg/kg at start of exposure.
[l]Butylated hydroxytoluene 300 mg/kg, i.p. for week 1, 83 mg/kg for week 2, and 150 mg/kg for weeks 3 to 52.
[m]12 mg/m^3 from 12 weeks of age to termination of exposure. Prior exposure (in utero) and of parents was 6 mg/m^3.
[n]120-121 males and 71-72 females examined histologically.
[o]Not all animals were exposed for full term, at least 10 males were killed at 3, 6, and 12 mo of exposure.
NS = Not specified.
NA = Not applicable.

Table 7-4. Tumor incidences in rats following intratracheal instillation of DE particles (DPM), extracted DPM, carbon black (CB), benzo[*a*]pyrene (B[*a*]P), or particles plus B[*a*]P

Experimental group	Number of animals	Total dose	Animals with tumors (percent)	Statistical significance[a]
Control	47	4.5 mL	0 (0)	-
DPM (original)	48	15 mg	8 (17)	< 0.01
DPM (extracted)	48	30 mg	10 (21)	< 0.001
DPM (extracted)	48	15 mg	2 (4)	NS
CB (printex)	48	15 mg	10 (21)	< 0.001
CB (lampblack)	48	14 mg	4 (8)	NS
B[*a*]P	47	30 mg	43 (90)	< 0.001
B[*a*]P	48	15 mg	12 (25)	< 0.001
DEP + B[*a*]P	48	15 mg + 170 µg B[*a*]P	4 (8)	NS
CB (printex) + B[*a*]P	48	15 mg + 443 µg B[*a*]P	13 (27)	< 0.001

Table 7-5. Tumorigenic effects of dermal application of acetone extracts of DPM

Number of animals	Strain/sex	Sample material	Time to first tumor (mo)	Survivors at time of first tumor	Total tumors	Duration of experiment (mo)
52	C57BL/40 F C57BL/12 M	Extract of DPM obtained during warmup	13	33	2	22
50	Strain A/M	Extract of DPM obtained during full load	15	8	4	23
25	Strain A/F	Extract of DPM obtained during full load	13	20	17	17

Source: Kotin et al., 1955.

General Motors Research Laboratories sponsored chronic inhalation studies at the Southwest Research Institute using male Fischer 344 rats, 30 per group, exposed to DPM concentrations of 0.25, 0.75, or 1.5 mg/m^3 (Kaplan et al., 1983; White et al., 1983). The animals were exposed in 12.6 m^3 exposure chambers. Airflow was adjusted to provide 13 changes per hour. Temperature was maintained at 22 ± 2 °C. The exposure protocol was 20 hr/day, 7 days/week for 9 to 15 months. Exposures were halted during normal working hours for servicing. Some animals were sacrificed following completion of exposure, while others were returned to clean air atmospheres for an additional 8 months. Control animals received clean air. Exhaust was generated by 5.7-L Oldsmobile engines (four different engines used throughout the experiment) operated at a steady speed and load simulating a 40-mph driving speed of a full-size passenger car.

Although five instances of bronchoalveolar carcinoma were observed in 90 rats exposed to DE for 15 months and held an additional 8 months in clean air, compared with none among controls, statistical significance was not achieved in any of the exposure groups. These included one tumor in the 0.25 mg/m^3 group, three in the 0.75 mg/m^3 group, and one in the 1.5 mg/m^3 group. Rats kept in clean-air chambers for 23 months did not exhibit any carcinomas. No tumors were observed in any of the 180 rats exposed to DE for 9 or 15 months without a recovery period, or in the respective controls for these groups. Equivocal results may again have been due to less-than-lifetime duration of the study as well as insufficient exposure concentrations. Although the increases in tumor incidences in the groups exposed for 15 months and held an additional 8 months in clean air were not statistically significant, relative to controls, they were slightly greater than the historic background incidence of 3.7% for this specific lesion in this strain of rat (Ward, 1983). The first definitive studies linking inhaled DE to induction of lung cancer in rats were reported by researchers in Germany, Switzerland, Japan, and the United States in the mid-to-late 1980s. In a study conducted at the Fraunhofer Institute exhaust-generating system and exposure atmosphere characteristics are presented in Appendix A. The type of engine used (3-cylinder, 43 bhp diesel) is normally used in mining situations and was of Toxicology and Aerosol Research, female Wistar rats were exposed for 19 hr/day, 5 days/week to both filtered and unfiltered (total) DE at an average particulate matter concentration of 4.24 mg/m^3. Animals were exposed for a maximum of 2.5 years. The exposure system as described by Heinrich et al. (1986a) used a 40 kilowatt 1.6-L diesel engine operated continuously under the U.S. 72 FTP driving cycle. The engines used European Reference Fuel with a sulfur content of 0.36%. Filtered exhaust was obtained by passing engine exhaust through a Luwa FP-65 HT 610 particle filter heated to 80 °C and a secondary series of filters (Luwa FP-85, Luwa NS-30, and Drager CH 63302) at room temperature. The filtered and unfiltered exhausts were diluted 1:17 with filtered air and passed through respective 12 m^3 exposure chambers. Mass

median aerodynamic diameter of DPM was 0.35 ± 0.10 μm (mean ± SD). The gas-phase components of the DE atmospheres are presented in Appendix A.

The effects of exposure to either filtered or unfiltered exhaust were described by Heinrich et al. (1986b) and Stöber (1986). Exposure to unfiltered exhaust resulted in 8 bronchoalveolar adenomas and 9 squamous cell tumors in 15 of 95 female Wistar rats examined, for a 15.8% tumor incidence. Although statistical analysis was not provided, the increase appears to be highly significant. In addition to the bronchioalveolar adenomas and squamous cell tumors, there was a high incidence of bronchioalveolar hyperplasia (99%) and metaplasia of the bronchioalveolar epithelium (65%). No tumors were reported among rats exposed to filtered exhaust (n = 92) or clean air (n = 96).

Mohr et al. (1986) provided a more detailed description of the lung lesions and tumors identified by Heinrich et al. (1986a,b) and Stöber (1986). Substantial alveolar deposition of carbonaceous particles was noted for rats exposed to unfiltered DE. Squamous metaplasia was observed in 65.3% of the rats breathing unfiltered DE, but not in the control rats. Of nine squamous cell tumors, one was characterized as a Grade I carcinoma (borderline atypia, few to moderate mitoses, and slight evidence of stromal invasion), and the remaining eight were classified as benign keratinizing cystic tumors.

Iwai et al. (1986b) examined the long-term effects of DE inhalation on female F344 rats. The exhaust was generated by a 2.4-L displacement truck engine. The exhaust was diluted 10:1 with clean air at 20 °C to 25 °C and 50% relative humidity. The engines were operated at 1,000 rpm with an 80% engine load. These operating conditions were found to produce exhaust with the highest particle concentration and lowest NO_2 and SO_2 content. For those chambers using filtered exhaust, proximally installed high-efficiency particulate air (HEPA) filters were used. Three groups of 24 rats each were exposed to unfiltered DE, filtered DE, or filtered room air for 8 hr/day, 7 days/week for 24 months. Particle concentration was 4.9 mg/m^3 for unfiltered exhaust. Concentrations of gas-phase exhaust components were 30.9 ppm NO_x, 1.8 ppm NO_2, 13.1 ppm SO_2, and 7.0 ppm CO.

No lung tumors were found in the 2-year control (filtered room air) rats, although one adenoma was noted in a 30-months control rat, providing a spontaneous tumor incidence of 4.5%. No lung tumors were observed in rats exposed to filtered DE. Nineteen of the 24 exposed to unfiltered exhaust survived for 2 years. Of these, 14 were randomly selected for sacrifice at this time. Four of the rats developed lung tumors; two of these were malignant. Five rats of this 2-year exposure group were subsequently placed in clean room air for 3 to 6 months and four eventually (time not specified) exhibited lung tumors (three malignancies). Thus, the lung tumor incidence for total tumors was 42.1% (8/19) and 26.3% (5/19) for malignant tumors in rats exposed to whole DE. The tumor types identified were adenoma (3/19), adenocarcinoma

(1/19), adenosquamous carcinoma (2/19), squamous carcinoma (1/19), and large-cell carcinoma (1/19). The lung tumor incidence in rats exposed to whole DE was significantly greater than that of controls ($p \leq 0.01$). Tumor data are summarized in Table 7-3. Malignant splenic lymphomas were detected in 37.5% of the rats in the filtered exhaust group and in 25.0% of the rats in the unfiltered exhaust group; these values were significantly ($p \leq 0.05$) greater than the 8.2% incidence noted in the control rats. The study demonstrates production of lung cancer in rats following 2-year exposure to unfiltered DE. In addition, splenic malignant lymphomas occurred during exposure to both filtered and unfiltered DE. This is the only report to date of tumor induction at an extrarespiratory site by inhaled DE in animals.

A chronic (up to 24 months) inhalation exposure study was conducted by Takemoto et al. (1986), in which female Fischer 344 rats were exposed to DE generated by a 269-cc YANMAR-40CE NSA engine operated at an idle state (1,600 rpm). Exposures were 4 hours/day, 4 days/week. The animals were exposed in a 376-L exposure chamber. Air flow was maintained at 120 L/min. Exhaust was diluted to produce a particle concentration of 2-4 mg/m^3. When not exposed the animals were maintained in an air-conditioned room at a temperature of 24 ± 2°C and a relative humidity of 55 ± 5% with 12 hr of light and darkness. Temperature and humidity in the exposure chambers was not noted. The particle concentration of the DE in the exposure chamber was 2 to 4 mg/m^3. B[a]P and 1-nitropyrene concentrations were 0.85 and 93 μg/g of particles, respectively. No lung tumors were reported in the diesel-exposed animals. It was also noted that the diesel engine employed in this study was originally used as an electrical generator and that its operating characteristics (not specified) were different from those of a diesel-powered automobile. However, the investigators deemed it suitable for assessing the effects of diesel emissions.

Mauderly et al. (1987) provided data affirming the carcinogenicity of automotive diesel engine exhaust in F344/Crl rats following chronic inhalation exposure. Male and female rats were exposed to diesel engine exhaust at nominal DPM concentrations of 0.35 (n = 366), 3.5 (n = 367), or 7.1 (n = 364) mg/m^3 for 7 hr/day, 5 days/week for up to 30 mo. Sham-exposed (n = 365) controls breathed filtered room air. A total of 230, 223, 221, and 227 of these rats (sham-exposed, low-, medium-, and high-exposure groups, respectively) were examined for lung tumors. These numbers include those animals that died or were euthanized during exposure and those that were terminated following 30 months of exposure. The exhaust was generated by 1980 model 5.7-L Oldsmobile V-8 engines operated through continuously repeating U.S. Federal Test Procedure (FTP) urban certification cycles. The engines were equipped with automatic transmissions connected to eddy-current dynamometers and flywheels simulating resistive and inertial loads of a midsize passenger car. The D-2 diesel control fuel (Phillips Chemical Co.) met U.S. EPA certification standards and contained approximately 30% aromatic

hydrocarbons and 0.3% sulfur. Following passage through a standard automotive muffler and tailpipe, the exhaust was diluted 10:1 with filtered air in a dilution tunnel and serially diluted to the final concentrations. The primary dilution process was such that particle coagulation was retarded. Mokler et al. (1984) provided a detailed description of the exposure system. No exposure-related changes in body weight or lifespan were noted for any of the exposed animals, nor were there any signs of overt toxicity. Collective lung tumor incidence was greater (z statistic, $p \leq 0.05$) in the high (7.1 mg/m^3) and medium (3.5 mg/m^3) exposure groups (12.8% and 3.6%, respectively) versus the control and low (0.35 mg/m^3) exposure groups (0.9% and 1.3%, respectively). In the high-dose group the incidences of tumor types reported were adenoma (0.4%), adenocarcinomas plus squamous cell carcinomas (7.5%), and squamous cysts (4.9%). In the medium-dose group adenomas were reported in 2.3% of animals, adenocarcinomas plus squamous cell carcinomas in 0.5%, and squamous cysts in 0.9%. In the low-exposure group adenocarcinomas plus squamous cell carcinomas were detected in 1.3% of the rats. Using the same statistical analysis of specific tumor types, adenocarcinoma plus squamous cell carcinoma and squamous cyst incidence was significantly greater in the high-exposure group, and the incidence of adenomas was significantly greater in the medium-exposure group. A significant ($p<0.001$) exposure-response relationship was obtained for tumor incidence relative to exposure concentration and lung burden of DPM. These data are summarized in Table 7-3. A logistic regression model estimating tumor prevalence as a function of time, dose (lung burden of DPM), and sex indicated a sharp increase in tumor prevalence for the high dose level at about 800 days after the commencement of exposure. A less pronounced, but definite, increase in prevalence with time was predicted for the medium-dose level. Significant effects were not detected at the low concentration. DPM (mg per lung) of rats exposed to 0.35, 3.5, or 7.1 mg of DPM/m^3 for 24 months were 0.6, 11.5, and 20.8, respectively, and affirmed the greater-than-predicted accumulation that was the result of decreased particle clearance following high-exposure conditions.

In summary, this study demonstrated the pulmonary carcinogenicity of high concentrations of whole, diluted DE in rats following chronic inhalation exposure. In addition, increasing lung particle burden resulting from this high-level exposure and decreased clearance was demonstrated. A logistic regression model presented by Mauderly et al. (1987) indicated that both lung DPM burden and exposure concentration may be useful for expressing exposure-effect relationships.

A long-term inhalation study (Ishinishi et al., 1988a; Takaki et al., 1989) examined the effects of emissions from a light-duty (LD) and a heavy-duty (HD) diesel engine on male and female Fischer 344/Jcl rats. The LD engines were 1.8-L, 4-cylinder, swirl-chamber-type power plants, and the HD engines were 11-L, 6-cylinder, direct-injection-type power plants. The

engines were connected to eddy-current dynamometers and operated at 1,200 rpm (LD engines) and 1,700 rpm (HD engines). Nippon Oil Co. JIS No. 1 or No. 2 diesel fuel was used. The 30-months whole-body exposure protocol (16 h/day, 6 days/week) used DPM concentrations of 0, 0.5, 1, 1.8, or 3.7 mg/m^3 from HD engines and 0, 0.1, 0.4, 1.1, or 2.3 mg/m^3 from LD engines. The animals inhaled the exhaust emissions from 1700 to 0900 h. Sixty-four male rats and 59 to 61 female rats from each exposure group were evaluated for carcinogenicity.

For the experiments using the LD series engines, the highest incidence of hyperplastic lesions plus tumors (72.6%) was seen in the highest exposure (2.3 mg/m^3) group. However, this high value was the result of the 70% incidence of hyperplastic lesions; the incidence of adenomas was only 0.8% and that of carcinomas 1.6%. Hyperplastic lesion incidence was considerably lower for the lower exposure groups (9.7%, 4.8%, 3.3%, and 3.3% for the 1.1, 0.4, and 0.1 mg/m^3 and control groups, respectively). The incidence of adenomas and carcinomas, combining males and females, was not significantly different among exposure groups (2.4%, 4.0%, 0.8%, 2.4%, and 3.3% for the 2.3, 1.1, 0.4, and 0.1 mg/m^3 groups and the controls, respectively).

For the experiments using the HD series engines, the total incidence of hyperplastic lesions, adenomas, and carcinomas was highest (26.6%) in the 3.7 mg/m^3 exposure group. The incidence of adenomas plus carcinomas for males and females combined equaled 6.5%, 3.3%, 0%, 0.8%, and 0.8% at 3.7, 1.8, 1, and 0.4 mg/m^3 and for controls, respectively. A statistically significant difference was reported between the 3.7 mg/m^3 and the control groups for the HD series engines. The carcinomas were identified as adenomas, adenosquamous carcinomas, and squamous cell carcinomas. Although the number of each was not reported, it was noted that the majority were squamous cell carcinomas. A progressive dose-response relationship was not demonstrated. Tumor incidence data for this experiment are presented in Table 7-3.

The Ishinishi et al. (1988a) study also included recovery tests in which rats exposed to whole DE (DPM concentration of 0.1 or 1.1 mg/m^3 for the LD engine and 0.5 or 1.8 mg/m^3 for the HD engine) for 12 months were examined for lung tumors following 6-, 12-, or 18-month recovery periods in clean air. The incidences of neoplastic lesions were low, and pulmonary DPM burden was lower than for animals continuously exposed to whole DE and not provided a recovery period. The only carcinoma observed was in a rat examined 12 months following exposure to exhaust (1.8 mg/m^3) from the HD engine.

Brightwell et al. (1986, 1989) studied the effects of DE on male and female F344 rats. The DE was generated by a 1.5-L Volkswagen engine that was computer-operated according to the U.S. 72 FTP driving cycle. The engine was replaced after 15 mo. The engine emissions were diluted by conditioned air delivered at 800 m^3/h to produce the high-exposure (6.6 mg/m^3) DE atmosphere. Further dilutions of 1:3 and 1:9 produced the medium- (2.2 mg/m^3) and low-

(0.7 mg/m^3) exposure atmospheres. The CO and NO_x concentrations (mean ± SD) were 32 ± 11 ppm and 8 ± 1 ppm in the high-exposure concentration chamber. The inhalation exposures were conducted overnight to provide five 16-h periods per week for 2 years; surviving animals were maintained for an additional 6 mo.

For males and females combined, a 1.2% (3/260), 0.7% (1/144), 9.7% (14/144), and 38.5% (55/143) incidence of primary lung tumors occurred in F344 rats following exposure to clean air or 0.7, 2.2, and 6.6 mg of DPM/m^3, respectively (Table 7-3). DE-induced tumor incidence in rats was dose-related and higher in females than in males (Table 7-3). These data included animals sacrificed at the interim periods (6, 12, 18, and 24 mo); therefore, the tumor incidence does not accurately reflect the effects of long-term exposure to the DE atmospheres. When tumor incidence is expressed relative to the specific intervals, a lung tumor incidence of 96% (24/25), 76% (19/25) of which were malignant, was reported for female rats in the high-dose group exposed for 24 months and held in clean air for the remainder of their lives. For male rats in the same group, the tumor incidence equaled 44% (12/27), of which 37% (10/27) were malignant. It was also noted that many of the animals exhibiting tumors had more than one tumor, often representing multiple histological types. The numbers and types of tumors identified in the rats exposed to DE included adenomas (40), squamous cell carcinomas (35), adenocarcinomas (19), mixed adenoma/adenocarcinomas (9), and mesothelioma (1). It should be noted that exposure during darkness (when increased activity would result in greater respiratory exchange and greater inhaled dose) could account, in part, for the high response reported for the rats.

Lewis et al. (1989) also examined the effects of inhalation exposure of DE and/or coal dust on tumorigenesis on F344 rats. Groups of 216 male and 72 female rats were exposed to clean air, whole DE (2 mg soot/m^3), coal dust (2 mg/m^3 respirable concentration; 5 to 6 mg/m^3 total concentration), or DE plus coal dust (1 mg/m^3 of each respirable concentration; 3.2 mg/m^3 total concentration) for 7 h/day, 5 days/week during daylight hours for up to 24 mo. Groups of 10 or more males were sacrificed at intermediate intervals (3, 6, and 12 mo). The DE was produced by a 7.0-L, 4-cycle, water-cooled Caterpillar Model 3304 engine using No. 2 diesel fuel (<0.5% sulfur by mass). The exhaust was passed through a Wagner water scrubber, which lowered the exhaust temperature and quenched engine backfire. The animals were exposed in 100-cubic-foot chambers. Temperature was controlled at 22 ± 2 °C and relative humidity at 50%±10%. The exhaust was diluted 27-fold with chemically and biologically filtered clean air to achieve the desired particle concentration.

Histological examination was performed on 120 to 121 male and 71 to 72 female rats terminated after 24 months of exposure. The exhaust exposure did not significantly affect the tumor incidence beyond what would be expected for aging F344 rats. There was no

postexposure period, which may explain, in part, the lack of significant tumor induction. The particulate matter concentration was also less than the effective dose in several other studies.

In a more recent study reported by Heinrich et al. (1995), female Wistar rats were exposed to whole DE (0.8, 2.5, or 7.0 mg/m^3) 18 h/day, 5 days/week for up to 24 mo, then held in clean air an additional 6 mo. The animals were exposed in either 6 or 12 m^3 exposure chambers. Temperature and relative humidity were maintained at 23-25 °C and 50%-70%, respectively. DE was generated by two 40-kw 1.6-L diesel engines (Volkswagen). One of them was operated according to the U.S. 72 cycle. The other was operated under constant load conditions. The first engine did not supply sufficient exhaust, which was filled by the second engine. Cumulative exposures for the rats in the various treatment groups were 61.7, 21.8, and 7.4 g/m^3 × h for the high, medium, and low whole-exhaust exposures. Significant increases in tumor incidences were observed in the high (22/100; $p<0.001$) and mid (11/200; $p<0.01$) exposure groups relative to clean-air controls (Table 7-3). Only one tumor (1/217), an adenocarcinoma, was observed in clean-air controls. Relative to clean-air controls, significantly increased incidences were observed in the high-exposure rats for benign squamous cell tumors (14/100; $p<0.001$), adenomas (4/100; $p<0.01$), and adenocarcinomas (5/100; $p<0.05$). Only the incidence of benign squamous cell tumors (7/200; $p<0.01$) was significantly increased in the mid-exposure group relative to the clean-air controls.

Particle lung burden and alveolar clearance also were determined in the Heinrich et al. (1995) study. Relative to clean air controls, alveolar clearance was significantly compromised by exposure to mid and high DE. For the high-diesel-exhaust group, 3-mo recovery time in clean air failed to reverse the compromised alveolar clearance.

In a study conducted at the Inhalation Toxicology Research Institute (Nikula et al., 1995) F344 rats (114-115 per sex per group) were exposed 16 hr/day, 5 days/week during daylight hours to DE diluted to achieve particle concentrations of 2.5 or 6.5 mg/m^3 for up to 24 mo. Controls (118 males, 114 females) were exposed to clean air. Surviving rats were maintained an additional 6 weeks in clean air, at which time mortality reached 90%. DE was generated with two 1988 Model LH6 General Motors 6.2-L V-8 engines burning D-2 fuel that met EPA certification standards. Chamber air flow was sufficient to provide about 15 exchanges per hour. Relative humidity was 40% to 70% and temperature ranged from 23 to 25 °C.

Following low and high DE exposure, the lung burdens were 36.7 and 80.7 mg, respectively, for females and 45.1 and 90.1 mg, respectively, for males. The percentages of susceptible rats (males and females combined) with malignant neoplasms were 0.9 (control), 3.3 (low DE), and 12.3 (high DE). The percentages of rats (males and females combined) with malignant or benign neoplasms were 1.4 (control), 6.2 (low DE), and 17.9 (high DE). All

primary neoplasms were associated with the parenchyma rather than the conducting airways of the lungs. The first lung neoplasm was observed at 15 mo. Among 212 males and females examined in the high-dose group, adenomas were detected in 23 animals, adenocarcinomas in 22 animals, squamous cell carcinomas in 3 animals, and an adenosquamous carcinoma in 1 animal. For further details see Table 7-3. Analysis of the histopathologic data suggested a progressive process from alveolar epithelial hyperplasia to adenomas and adenocarcinomas.

Iwai et al. (1997) carried out a series of exposures to both filtered and whole exhaust using a light-duty (2,369 mL) diesel engine. The protocol for engine operation was not stated. Groups of female SPF F344 Fischer rats were exposed for 2 years for 8 hr/day, 7 days/week, 8 hr/day, 6 days/week, or 18 hr/day, 3 days/week to either filtered exhaust or exhaust diluted to a particle concentration of 9.4, 3.2, and 5.1 mg/m^3, respectively. Cumulative exposure (mg/m^3 × hrs of exposure) equaled 274.4, 153.6, and 258.1 mg/m^3. The animals were then held for an additional 6 months in clean air. Lung tumors were reported in 5/121 (4%) of controls, 4/108 (4%) of those exposed to filtered exhaust, and 50/153 (35%) among those exposed to whole exhaust. Among rats exposed to whole DE the following number of tumors were detected; 57 adenomas, 24 adenocarcinomas, 2 benign squamous cell tumors, 7 squamous cell carcinomas, and 3 adenosquamous carcinomas. The authors stated that benign squamous cell tumors probably corresponded to squamous cysts in another classification.

7.3.1.2. *Mouse Studies*

A series of inhalation studies using strain A mice was conducted by Orthoefer et al. (1981). Strain A mice are usually given a series of intraperitoneal injections with the test agent; they are then sacrificed at about 9 months and examined for lung tumors. In the present series, inhalation exposure was substituted. DE was provided by one of two Nissan CN6-33 diesel engines having a displacement of 3244 cc and run on a Federal Short Cycle. Flow through the exposure chambers was sufficient to provide 15 air changes per hour. Temperature was maintained at 24 °C and relative humidity at 75%. In the first study, groups of 25 male Strong A strain (A/S) mice were exposed to irradiated DE (to simulate chemical reactions induced by sunlight) or nonirradiated DE (6 mg/m^3) for 20 h/day, 7 days/week. Additional groups of 40 Jackson A strain (S/J) mice (20 of each sex) were exposed similarly to either clean air or DE, then held in clean air until sacrificed at 9 months of age. No tumorigenic effects were detected at 9 months of age. Further studies were conducted in which male A/S mice were exposed 8 hr/day, 7 days/week until sacrifice (approximately 300 at 9 months of age and approximately 100 at 12 months of age). With the exception of those treated with urethan, the number of tumors per mouse did not exceed historical control levels in any of the studies. Exposure to DE,

however, significantly inhibited the tumorigenic effects of the 5-mg urethan treatment. Results are listed in Table 7-3.

Kaplan et al. (1982) also reported the effects of diesel exposure in strain A mice. Groups of male strain A/J mice were exposed for 20 h/day, 7 days/week for 90 days and held until 9 months of age. Briefly, the animals were exposed in inhalation chambers to DE generated by a 5.7-L Oldsmobile engine operated continuously at 40 mph at DPM concentrations of 0, 0.25, 0.75, or 1.5 mg/m^3. Controls were exposed to clean air. Temperature was maintained at 22 ± 2 °C and relative humidity at 50% ± 10% within the chambers. Among 458 controls and 485 exposed animals, tumors were detected in 31.4% of those breathing clean air versus 34.2% of those exposed to DE. The mean number of tumors per mouse also failed to show significant differences.

In a follow-up study, strain A mice were exposed to DE for 8 months (Kaplan et al., 1983; White et al., 1983). After exposure to the highest exhaust concentration (1.5 mg/m^3), the percentage of mice with pulmonary adenomas and the mean number of tumors per mouse were significantly less ($p<0.05$) than those for controls (25.0% vs. 33.5% and 0.30 ± 0.02 [S.E.] vs. 0.42 ± 0.03 [S.E.]) (Table 7-3).

Pepelko and Peirano (1983) summarized a series of studies on the health effects of diesel emissions in mice. Exhaust was provided by two Nissan CN 6-33, 6-cylinder, 3.24-L diesel engines coupled to a Chrysler A-272 automatic transmission and Eaton model 758-DG dynamometer. Sixty-day pilot studies were conducted at a 1:14 dilution, providing DPM concentrations of 6 mg/m^3. The engines were operated using the Modified California Cycle. These 20-hr/day, 7-days/week pilot studies using rats, cats, guinea pigs, and mice produced decreases in weight gain and food consumption. Therefore, at the beginning of the long-term studies, exposure time was reduced to 8 h/day, 7 days/week at an exhaust DPM concentration of 6 mg/m^3. During the final 12 months of exposure, however, the DPM concentration was increased to 12 mg/m^3. For the chronic studies, the engines were operated using the Federal Short Cycle. Chamber temperature was maintained at 24 °C and relative humidity at 50%. Airflow was sufficient for 15 changes per hour.

Pepelko and Peirano (1983) described a two-generation study using Sencar mice exposed to DE. Male and female parent-generation mice were exposed to DE at a DPM concentration of 6 mg/m^3 prior to (from weaning to sexual maturity) and throughout mating. The dams continued exposure through gestation, birth, and weaning. Groups of offspring (130 males and 130 females) were exposed to either DE or clean air. The exhaust exposure was increased to a DPM concentration of 12 mg/m^3 when the offspring were 12 weeks of age and was maintained until termination of the experiment when the mice were 15 months old.

The incidence of pulmonary adenomas (16.3%) was significantly increased in the mice exposed to DE compared with 6.3% in clean-air controls. The incidence in males and females combined was 10.2% in 205 animals examined compared with 5.1% in 205 clean-air controls. This difference was also significant. The incidence of carcinomas was not affected by exhaust exposure in either sex. These results provided the earliest evidence for cancer induction following inhalation exposure to DE. The increase in the sensitivity of the study, allowing detection of tumors at 15 mo, may have been the result of exposure from conception. It is likely that Sencar mice are sensitive to induction of lung tumors because they are also sensitive to induction of skin tumors. These data are summarized in Table 7-3.

Takemoto et al. (1986) reported the effects of inhaled DE (2 to 4 mg/m^3, 4 h/day, 4 days/week, for up to 28 mo) in ICR and C57BL mice exposed from birth. Details of the exposure conditions are presented in Section 7.3.2.1. All numbers reported are for males and females combined. Four adenomas and 1 adenocarcinoma were detected in 34 DE-exposed ICR mice autopsied at 13 to 18 mo, compared with 3 adenomas among 38 controls. Six adenomas and 3 adenocarcinomas were reported in 22 diesel-exposed ICR mice autopsied at 19 to 28 mo, compared with 3 adenomas and 1 adenocarcinoma in 22 controls. Four adenomas and 2 adenocarcinomas were detected in 79 C57BL mice autopsied at 13 to 18 mo, compared with none in 19 unexposed animals. Among males and females autopsied at 19 to 28 mo, 8 adenomas and 3 adenocarcinomas were detected in 71 exposed animals, compared with 1 adenoma among 32 controls. No significant increases in adenoma or adenocarcinoma were reported for either strain of exposed mice. However, the significance of the increase in the combined incidence of adenomas and carcinomas was not evaluated statistically. A statistical analysis by Pott and Heinrich (1990a) indicated that the difference in combined benign and malignant tumors between whole DE-exposed C57BL/6N mice and corresponding controls was significant at $p<.05$. See Table 7-3 for details of tumor incidence.

Heinrich et al. (1986b) and Stöber (1986), as part of a larger study, also evaluated the effects of DE in mice. Details of the exposure conditions reported by Heinrich et al. (1986a) are given in Section 7.3.1.1 and Appendix A. Following lifetime (19 h/day, 5 days/week, for a maximum of 120 weeks) exposure to DE diluted to achieve a particle concentration of 4.2 mg/m^3, 76 female NMRI mice exhibited a total lung tumor incidence of adenomas and adenocarcinomas combined of 32%. Tumor incidences reported for control mice (n = 84) equaled 11% for adenomas and adenocarcinomas combined. While the incidence of adenomas showed little change, adenocarcinomas increased significantly from 2.4% for controls to 17% for exhaust-exposed mice. In a follow-up study, however, Heinrich et al. (1995) reported a lack of tumorigenic response in either female NMRI or C57BL/6N mice exposed 17 h/day, 5

days/week for 13.5 to 23 months to whole DE diluted to produce a particle concentration of 4.5 mg/m^3. These data are summarized in Table 7-3.

The lack of a carcinogenic response in mice was reported by Mauderly et al. (1996). In this study, groups of 540 to 600 CD-1 male and female mice were exposed to whole DE (7.1, 3.5, or 0.35 mg DPM/m^3) for 7 hr/day, 5 days/week for up to 24 mo. Controls were exposed to filtered air. DE was provided by 5.7-L Oldsmobile V-8 engines operated continuously on the U.S. Federal Test Procedure urban certification cycle. The chambers were maintained at 25 °C-28 °C, relative humidity at 40%-60%, and a flow rate sufficient for 15 air exchanges per hour. Animals were exposed during the light cycle, which ran from 6:00 AM to 6:00 PM. DPM accumulation in the lungs of exposed mice was assessed at 6, 12, and 18 months of exposure and was shown to be progressive; DPM burdens were 0.2 ± 0.02, 3.7 ± 0.16, and 5.6 ± 0.39 mg for the low-, medium-, and high-exposure groups, respectively. The lung burdens in both the medium- and high-exposure groups exceeded that predicted by exposure concentration ratio for the low-exposure group. Contrary to what was observed in rats (Heinrich et al., 1986b; Stöber, 1986; Nikula et al., 1995; Mauderly et al., 1987), an exposure-related increase in primary lung neoplasms was not observed in the CD-1 mice, supporting the contention of a species difference in the pulmonary carcinogenic response to poorly soluble particles. The percentage incidence of mice (males and females combined) with one or more malignant or benign neoplasms was 13.4, 14.6, 9.7, and 7.5 for controls and low-, medium-, and high-exposure groups, respectively.

Although earlier studies provided some evidence for tumorigenic responses in diesel-exposed mice, no increases were reported in the two most recent studies by Mauderly et al. (1996) and Heinrich et al. (1995), which utilized large group sizes and were well designed and conducted. Overall, the results in mice must therefore be considered to be equivocal.

7.3.1.3. *Hamster Studies*

Heinrich et al. (1982) examined the effects of DE exposure on tumor frequency in female Syrian golden hamsters. Groups of 48 to 72 animals were exposed to clean air or whole DE at a mean DPM concentration of 3.9 mg/m^3. Inhalation exposures were conducted 7 to 8 hr/day, 5 days/week for 2 years. The exhaust was produced by a 2.4-L Daimler-Benz engine operated under a constant load and a constant speed of 2,400 rpm. Flow rate was sufficient for about 20 exchanges per hour in the 250-L chambers. No lung tumors were reported in either exposure group.

In a subsequent study, Syrian hamsters were exposed 19 hr/day, 5 days/week for a lifetime to DE diluted to a DPM concentration of 4.24 mg/m^3 (Heinrich et al., 1986b; Stöber, 1986). Details of the exposure conditions are reported in Appendix A. Ninety-six animals per

group were exposed to clean air or exhaust. No lung tumors were seen in either the clean-air group or in the DE-exposed group.

In a third study (Heinrich et al., 1989b), hamsters were exposed to exhaust from a Daimler-Benz 2.4-L engine operated at a constant load of about 15 kW and at a uniform speed of 2,000 rpm. The exhaust was diluted to an exhaust-clean air ratio of about 1:13, resulting in a mean particle concentration of 3.75 mg/m^3. Exposures were conducted in chambers maintained at 22 to 24 °C and 40% to 60% relative humidity for up to 18 mo. Surviving hamsters were maintained in clean air for up to an additional 6 mo. The animals were exposed 19 hr/day, 5 days/week beginning at noon each day, under a 12-hr light cycle starting at 7 AM. Forty animals per group were exposed to whole DE or clean air. No lung tumors were detected in either the clean-air or diesel-exposed hamsters.

Brightwell et al. (1986, 1989) studied the effects of DE on male and female Syrian golden hamsters. Groups of 52 males and 52 females, 6 to 8 weeks old, were exposed to DE at DPM concentrations of 0.7, 2.2, or 6.6 mg/m^3. They were exposed 16 hr/day, 5 days/week for a total of 2 years and then sacrificed. Exposure conditions are described in Section 7.3.1.1. No statistically significant (*t* test) relationship between tumor incidence and exhaust exposure was reported.

In summary, DE alone did not induce an increase in lung tumors in hamsters of either sex in several studies of chronic duration at high exposure concentrations.

7.3.1.4. *Monkey Studies*

Fifteen male cynomolgus monkeys were exposed to DE (2 mg/m^3) for 7 hr/day, 5 days/week for 24 months (Lewis et al., 1989). The same numbers of animals were also exposed to coal dust (2 mg/m^3 respirable concentration; 5 to 6 mg/m^3 total concentration), DE plus coal dust (1 mg/m^3 respirable concentration for each component; 3.2 mg/m^3 total concentration), or filtered air. Details of exposure conditions were listed previously in the description of the Lewis et al. (1989) study with rats (Section 7.3.1.1) and are listed in Appendix A.

None of the monkeys exposed to DE exhibited a significantly increased incidence of preneoplastic or neoplastic lesions. It should be noted, however, that the 24-mo time frame employed in this study may not have allowed the manifestation of tumors in primates, because this duration is only a small fraction of the monkeys' expected lifespan. In fact, there have been no near-lifetime exposure studies in nonrodent species.

7.3.2. Inhalation Studies (filtered DE)

Several studies have been conducted in which animals were exposed to DE filtered to remove PM. As these studies also included groups exposed to whole exhaust, details can be found in Sections 7.3.1.1 for rats, 7.3.1.2 for mice, and 7.3.1.3 for hamsters. Heinrich et al.

(1986b) and Stöber (1986) reported negative results for lung tumor induction in female Wistar rats exposed to filtered exhaust diluted to produce an unfiltered particle concentration of 4.24 mg/m^3. Negative results were also reported in female Fischer 344 rats exposed to filtered exhaust diluted to produce an unfiltered particle concentration of 4.9 mg/m^3 (Iwai et al., 1986a), in Fischer 344 rats of either sex exposed to filtered exhaust diluted to produce an unfiltered particle concentration of 6.6 mg/m^3 (Brightwell et al., 1989), in female Wistar rats exposed to filtered exhaust diluted to produce an unfiltered particle concentration of 7.0 mg/m^3 (Heinrich et al., 1995), and in female Fischer 344 rats exposed to filtered exhaust diluted to produce unfiltered particle concentrations of 5.1, 3.2, or 9.4 mg/m^3 (Iwai et al., 1997). In the Iwai et al. (1986a) study, splenic lymphomas were detected in 37.5% of the exposed rats compared with 8.2% in controls.

In the study reported by Heinrich at al. (1986a) and Stober (1986), primary lung tumors were seen in 29/93 NMRI mice (males and females combined) exposed to filtered exhaust, compared with 11/84 in clean-air controls, a statistically significant increase. In a repeat study by Heinrich et al. (1995), however, significant lung tumor increases were not detected in either female NMRI or C57BL/6N mice exposed to filtered exhaust diluted to produce an unfiltered particle concentration of 4.5 mg/m^3.

Filtered exhaust also failed to induce lung tumor induction in Syrian Golden hamsters (Heinrich et al., 1986a; Brightwell et al., 1989).

Although lung tumor increases were reported in one study and lymphomas in another, these results could not be confirmed in subsequent investigations. It is therefore concluded that little direct evidence exists for carcinogenicity of the vapor phase of DE in laboratory animals at concentrations tested.

7.3.3. Inhalation Studies (DE plus Cocarcinogens)

Details of the studies reported here have been described earlier and in Table 7-3. Tumor initiation with urethan (1 mg/kg body weight i.p. at the start of exposure) or promotion with butylated hydroxytolulene (300 mg/kg body weight i.p. week 1, 83 mg/kg week 2, and 150 mg/kg for weeks 3-52) did not influence tumorigenic responses in Sencar mice of both sexes exposed to concentrations of DE up to 12 mg/m^3 (Pepelko and Peirano, 1983).

Heinrich et al. (1986b) exposed Syrian hamsters of both sexes to DE diluted to a particle concentration of 4 mg/m^3. See Section 7.3.1.1 for details of the exposure conditions. At the start of exposure the hamsters received either one dose of 4.5 mg diethylnitrosamine (DEN) subcutaneously per kg body weight or 20 weekly intratracheal instillations of 250 μ*g* B[*a*]P. Female NMRI mice received weekly intratracheal instillations of 50 or 100 μ*g* B[*a*]P for 10 or 20 weeks, respectively, or 50 μ*g* dibenz[ah]anthracene (DBA) for 10 weeks. Additional groups of 96 newborn mice received one s.c. injection of 5 or 10 μ*g* DBA between 24 and 48 hr after birth. Female Wistar rats received weekly subcutaneous injections of dipentylnitrosamine

(DPN) at doses of 500 and 250 mg/kg body weight, respectively, during the first 25 weeks of exhaust inhalation exposure. Neither DEN, DBA, or DPN treatment enhanced any tumorigenic responses to DE. Response to B[*a*]P did not differ from that of BaP alone in hamsters, but results were inconsistent in mice. Although 20 B[*a*]P instillations induced a 71% tumor incidence in mice, concomitant diesel exposure resulted in only a 41% incidence. However, neither 10 B[*a*]P instillations nor DBA instillations induced significant effects.

Takemoto et al. (1986) exposed Fischer 344 rats for 2 years to DE at particle concentrations of 2 to 4 mg/m^3. One month after start of inhalation exposure one group of rats received di-isopropyl-nitrosamine (DIPN) administered i.p. at 1 mg/kg weekly for 3 weeks. Among injected animals autopsied at 18 to 24 mo, 10 adenomas and 4 adenocarcinomas were reported in 21 animals exposed to clean air, compared with 12 adenomas and 7 adenocarcinomas in 18 diesel-exposed rats. According to the authors, the incidence of adenocarcinomas was not significantly increased by exposure to DE.

Brightwell et al. (1989) investigated the concomitant effects of DE and DEN in Syrian hamsters exposed to DE diluted to produce particle concentrations of 0.7, 2.2, or 6.6 mg/m^3 for 2 years. The animals received a single dose of 4.5 mg DEN s.c. 3 days prior to start of inhalation exposure. DEN did not affect the lack of responsiveness to DE alone. Heinrich et al. (1989b) also exposed Syrian hamsters of both sexes to DE diluted to a particle concentration of 3.75 mg/m^3 for up to 18 mo. After 2 weeks of exposure, groups were treated with either 3 or 6 mg DEN/kg body weight, respectively. Again, DEN did not significantly influence the lack of tumorigenic responses to DE.

Heinrich et al. (1989a) investigated the effects of DPN in female Wistar rats exposed to DE diluted to achieve a particle concentration of 4.24 mg/m^3 for 2-2.5 years. DPN at doses of 250 and 500 mg/kg body weight was injected subcutaneously once a week for the first 25 weeks of exposure. The tumorigenic responses to DPN were not affected by exposure to DE. For details of exposure conditions of the hamster studies see Section 7.3.1.3.

Heinrich et al. (1986a) and Mohr et al. (1986) compared the effects of exposure to particles having only a minimal carbon core but a much greater concentration of PAHs than DPM does. The desired exposure conditions were achieved by mixing coal oven flue gas with pyrolyzed pitch. The concentration of B[a]P and other PAHs per milligram of DPM was about three orders of magnitude greater than that of DE. Female rats were exposed to the flue gas-pyrolyzed pitch for 16 hr/day, 5 days/week at particle concentrations of 3 to 7 mg/m^3 for 22 mo, then held in clean air for up to an additional 12 mo. Among 116 animals exposed, 22 tumors were reported in 21 animals, for an incidence of 18.1%. One was a bronchioloalveolar adenoma, one was a bronchioloalveolar carcinoma, and 20 were squamous cell tumors. Among the latter, 16 were classified as benign keratinizing cystic tumors and 4 were classified as carcinomas. No tumors were reported in 115 controls. The tumor incidence in this study was comparable to that reported previously for the DE-exposed animals.

In analyzing the studies of Heinrich et al. (1986a,b), Heinrich (1990b), Mohr et al. (1986), and Stöber (1986), it must be noted that the incidence of lung tumors occurring following exposure to whole DE, coal oven flue gas, or carbon black (15.8%, 18.1%, and 8% to 17%, respectively) was very similar. This occurred despite the fact that the PAH content of the PAH-enriched pyrolyzed pitch was more than three orders of magnitude greater than that of DE; carbon black, on the other hand, had only traces of PAHs. Based on these findings, particle-associated effects appear to be the primary cause of diesel-exhaust-induced lung cancer in rats exposed at high concentrations. This issue is discussed further in Chapter 7.

7.3.4. Lung Implantation or Intratracheal Instillation Studies

7.3.4.1. *Rat Studies*

Grimmer et al. (1987), using female Osborne Mendel rats (35 per treatment group), provided evidence that PAHs in DE that consist of four or more rings have carcinogenic potential. Condensate was obtained from the whole exhaust of a 3.0-L passenger-car diesel engine connected to a dynamometer operated under simulated city traffic driving conditions. This condensate was separated by liquid-liquid distribution into hydrophilic and hydrophobic fractions representing 25% and 75% of the total condensate, respectively. The hydrophilic, hydrophobic, or reconstituted hydrophobic fractions were surgically implanted into the lungs of the rats. Untreated controls, vehicle (beeswax/trioctanoin) controls, and positive (B[a]P) controls were also included in the protocol (Table 7-6). Fraction IIb (made up of PAHs with four to seven rings), which accounted for only 0.8% of the total weight of DPM condensate, produced the highest incidence of carcinomas following implantation into rat lungs. A carcinoma incidence of 17.1% was observed following implantation of 0.21 mg IIb/rat, whereas the nitro-PAH fraction (IId) at 0.18 mg/rat accounted for only a 2.8% carcinoma incidence. Hydrophilic fractions of the DPM extracts, vehicle (beeswax/trioctanoin) controls, and untreated controls failed to exhibit carcinoma formation. Administration of all hydrophobic fractions (IIa-d) produced a carcinoma incidence (20%) similar to the summed incidence of fraction IIb (17.1%) and IId (2.8%). The B[a]P positive controls (0.03, 0.1, 0.3 mg/rat) yielded a carcinoma incidence of 8.6%, 31.4%, and 77.1%, respectively. The study showed that the tumorigenic agents were primarily four- to seven-ring PAHs and, to a lesser extent, nitroaromatics. However, these studies demonstrated that simultaneous administration of various PAH compounds resulted in a varying of the tumorigenic effect, thereby implying that the tumorigenic potency of PAH mixtures may not depend on any one individual PAH. This study did not provide any information regarding the bioavailability of the particle-associated PAHs that might be responsible for carcinogenicity.

Kawabata et al. (1986) compared the effects of activated carbon and DE on lung tumor formation. One group of 59 F344 rats was intratracheally instilled with DPM (1 mg/week for 10

Table 7-6. Tumor incidence and survival time of rats treated by surgical lung implantation with fractions from DE condensate (35 rats/group)

Material portion by weight (%)	Dose (mg)	Median survival time in weeks (range)	Number of carcinomas[a]	Number of adenomas[b]	Carcinoma incidence (%)
Hydrophilic fraction (I) (25)	6.7	97 (24-139)	0	1	0
Hydrophobic fraction (II) (75)	20.00	99 (50-139)	50601	1000	14.2
Nonaromatics +					
PAC[c] 2 + 3 rings (IIa) (72)	19.22	103 (25-140)			0
PAH[d] 4 to 7 rings (IIb) (0.8)	0.21	102 (50-140)			17.1
Polar PAC (IIc) (1.1)	0.29	97 (44-138)			0
Nitro-PAH (IId) (0.7)	0.19	106 (32-135)			2.8
Reconstituted hydrophobics (Ia, b, c, d) (74.5)	19.91	93 (46-136)	70027113	101000	20.0
Control, unrelated		110 (23-138)			0
Control (beeswax/trioctanoin)		103 (51-136)			0
B[*a*]P	0.3	69 (41-135)			77.1
	0.1	98 (22-134)			31.4
	0.03	97 (32-135)			8.6

[a]Squamous cell carcinoma.

[b]Bronchiolar/alveolar adenoma.
[c]PAC = polycyclic aromatic compounds.
[d]PAH = polycyclic aromatic hydrocarbons.

Source: Adapted from Grimmer et al., 1987.

weeks). A second group of 31 rats was instilled with activated carbon using the same dosing regime. Twenty-seven rats received only the solvent (buffered saline with 0.05% Tween 80), and 53 rats were uninjected. Rats dying after 18 months were autopsied. All animals surviving 30 months or more postinstillation were sacrificed and evaluated for histopathology. Among 42 animals exposed to DPM surviving 18 months or more, tumors were reported in 31, including 20 malignancies. In the subgroup surviving for 30 mo, tumors were detected in 19 of 20 animals, including 10 malignancies. Among the rats exposed to activated carbon, the incidence of lung tumors equaled 11 of 23 autopsied, with 7 cases of malignancy. Data for those dying between 18 and 30 months and those sacrificed at 30 months were not reported separately. Statistical analysis indicated that activated carbon induced a significant increase in lung tumor incidence compared with no tumors in 50 uninjected controls and 1 tumor in 23 solvent-injected controls. The tumor incidence was significantly greater in the DPM-instilled group and was significantly greater than the increase in the carbon-instilled group.

A study reported by Rittinghausen et al. (1997) suggested that organic constituents of diesel particles play a role in the induction of lung tumors in rats. An incidence of 16.7% pulmonary cystic keratinizing squamous cell lesions was noted in rats intratracheally instilled with 15 mg whole DE particles, compared with 2.1% in rats instilled with 15 mg particles extracted to remove all organic constituents, and none among controls. Instillation of 30 mg of extracted particles induced a 14.6% incidence of squamous lesions, indicating the greater effectiveness of particles alone as lung particle overload increased.

Iwai et al. (1997) instilled 2, 4, 8, and 10 mg of whole diesel particles over a 2- to 10-week period into female F/344 rats, 50 or more per group. Tumors were reported in 6%, 20%, 43%, and 74% of the rats, with incidence of malignant tumors equal to 2%, 13%, 34%, and 48%, respectively. In a second experiment comparing whole with extracted diesel particles, tumor incidence equaled 1/48 (2%) in uninjected controls, 3/55 (5%) in solvent controls, 12/56 (21%) in extracted diesel particles, and 13/106 (12%) in animals injected with unextracted particles. Although the extracted particles appeared to be more potent, when converted to a lung burden basis (mg/100 mg dry lung) the incidence was only 14% among those exposed to extracted exhaust compared with 31% in those exposed to whole particles.

Dasenbrock et al. (1996) conducted a study to determine the relative importance of the organic constituents of diesel particles and particle surface area in the induction of lung cancer in rats. Fifty-two female Wistar rats were intratracheally instilled with 16-17 doses of DPM, extracted DPM, printex carbon black (PR), lampblack (LB), B[*a*]P, DPM + B[*a*]P, or PR + B[*a*]P. The animals were held for a lifetime or sacrificed when moribund. The lungs were necropsied and examined for tumors. Diesel particles were collected from a Volkswagen 1.6-L engine operating on a US FTP-72 driving cycle. The mass median aerodynamic diameter (MMAD) of the diesel particles was 0.25 μm and the specific surface area was 12 m^2/gm.

Following extraction with toluene, specific surface area increased to 138 m^2/gm. The MMAD for extracted PR was equal to 14 nm, while the specific surface area equaled 271 m^2/gm. The MMAD for extracted lampblack was equal to 95 nm, with a specific surface area equal to 20 m^2/gm. The B[*a*]P content of the treated particles was 11.3 mg per gm diesel particles and 29.5 mg B[*a*]P per gm PR. Significant increases in lung tumors were detected in rats instilled with 15 mg unextracted DPM and 30 mg extracted DPM, but not 15 mg extracted DPM. Printex CB was more potent than lampblack CB for induction of lung tumors, whereas B[*a*]P was effective only at high doses. Total dose and tumor responses are shown in Table 7-4.

A number of conclusions can be drawn from these results. First of all, particles devoid of organics are capable of inducing lung tumor formation, as indicated by positive results in the groups treated with high-dose extracted diesel particles and printex. Nevertheless, toluene extraction of organics from diesel particles results in a decrease in potency, indicating that the organic fraction does play a role in cancer induction. A relationship between cancer potency and particle surface area was also suggested by the finding that printex with a large specific surface area was more potent than either extracted DPM or lampblack, which have smaller specific areas. Finally, while very large doses of B[*a*]P are very effective in the induction of lung tumors, smaller doses adsorbed to particle surfaces had little detectable effect, suggesting that other organic components of DE may be of greater importance in the induction of lung tumors at low doses pf B[*a*]P (0.2-0.4 mg).

7.3.4.2. *Syrian Hamster Studies*

Kunitake et al. (1986) and Ishinishi et al. (1988b) conducted a study in which total doses of 1.5, 7.5, or 15 mg of a dichloromethane extract of DPM were instilled intratracheally over 15 weeks into male Syrian hamsters that were then held for their lifetimes. The tumor incidences of 2.3% (1/44), 0% (0/56), and 1.7% (1/59) for the high-, medium-, and low-dose groups, respectively, did not differ significantly from the 1.7% (1/56) reported for controls. Addition of 7.5 mg of B[a]P to a DPM extract dose of 1.5 mg resulted in a total tumor incidence of 91.2% and malignant tumor incidence of 88%. B[a]P (7.5 mg over 15 weeks) alone produced a tumor incidence rate of 88.2% (85% of these being malignant), which was not significantly different from the DPM extract + B[a]P group. Intratracheal administration of 0.03 μg B[a]P, the equivalent content in 15 mg of DPM extract, failed to cause a significant increase in tumors in rats. This study demonstrated a lack of detectable interaction between DPM extract and B[a]P, the failure of DPM extract to induce carcinogenesis, and the propensity for respiratory tract carcinogenesis following intratracheal instillation of high doses of B[a]P. For studies using the DPM extract, some concern must be registered regarding the known differences in chemical composition between DPM extract and DPM. As with all intratracheal instillation protocols, DPM extract lacks the complement of volatile chemicals found in whole DE.

The effects on hamsters of intratracheally instilled DPM suspension, DPM with Fe_2O_3, or DPM extract with Fe_2O_3 as the carrier were studied by Shefner et al. (1982). The DPM component in each of the treatments was administered at concentrations of 1.25, 2.5, or 5.0 mg/week for 15 weeks to groups of 50 male Syrian golden hamsters. The total volume instilled was 3.0 mL (0.2 mL/week for 15 weeks). The DPM and dichloromethane extracts were suspended in physiological saline with gelatin (0.5% w/v), gum arabic (0.5% w/v), and propylene glycol (10% by volume). The Fe_2O_3 concentration, when used, was 1.25 mg/0.2 mL of suspension. Controls received vehicle and, where appropriate, carrier particles (Fe_2O_3) without the DPM component. Two replicates of the experiments were performed. Adenomatous hyperplasia was reported to be most severe in those animals treated with DPM or DPM plus Fe_2O_3 particles and least severe in those animals receiving DPM plus Fe_2O_3. Of the two lung adenomas detected microscopically, one was in an animal treated with a high dose of DPM and the other was in an animal receiving a high dose of DPM extract. Although lung damage was increased by instillation of DPM, there was no evidence of tumorigenicity.

7.3.4.3. *Mouse Studies*

Ichinose et al. (1997a) intratracheally instilled 36 four-week-old male ICR mice per group weekly for 10 weeks with sterile saline or 0.05, 0.1, or 0.2 mg DPM. Particles were collected from a 2.74-L four-cylinder Isuzu engine run at a steady speed of 1,500 rpm under a load of 10 torque (kg/m). Twenty-four hours after the last instillation, six animals per group were sacrificed for measurement of lung 8-hydroxydeoxyguanosine (8-OHdG). The remaining animals were sacrificed after 12 months for histopathological analysis. Lung tumor incidence varied from 4/30 (13.3%) for controls to 9/30 (30%), 9/29 (31%), and 7/29 (24.1%) for mice instilled with 0.05, 0.1, and 0.2 mg/week, respectively. The increase in animals with lung tumors compared with controls was statistically significant for the 0.1 mg dose group, the only group analyzed statistically. Increases in 8-OHdG, an indicator of oxidative DNA damage, correlated well with the increase in tumor incidence in the 0.05 mg dose group, although less so with the other two. The correlation coefficients $r = 0.916$, 0.765, and 0.677 for the 0.05, 0.10, and 0.20 mg DPM groups, respectively.

In a similar study, 33 four-week-old male ICR mice per group were intratracheally instilled weekly for 10 weeks with sterile saline, 0.1 mg DPM, or 0.1 mg DPM from which the organic constituents were extracted with hexane (Ichinose et al., 1997b). Exhaust was collected from a 2.74-L four-cylinder Izuzu engine run at a steady speed of 2,000 rpm under a load of 6 torque (kg/m). Twenty-four hours after the last instillation, six animals per group were sacrificed for measurement of 8-OHdG. Surviving animals were sacrificed after 12 mo. The incidence of lung tumors increased from 3/27 (11.1%) among controls to 7/27 (25.9%) among those instilled with extracted diesel particles and 9/26 (34.6%) among those instilled with

unextracted particles. The increase in number of tumor-bearing animals was statistically significant compared with controls ($p<0.05$) for the group treated with unextracted particles. The increase in 8-OHdG was highly correlated with lung tumor incidence, r = 0.99.

7.3.5. Subcutaneous and Intraperitoneal Injection Studies

7.3.5.1. *Mouse Studies*

In addition to inhalation studies, Orthoefer et al. (1981) also tested the effects of i.p. injections of DPM on male (A/S) strain mice. Three groups of 30 mice were injected with 0.1 mL of a suspension (particles in distilled water) containing 47, 117, or 235 μg of DPM collected from Fluoropore filters in the inhalation exposure chambers. The exposure system and exposure atmosphere are described in Appendix A. Vehicle controls received injections of particle suspension made up of particulate matter from control exposure filters, positive controls received 20 mg of urethan, and negative controls received no injections. Injections were made three times weekly for 8 weeks, resulting in a total DPM dose of 1.1, 2.8, and 5.6 mg for the low-, medium-, and high-dose groups and 20 mg of urethan for the positive control group. These animals were sacrificed after 26 weeks and examined for lung tumors. For the low-, medium-, and high-dose DPM groups, the tumor incidence was 2/30, 10/30, and 8/30, respectively. The incidence among urethan-treated animals (positive controls) was 100% (29/29), with multiple tumors per animal. The tumor incidence for the DPM-treated animals did not differ significantly from that of vehicle controls (8/30) or negative controls (7/28). The number of tumors per mouse was also unaffected by treatment.

In further studies conducted by Orthoefer et al. (1981), an attempt was made to compare the potency of DPM with that of other environmental pollutants. Male and female Strain A mice were injected i.p. three times weekly for 8 weeks with DPM, DPM extracts, or various environmental mixtures of known carcinogenicity, including cigarette smoke condensate, coke oven emissions, and roofing tar emissions. Injection of urethan or dimethylsulfoxide (DMSO) served as positive or vehicle controls, respectively. In addition to DPM from the Nissan diesel previously described, an eight-cylinder Oldsmobile engine operated at the equivalent of 40 mph was also used to compare emission effects from different makes and models of diesel engine. The mice were sacrificed at 9 months of age and their lungs examined for histopathological changes. The only significant findings, other than for positive controls, were small increases in numbers of lung adenomas per mouse in male mice injected with Nissan DPM and in female mice injected with coke oven extract. Furthermore, the increase in the extract-treated mice was significant only in comparison with uninjected controls (not injected ones) and did not occur when the experiment was repeated. Despite the use of a strain of mouse known to be sensitive to tumor induction, the overall findings of this study were negative. The authors provided several possible explanations for these findings, the most likely of which were (1) the carcinogens that

were present were very weak, or (2) the concentrations of the active components reaching the lungs were insufficient to produce positive results.

Kunitake et al. (1986) conducted studies using DPM extract obtained from a 1983 HD MMC—6D22P 11-L V-6 engine. Five s.c. injections of DPM extract (500 mg/kg per injection) resulted in a significant ($p<0.01$) increase in subcutaneous tumors for female C57BL mice (5/22 [22.7%] vs. 0/38 among controls). Five s.c. doses of DPM extract of 10, 25, 30, 100, or 200 mg/kg failed to produce a significant increase in tumor incidence. One of 12 female ICR mice (8.3%) and 4 of 12 male ICR mice (33.3%) developed malignant lymphomas following neonatal s.c. administration of 10 mg of DPM extract per mouse. The increase in malignant lymphoma incidence for the male mice was statistically significant at $p<0.05$ compared with an incidence of 2/14 (14.3%) among controls. Treatment of either sex with 2.5 or 5 mg of DPM extract per mouse did not result in statistically significant increases in tumor incidence.

Additional studies using DPM extract from LD (1.8-L, 4-cylinder) as well as HD engines with female ICR and nude mice (BALB/c/cA/JCL-nu) were also reported (Kunitake et al., 1988). Groups of 30 ICR and nude mice each were given a single s.c. injection of 10 mg HD extract, 10 mg HD + 50 μg 12-O-tetradecanoylphorbol 13-acetate (TPA), 10 mg LD extract + 50 μg TPA, or 50 μg TPA. No malignant tumors or papillomas were observed. One papillomatous lesion was observed in an ICR mouse receiving LD extract + TPA, and acanthosis was observed in one nude mouse receiving only TPA.

In what appears to be an extension of the Kunitake et al. (1986) s.c. injection studies, Takemoto et al. (1988) presented additional data for subcutaneously administered DPM extract from HD and LD diesel engines. In this report, the extracts were administered to 5-week-old and neonatal (<24 hr old) C57BL mice of both sexes. DPM extract from HD or LD engines was administered weekly to the 5-week-old mice for 5 weeks at doses of 10, 25, 50, 100, 200, or 500 mg/kg, with group sizes ranging from 15 to 54 animals. After 20 weeks, comparison with a control group indicated a significant increase in the incidence of subcutaneous tumors for the 500 mg/kg HD group (5 of 22 mice [22.7%], $p<0.01$), the 100 mg/kg LD group (6 of 32 [18.8%],
$p<0.01$), and the 500 mg/kg LD group (7 of 32 [21.9%], $p<0.01$) in the adult mouse experiments. The tumors were characterized as malignant fibrous histiocytomas. No tumors were observed in other organs. The neonates were given single doses of 2.5, 5, or 10 mg DPM extract subcutaneously within 24 hr of birth. There was a significantly higher incidence of malignant lymphomas in males receiving 10 mg of HD extract and of lung tumors for males given 2.5 mg HD extract and for males given 5 mg and females given 10 mg LD extract. A dose-related trend that was not significant was observed for the incidences of liver tumors for both the HD extract- and LD extract-treated neonatal mice. The incidence of mammary tumors in female mice and multiple-organ tumors in male mice was also greater for some extract-treated

mice, but was not dose related. The report concluded that LD DPM extract showed greater carcinogenicity than did HD DPM extract.

7.3.6. Dermal Studies

7.3.6.1. *Mouse Studies*

In one of the earliest studies of diesel emissions, the effects of dermal application of extract from DPM were examined by Kotin et al. (1955). Acetone extracts were prepared from the DPM of a diesel engine (type and size not provided) operated at warmup mode and under load. These extracts were applied dermally three times weekly to male and female C57BL and strain A mice. Results of these experiments are summarized in Table 7-5. In the initial experiments using 52 (12 male, 40 female) C57BL mice treated with DPM extract from an engine operated in warmup mode, two papillomas were detected after 13 mo. Four tumors were detected 16 months after the start of treatment in 8 surviving of 50 exposed male strain A mice treated with DPM extract from an engine operated under full load. Among female strain A mice treated with DPM extract from an engine operated under full load, 17 tumors were detected in 20 of 25 mice surviving longer than 13 mo. This provided a significantly increased tumor incidence of 85%. Carcinomas as well as papillomas were seen, but the numbers were not reported.

Depass et al. (1982) examined the potential of DPM and dichloromethane extracts of DPM to act as complete carcinogens, carcinogen initiators, or carcinogen promoters. In skin-painting studies, the DPM was obtained from an Oldsmobile 5.7-L diesel engine operated under constant load at 65 km/h. The DPM was collected at a temperature of 100°C. Groups of 40 C3H/HeJ mice were used because of their low spontaneous tumor incidence. For the complete carcinogenesis experiments, DPM was applied as a 5% or 10% suspension in acetone. Dichloromethane extract was applied as 5%, 10%, 25%, or 50% suspensions. Negative controls received acetone, and positive controls received 0.2% B[a]P. For tumor-promotion experiments, a single application of 1.5% B[a]P was followed by repeated applications of 10% DPM suspension, 50% DPM extract, acetone only (vehicle control), 0.0001% phorbol 12-myristate 13-acetate (PMA) as a positive promoter control, or no treatment (negative control). For the tumor-initiation studies, a single initiating dose of 10% diesel particle suspension, 50% diesel particle extract, acetone, or PMA was followed by repeated applications of 0.0001% PMA. Following 8 months of treatment, the PMA dose in the initiation and promotion studies was increased to 0.01%. Animals were treated three times per week in the complete carcinogenesis and initiation experiments and five times per week in promotion experiments. All test compounds were applied to a shaved area on the back of the mouse.

In the complete carcinogenesis experiments, one mouse receiving the high-dose (50%) suspension of extract developed a squamous cell carcinoma after 714 days of treatment. Tumor

incidence in the B[a]P group was 100%, and no tumors were observed in any of the other groups. For the promotion studies, squamous cell carcinomas with pulmonary metastases were identified in one mouse of the 50% DPM extract group and in one in the 25% extract group. Another mouse in the 25% extract group developed a grossly diagnosed papilloma. Nineteen positive control mice had tumors (11 papillomas, 8 carcinomas). No tumors were observed for any of the other treatment groups. For the initiation studies, three tumors (two papillomas and one carcinoma) were identified in the group receiving DPM suspension and three tumors (two papillomas and one fibrosarcoma) were found in the DPM extract group. These findings were reported to be statistically insignificant using the Breslow and Mantel-Cox tests.

Although these findings were not consistent with those of Kotin et al. (1955), the occurrence of a single carcinoma in a strain known to have an extremely low spontaneous tumor incidence may be of importance. Furthermore, a comparison between studies employing different strains of mice with varying spontaneous tumor incidences may result in erroneous assumptions.

Nesnow et al. (1982) studied the formation of dermal papillomas and carcinomas following dermal application of dichloromethane extracts from coke oven emissions, roofing tar, DPM, and gasoline engine exhaust. DPM from five different engines, including a preproduction Nissan 220C, a 5.7-L Oldsmobile, a prototype Volkswagen Turbo Rabbit, a Mercedes 300D, and a HD Caterpillar 3304, was used for various phases of the study. Male and female Sencar mice (40 per group) were used for tumor initiation, tumor promotion, and complete carcinogenesis studies. For the tumor-initiation experiments, the DPM extracts were topically applied in single doses of 100, 500, 1,000, or 2,000 μg/mouse. The high dose (10,000 μg/mouse) was applied in five daily doses of 2,000 μg. One week later, 2 μg of the tumor promoter TPA was applied topically twice weekly. The tumor-promotion experiments used mice treated with 50.5 μg of B[a]P followed by weekly (twice weekly for high dose) topical applications (at the aforementioned doses) of the extracts. For the complete carcinogenesis experiments, the test extracts were applied weekly (twice weekly for the high doses) for 50 to 52 weeks. Only extracts from the Nissan, Oldsmobile, and Caterpillar engines were used in the complete carcinogenesis experiments.

In the tumor-initiation studies, both B[a]P alone and the Nissan engine DPM extract followed by TPA treatment produced a significant increase in tumor (dermal papillomas) incidence at 7 to 8 weeks postapplication. By 15 weeks, the tumor incidence was greater than 90% for both groups. No significant carcinoma formation was noted for mice in the tumor-initiation experiments following exposure to DPM extracts of the other diesel engines, although the Oldsmobile engine DPM extract at 2.0 mg/mouse did produce a 40% papilloma incidence in male mice at 6 mo. This effect, however, was not dose dependent.

B[a]P (50.5 μg/week), coke oven extract (at 1.0, 2.0, or 4.0 mg/week), and the highest dose of roofing tar extract (4.0 mg/week) all tested positive for complete carcinogenesis activity. DPM extracts from only the Nissan, Oldsmobile, and Caterpillar engines were tested for complete carcinogenic potential, and all three proved to be negative using the Sencar mouse assay.

The results of the dermal application experiments by Nesnow et al. (1982) are presented in Table 7-7. The tumor initiation-promotion assay was considered positive if a dose-dependent response was obtained and if at least two doses provided a papilloma-per-mouse value that was three times or greater than that of the background value. Based on these criteria, only emissions from the Nissan were considered positive. Tumor initiation and complete carcinogenesis assays required that at least one dose produce a tumor incidence of at least 20%. None of the DPM samples yielded positive results based on this criterion.

Kunitake et al. (1986, 1988) evaluated the effects of a dichloromethane extract of DPM obtained from a 1983 MMC M-6D22P 11-L V-6 engine. An acetone solution was applied in 10 doses every other day, followed by promotion with 2.5 μg of TPA three times weekly for 25 weeks. Exposure groups received a total dose of 0.5, 5, 15, or 45 mg of extract. Papillomas were reported in 2 of 50 animals examined in the 45 mg exposure group and in 1 of 48 in the 15 mg group compared with 0 of 50 among controls. Differences, however, were not statistically significant.

7.3.7. Summary and Conclusions of Laboratory Animal Carcinogenicity Studies

As early as 1955, Kotin et al. (1955) provided evidence for tumorigenicity and carcinogenicity of acetone extracts of DPM following dermal application and also provided data suggesting a difference in this potential depending on engine operating mode. Until the early 1980s, no chronic studies assessing inhalation of DE, the relevant mode for human exposure, had been reported. Since then long-term inhalation bioassays with DE have been carried out in the United States, Germany, Switzerland, and Japan, testing responses of rats, mice, and Syrian hamsters, and to a limited extent cats and monkeys.

Table 7-7. Dermal tumorigenic and carcinogenic effects of various emission extracts

	Tumor initiation		Complete carcinogenesis	Tumor promotion
Sample	**Papillomas[a]**	**Carcinomas[b]**	**Carcinomas[b]**	**Papillomas[a]**
Benzo[*a*]pyrene	+/+[c]	+/+	+/+	+/+
Topside coke oven	+/+	-/+	ND[d]	ND
Coke oven main	+/+	+/+	+/+	+/+
Roofing tar	+/+	+/+	+/+	+/+
Nissan	+/+	+/+	-/-	ND
Oldsmobile	+/+	-/-	-/-	ND
VW Rabbit	+/+	-/-	I[e]	ND
Mercedes	+/-	-/-	ND	ND
Caterpillar	-/-	-/-	-/-	ND
Residential furnace	-/-	-/-	ND	ND
Mustang	+/+	-/+	ND	ND

[a]Scored at 6 mo.

[b]Cumulative score at 1 year.

[c]Male/female.

[d]ND = Not determined.

[e]I = Incomplete.

Source: Nesnow et al., 1982.

It can be reasonably concluded that with adequate exposure, inhalation of DE is capable of inducing lung cancer in rats. Responses best fit cumulative exposure (concentration × daily exposure duration × days of exposure). Examination of rat data shown in Table 7-8 indicates a trend of increasing tumor incidence at exposures exceeding 1×10^4 mg·hr/m^3. Exposures greater than approximately this value result in lung particle overload, characterized by slowed particle clearance and lung pathology, as discussed in Chapters 3 and 5, respectively. Tumor induction at high doses may therefore be primarily the result of lung particle overload with associated inflammatory responses. Although tumorigenic responses could not be detected under non-particle-overload conditions, the animal experiments lack sensitivity to determine if a threshold exists. However, studies such as those reported by Driscoll et al. (1996) support the existence of a threshold if it is assumed that inflammation is a prerequisite for lung tumor induction. If low-dose effects do occur, it can be hypothesized that the organic constituents are playing a role. See Chapter 7 for a discussion of this issue.

Although rats develop adenomas, adenocarcinomas, and adenosquamous cell carcinomas, they also develop squamous keratinizing lesions. This latter spectrum appears for the most part to be peculiar to the rat. In a recent workshop aimed at classifying these tumors (Boorman et al., 1996), it was concluded that when these lesions occur in rats as part of a carcinogenicity study, they must be evaluated on a case-by-case basis and regarded as a part of the total biologic profile of the test article. If the only evidence of tumorigenicity is the presence of cystic keratinizing epitheliomas, it may not have relevance to human safety evaluation of a substance or particle. Their use in quantifying cancer potency is even more questionable.

The evidence for response of common strains of laboratory mice exposed under standard inhalation protocols is equivocal. Inhalation of DE induced significant increases in lung tumors in female NMRI mice (Heinrich et al., 1986b; Stöber, 1986) and in female Sencar mice (Pepelko and Peirano, 1983). An apparent increase was also seen in female C57BL mice (Takemoto et al., 1986). However, in a repeat of their earlier study, Heinrich et al. (1995) failed to detect lung tumor induction in either NMRI or C57BL/6N mice. No increases in lung tumor rates were reported in a series of inhalation studies using strain A mice (Orthoefer et al., 1981; Kaplan et al., 1982, 1983; White et al., 1983). Finally, Mauderly et al. (1996) reported no tumorigenic responses in CD-1 mice exposed under conditions resulting in positive responses in rats. The successful induction of lung tumors in mice by Ichinose et al. (1997a,b) via intratracheal instillation may have been the result of focal deposition of larger doses. Positive effects in Sencar mice may be due to use of a strain sensitive to tumor induction in epidermal tissue by organic agents, as well as exposure from conception, although proof for such a hypothesis is lacking.

Table 7-8. Cumulative (concentration × time) exposure data for rats exposed to whole DE

Study	Exposure rate/duration (hr/week, mo)	Total exposure time (hr)	Particle concentration (mg/m^3)	Cumulative exposure ($mg \cdot hr/m^3$) Per week	Cumulative exposure ($mg \cdot hr/m^3$) Total	Tumor incidence (%)[a]
Mauderly et al. (1987)	35, 30	4.20042004e+15	0	0	14701470029820	0.9
	35, 30		0.35	12.25		1.3
	35, 30		3.5	122.5		3.6
	35, 30		7.1	248.5		12.8
Nikula et al. (1995)	80, 23	736073607360	0	0	1840047840	1.0
	80, 23		2.5	200.0		7.0
	80, 23		6.5	520.0		18.0
Heinrich et al. (1986a)	95, 35	1330013300	4.24	402.8	56392	17.8
	95, 35					
Heinrich et al. (1995)	90, 24	8.64086409e+15	0	0	74002180061700	0
	90, 24		0.8	72.0		0
	90, 24		2.5	225.0		5.5
	90, 24		7.0	630.0		22.0
Ishinishi et al. (1988a)	96, 30	1.15201152e+49	0	0	1.1524	3.3
(Light-duty engine)	96, 30		0.1	9.6	60813e+37	2.4
	96, 30		0.4	38.4		0.8
	96, 30		1.1	105.6		4.1
(Heavy-duty engine)	96, 30		2.3	220.8		2.4
	96, 30		0	0		0.8
	96, 30		0.5	48.0		0.8
	96, 30		1.0	96.0		0
	96, 30		1.8	172.8		3.3
	96, 30		3.7	355.2		6.5

Table 7-8. Cumulative (concentration × time) exposure data for rats exposed to whole DE (continued)

Study	Exposure rate/duration (hr/week, mo)	Total exposure time (hr)	Particle concentration (mg/m^3)	Cumulative exposure ($mg \cdot hr/m^3$) Per week	Cumulative exposure ($mg \cdot hr/m^3$) Total	Tumor incidence (%)[a]
Brightwell et al. (1989)	80, 24	7.6807681e+15	0	0	53761689650688	1.2
	80, 24		0.7	56.0		0.7
	80, 24		2.2	176.0		9.7
	80, 24		6.6	528.0		38.5
Kaplan et al. (1983)	140, 15	8.4008401e+15	0	0	2100630012600	0
	140, 15		0.25	35.0		3.3
	140, 15		0.75	105.0		10.0
	140, 15		1.5	210.0		3.3
Iwai et al. (1986b)	56, 24	53765376	4.9	274.4	26342	36.8
	56, 24					
Takemoto et al. (1986)	16, 18-24	1,152-1,536	0	0	0	0
	16, 18-24	1,152-1,536	2-4	32-64	3,456-4,608	
Karagianes et al. (1981)	30, 20	24002400	8.3	249	19920	16.6
	30, 20					
Iwai et al. (1997)	56, 24	537649925616	9.4	526154275	5.47041597e+14	421242
	48, 24		3.2			
	54, 24		5.1			

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Attempts to induce significant increases in lung tumors in Syrian hamsters by inhalation of whole DE were unsuccessful (Heinrich et al., 1982, 1986b, 1989b; Brightwell et al., 1986). However, hamsters are considered to be relatively insensitive to lung tumor induction. For example, while cigarette smoke, a known human carcinogen, was shown to induce laryngeal cancer in hamsters, the lungs were relatively unaffected (Dontenwill et al., 1973).

Neither cats (Pepelko and Peirano, 1983 [see Chapter 7]) nor monkeys (Lewis et al., 1989) developed tumors following 2-year exposure to DE. The duration of these exposures, however, was likely to be inadequate for these two longer-lived species, and group sizes were quite small. Exposure levels were also below the maximum tolerated dose (MTD) in the monkey studies and, in fact, only borderline for detection of lung tumor increases in rats.

Long-term exposure to DE filtered to remove particulate matter failed to induce lung tumors in rats (Heinrich et al., 1986b; Iwai et al., 1986b; Brightwell et al., 1989), or in Syrian hamsters (Heinrich et al., 1986b; Brightwell, 1989). A significant increase in lung carcinomas was reported by Heinrich et al. (1986b) in NMRI mice exposed to filtered exhaust. However, in a more recent study the authors were unable to confirm earlier results in either NMRI or C57BL/6N mice (Heinrich et al., 1995). Although filtered exhaust appeared to potentiate the carcinogenic effects of DEN (Heinrich et al., 1982), because of the lack of positive data in rats and equivocal or negative data in mice it can be concluded that filtered exhaust is either not carcinogenic or has a low cancer potency.

Kawabata et al. (1986) demonstrated the induction of lung tumors in Fischer 344 rats following intratracheal instillation of DPM. Rittinghausen et al. (1997) reported an increase in cystic keratinizing epitheliomas following intratracheal instillation of rats with either original DPM or DPM extracted to remove the organic fraction, with the unextracted particles inducing a slightly greater effect. Grimmer et al. (1987) showed not only that an extract of DPM was carcinogenic when instilled in the lungs of rats, but also that most of the carcinogenicity resided in the portion containing PAHs with four to seven rings. Intratracheal instillation did not induce lung tumors in Syrian hamsters (Kunitake et al., 1986; Ishinishi et al., 1988b).

Dermal exposure and s.c. injection in mice provided additional evidence for tumorigenic effects of DPM. Particle extracts applied dermally to mice have been shown to induce significant skin tumor increases in two studies (Kotin et al., 1955; Nesnow et al., 1982). Kunitake et al. (1986) also reported a marginally significant increase in skin papillomas in ICR mice treated with an organic extract from an HD diesel engine. Negative results were reported by Depass et al. (1982) for skin-painting studies using mice and acetone extracts of DPM suspensions. However, in this study the exhaust particles were collected at temperatures of 100 °C, which would minimize the condensation of vapor-phase organics and, therefore, reduce the availability of potentially carcinogenic compounds that might normally be present on DE particles. A significant increase in the incidence of sarcomas in female C57Bl mice was reported by Kunitake et al. (1986) following s.c. administration of LD DPM extract at doses of

500 mg/kg. Takemoto et al. (1988) provided additional data for this study and reported an increased tumor incidence in the mice following injection of LD engine DPM extract at doses of 100 and 500 mg/kg. Results of i.p. injection of DPM or DPM extracts in strain A mice were generally negative (Orthoefer et al., 1981; Pepelko and Peirano, 1983), suggesting that the strain A mouse may not be a good model for testing diesel emissions.

Results of experiments using tumor initiators such as DEN, B[a]P, DPN, or DBA (Brightwell et al., 1986; Heinrich et al., 1986b; Takemoto et al., 1986) were generally inconclusive regarding the tumor-promoting potential of either filtered or whole DE. A report by Heinrich et al. (1982), however, indicated that filtered exhaust may promote the tumor-initiating effects of DEN in hamsters.

Several reports (Wong et al., 1985; Bond et al., 1990) affirm observations of the potential carcinogenicity of DE by providing evidence for DNA damage in rats. These findings are discussed in more detail in Chapter 3, Section 3.6. Evidence for the mutagenicity of organic agents present in diesel engine emissions is also provided in Chapter 4.

Evidence for the importance of the carbon core was initially provided by studies of Kawabata et al. (1986), which showed induction of lung tumors following intratracheal instillation of carbon black that contained no more than traces of organics, and studies of Heinrich (1990b) that indicated that exposure via inhalation to carbon black (Printex 90) particles induced lung tumors at concentrations similar to those effective in DPM studies. Additional studies by Heinrich et al. (1995) and Nikula et al. (1995) confirmed the capability of carbon particles to induce lung tumors. Induction of lung tumors by other particles of low solubility, such as titanium dioxide (Lee et al., 1986), confirmed the capability of particles to induce lung tumors. Pyrolyzed pitch, on the other hand, essentially lacking a carbon core but having much higher PAH concentrations than DPM, also was effective in tumor induction (Heinrich et al., 1986a, 1994).

The relative importance of the adsorbed organics, however, remains to be elucidated and is of some concern because of the known carcinogenic capacity of some of these chemicals. These include polycyclic aromatics as well as nitroaromatics, as described in Chapter 2. Organic extracts of particles also have been shown to induce tumors in a variety of injection, intratracheal instillation, and skin-painting studies, and Grimmer et al. (1987) have, in fact, shown that the great majority of the carcinogenic potential following instillation resided in the fraction containing four- to seven-ring PAHs.

In summary, based on positive inhalation studies in rats exposed to high concentrations, intratracheal instillation studies in rats and mice exposed to high doses, and supported by positive mutagenicity studies, the evidence for carcinogenicity of DE is considered to be adequate in animals. The contribution of the various fractions of DE to the carcinogenic response is less certain. Exposure to filtered exhaust generally failed to induce lung tumors. The presence of known carcinogens adsorbed to diesel particles and the demonstrated

tumorigenicity of particle extracts in a variety of injection, instillation, and skin-painting studies indicate a carcinogenic potential for the organic fraction. Studies showing that long-term exposure at high concentrations of poorly soluble particles (e.g., carbon black, TiO_2) can also induce tumors, on the other hand, have provided definitive evidence that the carbon core of the diesel particle is primarily instrumental in the carcinogenic response observed in rats under sufficient exposure conditions. The ability of DE to induce lung tumors at non-particle-overload conditions, and the relative contribution of the particles' core versus the particle-associated organics (if effects do occur at low doses) remains to be determined.

7.4. MODE OF ACTION OF DIESEL EXHAUST-INDUCED CARCINOGENESIS

As noted in Chapter 2, DE is a complex mixture that includes a vapor phase and a particle phase. The particle phase consists of an insoluble carbon core with a large number of organic compounds, as well as inorganic compounds such as sulfates, adsorbed to the particle surface. Some of the semivolatile and particle-associated compounds, in particular PAHs, nitro-PAHs, oxy-PAHs, and oxy-nitro-PAHs (Scheepers and Bos, 1992), are considered likely to be carcinogenic in humans. The vapor phase also contains a large number of organic compounds, including several known or probable carcinogens such as benzene and 1,3-butadiene. Because exposure to the vapor phase alone, even at high concentrations, failed to induce lung cancer in laboratory animals (Heinrich et al., 1986b), the mode-of-action discussion will focus on the particulate matter phase. Additive or synergistic effects of vapor-phase components, however, cannot be ruled out, as chronic inhalation bioassays involving exposure to diesel particles alone have not been carried out.

Several hypotheses regarding the primary mode of action of DE have been proposed. Initially it was generally believed that cancer was induced by particle-associated organics acting via a genotoxic mechanism. By the late 1980s, however, studies indicated that carbon particles virtually devoid of organics could also induce lung cancer at sufficient inhaled concentrations (Heinrich, 1990b). This finding provided support for a hypothesis originally proposed by Vostal (1986) that induction of lung tumors arising in rats exposed to high concentrations of DE is related to overloading of normal lung clearance mechanisms, accumulation of particles, and cell damage followed by regenerative cell proliferation. The action of particles is therefore mediated by epigenetic mechanisms that can be characterized more by promotional than initiation stages of the carcinogenic process. More recently several studies have focused upon the production of reactive oxygen species generated from particle-associated organics, which may induce oxidative DNA damage at exposure concentrations lower than those required to produce lung particle overload. Because it is likely that more than one of these factors is involved in the carcinogenic process, a key consideration is their likely relative contribution at different exposure levels. The following discussion will therefore consider the possible relationship of the organic components of exhaust, inflammatory responses associated with lung particle overload, reactive oxygen

species, and physical characteristics of diesel particles to cancer induction, followed by a hypothesized mode of action, taking into account the likely contribution of the factors discussed.

7.4.1. Potential Role of Organic Exhaust Components in Lung Cancer Induction

More than 100 carcinogenic or potentially carcinogenic components have been specifically identified in diesel emissions, including various PAHs and nitroarenes such as 1-nitropyrene (1-NP) and dinitropyrenes (DNPs). The majority of these compounds are adsorbed to the carbon core of the particulate phase of the exhaust and, if desorbed, may become available for biological processes such as metabolic activation to mutagens. Among such compounds identified from DE are B[*a*]P, dibenz[*a,h*]anthracene, pyrene, chrysene, and nitroarenes such as 1-NP, 1,3-DNP, 1,6-DNP, and 1,8-DNP, all of which are mutagenic, carcinogenic, or implicated as procarcinogens or cocarcinogens (Stenback et al., 1976; Weinstein and Troll, 1977; Thyssen et al., 1981; Pott and Stöber, 1983; Howard et al., 1983; Hirose et al., 1984; Nesnow et al., 1984; El-Bayoumy et al., 1988). More recently Enya et al. (1997) reported isolation of 3-nitrobenzanthrone, one of the most powerful direct-acting mutagens known to date, from the organic extracts of DE.

Grimmer et al. (1987) separated DE particle extract into a water- and a lipid-soluble fraction, and the latter was further separated into a PAH-free, a PAH-containing, and a polar fraction by column chromatography. These fractions were then tested in Osborne-Mendel rats by pulmonary implantation at doses corresponding to the composition of the original DE. The water-soluble fraction did not induce tumors; the incidences induced by the lipid-soluble fractions were 0% with the PAH-free fraction, 25% with the PAH and nitro-PAH- containing fractions, and 0% with the polar fraction. The PAH and nitro-PAH-containing fraction, comprising only 1% by weight of the total extract, was thus shown to be responsible for most, if not all, of the carcinogenic activity.

Exposure of rats by inhalation to 2.6 mg/m^3 of an aerosol of tar-pitch condensate with no carbon core but containing 50 μg/m^3 B[*a*]P along with other PAHs for 10 months induced lung tumors in 39% of the animals. The same amount of tar-pitch vapor condensed onto the surface of carbon black particles at 2 and 6 mg/m^3 resulted in tumor rates that were roughly two times higher (89% and 72%). Because exposure to 6 mg/m^3 carbon black almost devoid of extractable organic material induced a lung tumor rate of 18%, the combination of PAHs and particles increases their effectiveness (Heinrich et al., 1994). Although this study shows the tumor-inducing capability of PAHs resulting from combustion, it should be noted that the B[*a*]P content in the coal-tar pitch was about three orders of magnitude greater than in diesel soot. Moreover, because organics are present on diesel particles in a thinner layer and the particles are quite convoluted, they may be more tightly bound and less bioavailable. Nevertheless, these studies provide evidence supporting the involvement of organic constituents of diesel particles in the carcinogenic process.

Exposure of humans to related combustion emissions provides some evidence for the involvement of organic components. Mumford et al. (1989) reported greatly increased human lung cancer mortality in Chinese communes burning so-called smoky coal, but not wood, in unvented open-pit fires used for heating and cooking. Although particle concentrations were similar, PAH levels were five to six times greater in the air of communes burning smoky coal. Coke oven emissions, containing high concentrations of PAHs but lacking an insoluble carbon core, have also been shown to be carcinogenic in humans (Lloyd, 1971).

Adsorption of PAHs to a carrier particle such as hematite, CB, aluminum, or titanium dioxide enhances their carcinogenic potency (Farrell and Davis, 1974). As already noted, adsorption to carbon particles greatly enhanced the tumorigenicity of pyrolyzed pitch condensate containing B[*a*]P and other aromatic carcinogens (Heinrich et al., 1995). The increased effectiveness can be partly explained by more efficient transport to the deep lung. Slow release also enhances residence time in the lungs and prevents overwhelming of activating pathways. As discussed in Chapter 3, free organics are likely to be rapidly absorbed into the bloodstream, which may explain why the vapor-phase component of exhaust is relatively ineffective in the induction of pathologic or carcinogenic effects.

Even though the organic constituents may be tightly bound to the particle surface, significant elution is still likely because particle clearance half-times are nearly 1 year in humans (Bohning et al., 1982). Furthermore, Gerde et al. (1991) presented a model demonstrating that large aggregates of inert dust containing crystalline PAHs are unlikely to form at doses typical of human exposure. This allows the particles to deposit and react with the surrounding lung medium, without interference from other particles. Particle-associated PAHs can then be expected to be released more rapidly from the particles. Bond et al. (1984) provided evidence that alveolar macrophages from beagle dogs metabolized B[*a*]P coated on diesel particles to proximate carcinogenic forms. Unless present on the particle surface, B[*a*]P is more likely to pass directly into the bloodstream and escape activation by phagocytic cells.

The importance of DE-associated PAHs in the induction of lung cancer in humans may be enhanced because of the possibility that the human lung is more sensitive to these compounds than are rat lungs. Rosenkranz (1996) summarized information indicating that in humans and mice, large proportions of lung cancers contain both mutated *p*53 suppressor genes and K-*ras* genes. Induction of mutations in these genes by genotoxins, however, is much lower in rats than in humans or mice.

B[*a*]P, although only one of many PAHs present in DE, is the one most extensively studied. Bond et al. (1983, 1984) demonstrated metabolism of particle-associated B[*a*]P and free B[*a*]P by alveolar macrophages (AM) and by type II alveolar cells. The respiratory tract cytochrome P-450 systems have an even greater concentration in the nonciliated bronchiolar cells (Boyd, 1984). It is worth noting that bronchiolar adenomas that develop following diesel exposure have been found to resemble both Type II and nonciliated bronchiolar cells. It should

also be noted that any metabolism of procarcinogens by these latter two cell types probably involves the preextraction of carcinogens in the extracellular lining fluid and/or other endocytotic cells, as they are not especially important in phagocytosis of particles. Thus, bioavailability is an important issue in assessing the relative importance of PAHs.

Additionally, a report by Borm et al. (1997) indicates that incubating rat lung epithelial-derived cells with human polymorphonucleocytes (PMNs) (either unactivated or activated by preexposure to phorbol myristate acetate) increases DNA adduct formation caused by exposure to B[*a*]P; at 0.05 to 0.5 micromolar concentration, addition of more activated PMN in relation to the number of lung cells further increased adduct formation in a dose-dependent manner. The authors suggest that "an inflammatory response in the lung may increase the biologically effective dose of PAHs, and may be relevant to data interpretation and risk assessment of PAH-containing particles." These data raise the possibility that DE exposure at low concentrations may result in levels of neutrophil influx that would not necessarily be detectable via histopathological examination as acute inflammation, but that might be effective at amplifying any potential DE genotoxic effect.

Nitro-PAHs have also been implicated as potentially involved in diesel-exhaust-induced lung cancer. Although the nitro-PAH fraction of diesel was less effective than PAHs in the induction of lung cancer when implanted into the lungs of rats (Grimmer et al., 1987), in a study of various extracts of DE particles, 30%-40% of the total mutagenicity could be attributed to a group of six nitroarenes (Salmeen et al., 1984). Moreover, Gallagher et al. (1994) reported results suggesting that DNA adducts are formed from nitro-PAHs present in DNA and may play a role in the carcinogenic process. Nitroarenes, however, quantitatively represent a very small percentage of diesel particle extract (Grimmer et al., 1987), making their role in the tumorigenic response uncertain.

The induction of DNA adducts in humans occupationally exposed to DE indicates the likelihood that PAHs are participating in the tumorigenic response, and that these effects can occur at exposure levels less than those required to induce lung particle overload. Distinct adduct patterns were found among garage workers occupationally exposed to DE when compared with nonexposed controls (Nielsen and Autrup, 1994). Furthermore, the findings were concordant with the adduct patterns observed in groups exposed to low concentrations of PAHs from combustion processes. Hemminki et al. (1994) also reported significantly elevated levels of DNA adducts in lymphocytes from garage workers with known DE exposure compared with unexposed mechanics. Hou et al. (1995) found elevated adduct levels in bus maintenance workers exposed to DE. Although no difference in mutant frequency was observed between the groups, the adduct levels were significantly different (3.2 vs. 2.3×10^{-8}). Nielsen et al. (1996b) measured three biomarkers in DE-exposed bus garage workers: lymphocyte DNA adducts, hydroxyethylvaline adducts in hemoglobin, and 1-hydroxypyrene in urine. Significantly increased levels were reported for all three. Qu et al. (1996) detected increased adduct levels, as

well as increases in some individual adducts, in the blood of underground coal miners exposed to DE.

7.4.2. Role of Inflammatory Cytokines and Proteolytic Enzymes in the Induction of Lung Cancer in Rats by Diesel Exhaust

It is well recognized that the deposition of particles in the lung can result in the efflux of PMNs from the vascular compartment into the alveolar space compartment in addition to expanding the AM population size. Following acute exposures, the influx of the PMNs is transient, lasting only a few days (Adamson and Bowden, 1978; Bowden and Adamson, 1978; Lehnert et al., 1988). During chronic exposure the numbers of PMNs lavaged from the lungs of diesel-exposed rats generally increased with increasing exposure duration and inhaled DPM concentration (Strom, 1984). Strom (1984) also found that PMNs in diesel-exposed lungs remained persistently elevated for at least 4 months after cessation of exposure, a potential mechanism that may be related to an ongoing release of phagocytized particles. Evidence in support of this possibility was reported by Lehnert et al. (1989) in a study in which rats were intratracheally instilled with 0.85, 1.06, or 3.6 mg of polystyrene particles. The PMNs were not found to be abnormally abundant during the clearance of the two lower lung burdens, but they became progressively elevated in the lungs of the animals in which alveolar-phase clearance was inhibited. Moreover, the particle burdens in the PMNs became progressively greater over time. Such findings are consistent with an ongoing particle relapse process, in which particles released by dying phagocytes are ingested by new ones.

The inflammatory response, characterized by efflux of PMNs from the vascular compartment, is mediated by inflammatory chemokines. Driscoll et al. (1996) reported that inhalation of high concentrations of carbon black stimulated the release of macrophage inflammatory protein 2 (MIP-2) and monocyte chemotactic protein I (MCP-I). They also reported a concomitant increase in hprt mutants. In a following study it was shown that particle exposure stimulates production of tumor necrosis factor TNF-α, an agent capable of activating expression of several proteins that promote both adhesion of leucocytes and chemotaxis (Driscoll et al., 1997a). In addition, alveolar macrophages also have the ability to release several other effector molecules or cytokines that can regulate numerous functions of other lung cells, including their rates of proliferation (Bitterman et al., 1983; Jordana et al., 1988; Driscoll et al., 1996).

Another characteristic of AMs and PMNs under particle overload conditions is the release of a variety of potentially destructive hydrolytic enzymes, a process known to occur simultaneously with the phagocytosis of particles (Sandusky et al., 1977). The essentially continual release of such enzymes during chronic particle deposition and phagocytosis in the lung may be detrimental to the alveolar epithelium, especially to Type I cells. Evans et al. (1986) showed that injury to Type I cells is followed shortly thereafter by a proliferation of Type

II cells. Type II cell hyperplasia is a common feature observed in animals that have received high lung burdens of various types of particles, including unreactive polystyrene microspheres. Exaggerated proliferation as a repair or defensive response to DPM deposition may have the effect of amplifying the likelihood of neoplastic transformation in the presence of carcinogens beyond that which would normally occur with lower rates of proliferation, assuming an increase in the cycling of target cells and the probability of a neoplastic-associated genomic disturbance.

7.4.3. Role of Reactive Oxygen Species in Lung Cancer Induction by Diesel Exhaust

Phagocytes from a variety of rodent species produce elevated levels of oxidant reactants in response to challenges, with the physiochemical characteristics of a phagocytized particle being a major factor in determining the magnitude of the oxidant-producing response. Active oxygen species released by the macrophages and lymphatic cells can cause lipid peroxidation in the membrane of lung epithelial cells. These lipid peroxidation products can initiate a cascade of oxygen free radicals that progress through the cell to the nucleus, where they damage DNA. If this damage occurs during the epithelial cell's period of DNA synthesis, there is some probability that the DNA will be replicated unrepaired (Lechner and Mauderly, 1994). The generation of reactive oxygen species by both AMs and PMNs should therefore be considered as one potential factor of what probably is a multistep process that culminates in the development of lung tumors in response to chronic deposition of DPM.

Even though products of phagocytic oxidative metabolism, including superoxide anions, hydrogen peroxide, and hydroxyl radicals, can kill tumor cells (Klebanoff and Clark, 1978), and the reactive oxygen species can peroxidize lipids to produce cytotoxic metabolites such as malonyldialdehyde, some products of oxidative metabolism apparently can also interact with DNA to produce mutations. Cellular DNA is damaged by oxygen free radicals generated from a variety of sources (Ames, 1983; Trotter, 1980). Along this line, Weitzman and Stossel (1981) found that human peripheral leukocytes are mutagenic in the Ames assay. This mutagenic activity was related to PMNs and blood monocytes; blood lymphocytes alone were not mutagenic. These investigators speculated that the mutagenic activity of the phagocytes was a result of their ability to produce reactive oxygen metabolites, inasmuch as blood leukocytes from a patient with chronic granulomatous diseases, in which neutrophils have a defect in the NADPH oxidase generating system (Klebanoff and Clark, 1978), were less effective in producing mutations than were normal leukocytes. Of related significance, Phillips et al. (1984) demonstrated that the incubation of Chinese hamster ovary cells with xanthine plus xanthine oxidase (a system for enzymatically generating active oxygen species) resulted in genetic damage hallmarked by extensive chromosomal breakage and sister chromatid exchange and produced an increase in the frequency of thioguanidine-resistant cells (HGPRT test). Aside from interactions of oxygen species with DNA, increasing evidence also points to an important role of

phagocyte-derived oxidants and/or oxidant products in the metabolic activation of procarcinogens to their ultimate carcinogenic form (Kensler et al., 1987).

Driscoll et al. (1997b) have demonstrated that exposure to doses of particles producing significant neutrophilic inflammation are associated with increased mutation in rat alveolar type II cells. The ability of particle-elicited macrophages and neutrophils to exert a mutagenic effect on epithelial cells in vitro supports a role for these inflammatory cells for the in vivo mutagenic effects of particle exposure. The inhibition of bronchoalveolar lavage cell-induced mutations by catalase implies a role for cell-derived oxidants in this response.

Hatch and co-workers (1980) have demonstrated that interactions of guinea pig AMs with a wide variety of particles, such as silica, metal oxide-coated fly ash, polymethylmethacrylate beads, chrysotile asbestos, fugitive dusts, polybead carboxylate microspheres, glass and latex beads, uncoated fly ash, and fiberglass increase the production of reactive oxygen species. Similar findings have been reported by numerous investigators for human, rabbit, mouse, and guinea pig AMs (Drath and Karnovsky, 1975; Allen and Loose, 1976; Beall et al., 1977; Lowrie and Aber, 1977; Miles et al., 1977; Rister and Baehner, 1977; Hoidal et al., 1978). PMNs are also known to increase production of superoxide radicals, hydrogen peroxide, and hydroxyl radicals in response to membrane-reactive agents and particles (Goldstein et al., 1975; Weiss et al., 1978; Root and Metcalf, 1977). Although these responses may occur at any concentration, they are likely to be greatly enhanced at high exposure concentrations with slowed clearance and lung particle overload.

Reactive oxygen species can also be generated from particle-associated organics. Sagai et al. (1993) reported that DPM can nonenzymatically generate active oxygen species (e.g., superoxide [O_2^-] and hydroxyl radical [$^{\cdot}OH$] in vitro without any biologically activating systems) such as microsomes, macrophages, hydrogen peroxide, or cysteine. Because DPM washed with methanol could no longer produce these radicals, it was concluded that the active components were compounds extractable with organic solvents. However, the nonenzymatic contribution to the DPM-promoted active oxygen production was negligible compared with that generated via an enzymatic route (Ichinose et al., 1997a). They reported that O_2^- and $^{\cdot}OH$ can be enzymatically generated from DPM by the following process. Soot-associated quinone-like compounds are reduced to the semiquinone radical by cytochrome P-450 reductase. These semiquinone radicals then reduce O_2 to O_2^-, and the produced superoxide reduces ferric ions to ferrous ions, which catalyzes the homobiotic cleavage of H_2O_2 dismutated from O_2 by superoxide dismutase or spontaneous reactions to produce $^{\cdot}OH$. According to Kumagai et al. (1997), while quinones are likely to be the favored substrates for this reaction, the participation of nitroaromatics cannot be ruled out.

One of the critical lesions to DNA bases generated by oxygen free radicals is 8-hydroxydeoxyguanosine (8-OHdG). The accumulation of 8-OhdG as a marker of oxidative DNA damage could be an important factor in enhancing the mutation rate leading to lung cancer

(Ichinose et al., 1997a). For example, formation of 8-OHdG adducts leads to G:C to T:A transversions unless repaired prior to replication. Nagashima et al. (1995) demonstrated that the production of (8-OHdG) is induced in mouse lungs by intratracheal instillation of DPM. Ichinose et al. (1997b) reported further that although intratracheal instillation of DPM in mice induced a significant increase in lung tumor incidence, comparable increases were not reported when mice were instilled with extracted DPM (to remove organics). Lung injury was also less in the mice instilled with extracted DPM. Moreover, increases in 8-OHdG in the mice instilled with unextracted DPM correlated very well with increases in tumor rates. In a related study, Ichinose et al. (1997a) intratracheally instilled small doses of DPM, 0.05, 0.1, or 0.2 mg weekly for 3 weeks, in mice fed standard or high-fat diets either with or without β-carotene. High dietary fat enhanced DPM-induced lung tumor incidence, whereas β-carotene, which may act as a free radical scavenger, partially reduced the tumorigenic response. Formation of 8-OHdG was again significantly correlated with lung tumor incidence in these studies, except at the highest dose. Dasenbrock et al. (1996) reported that extracted DPM, intratracheally instilled into rats (15 mg total dose) induced only marginal increases in lung tumor induction, while unextracted DPM was considerably more effective. Although adducts were not measured in this study, it nevertheless provides support for the likelihood that activation of organic metabolites and/or generation of oxygen free radicals from organics are involved in the carcinogenic process.

Additional support for the involvement of particle-associated radicals in tissue damage was provided by the finding that pretreatment with superoxide dismutase (SOD), an antioxidant, markedly reduced lung injury and death due to instillation of DPM. Similarly, Hirafuji et al. (1995) found that the antioxidants catalase, deferoxamine, and MK-447 inhibited the toxic effects of DPM on guinea pig tracheal cells and tissues in vitro.

Although the data presented supported the hypothesis that generation of reactive oxygen species resulting from exposure to DPM is involved in the carcinogenic process, it should be noted that 8-OHdG is efficiently repaired and that definitive proof of a causal relationship in humans is still lacking. It is also uncertain whether superoxide or hydroxyl radicals chemically generated by DPM alone promote 8-OHdG production in vivo and induce lung toxicity, because SOD is extensively located in mammalian tissues. Nevertheless, demonstration that oxygen free radicals can be generated from particle-associated organics, that their presence will induce adduct formation and DNA damage unless repaired, that tumor induction in experimental animals correlates with OhdG adducts, and that treatment with antioxidant limits lung damage, provides strong support for the involvement of oxygen free radicals in the toxicologic and carcinogenic response to DE.

7.4.4. Relationship of Physical Characteristics of Particles to Cancer Induction

The biological potential of inhaled particles is strongly influenced by surface chemistry and character. For example, the presence of trace metal compounds such as aluminum and iron, as well as ionized or protonated sites, is important in this regard (Langer and Nolan, 1994). A

major factor is specific surface area (surface area/mg). PMNs characteristically are increased abnormally in the lung by DE exposure, but their presence in the lungs does not appear to be excessive following the pulmonary deposition of even high lung burdens of spherical TiO_2 particles in the 1-2 μm diameter range (Strom, 1984). In these studies lung tumors were detected only at an inhaled concentration of 250 $\mu g/m^3$. In a more recent study in which rats were exposed to TiO_2 in the 15-40 nm size range, inhibition of particle clearance and tumorigenesis were induced at concentrations of 10 mg/m^3 (Heinrich et al., 1995). Comparison of several chronic inhalation studies correlating particle mass and particle surface area retained in the lung with tumor incidence indicated that particle surface area is a much better dosimeter than particle mass (Oberdörster and Yu, 1990; Driscoll et al., 1996). Heinrich et al. (1995) also found that lung tumor rates increased with specific particle surface area following exposure to DE, carbon black, or titanium dioxide, irrespective of particle type. Langer and Nolan (1994) reported that the hemolytic potential of Min-U-Sil15, a silica flour, increased in direct relationship to specific surface area at nominal particle diameters ranging from 0.5 to 20 μm.

Ultrafine particles appear to be more likely to be taken up by lung epithelial cells. Riebe-Imre et al. (1994) reported that CB is taken up by lung epithelial cells in vitro, inducing chromosomal damage and disruption of the cytoskeleton, lesions that closely resemble those present in tumor cells. Johnson et al. (1993) reported that 20-nm polytetrafluoroethylene particles are taken up by pulmonary epithelial cells as well as polymorphonuclear leucocytes, inducing an approximate 4-, 8-, and 40-fold increase in the release of interleukin-1 alpha and beta, inducible nitric oxide synthetase, and macrophage inflammatory protein, respectively.

The carcinogenic potency of diesel particles, therefore, appears to be related, at least to some extent, to their small size and convoluted shape, which results in a large specific particle surface area. Toxicity and carcinogenicity increased with decreasing particle size into the submicron range. For example, Heinrich et al. (1995) have shown that ultrafine titanium dioxide (approximately 0.2 μm diameter) is much more toxic than particles with a 10-fold greater diameter of the same composition used in an earlier study by Lee et al. (1986). This increase in toxicity has been noted with even smaller particles. For example, carbon black particles 20 nm in diameter were shown to be significantly more toxic than 50 nm particles (Murphy et al., 1999). The relationship between particle size and toxicity is of concern because, as noted in Chapter 2, approximately 50%-90% of the number of particles in DE are in the size range from 5 to 50 nm. Other than disruption of the cytoskeleton of epithelial cells, there is little information regarding the means by which particle size influences carcinogenicity as well as noncancer toxicity.

7.4.5. Integrative Hypothesis for Diesel-Induced Lung Cancer

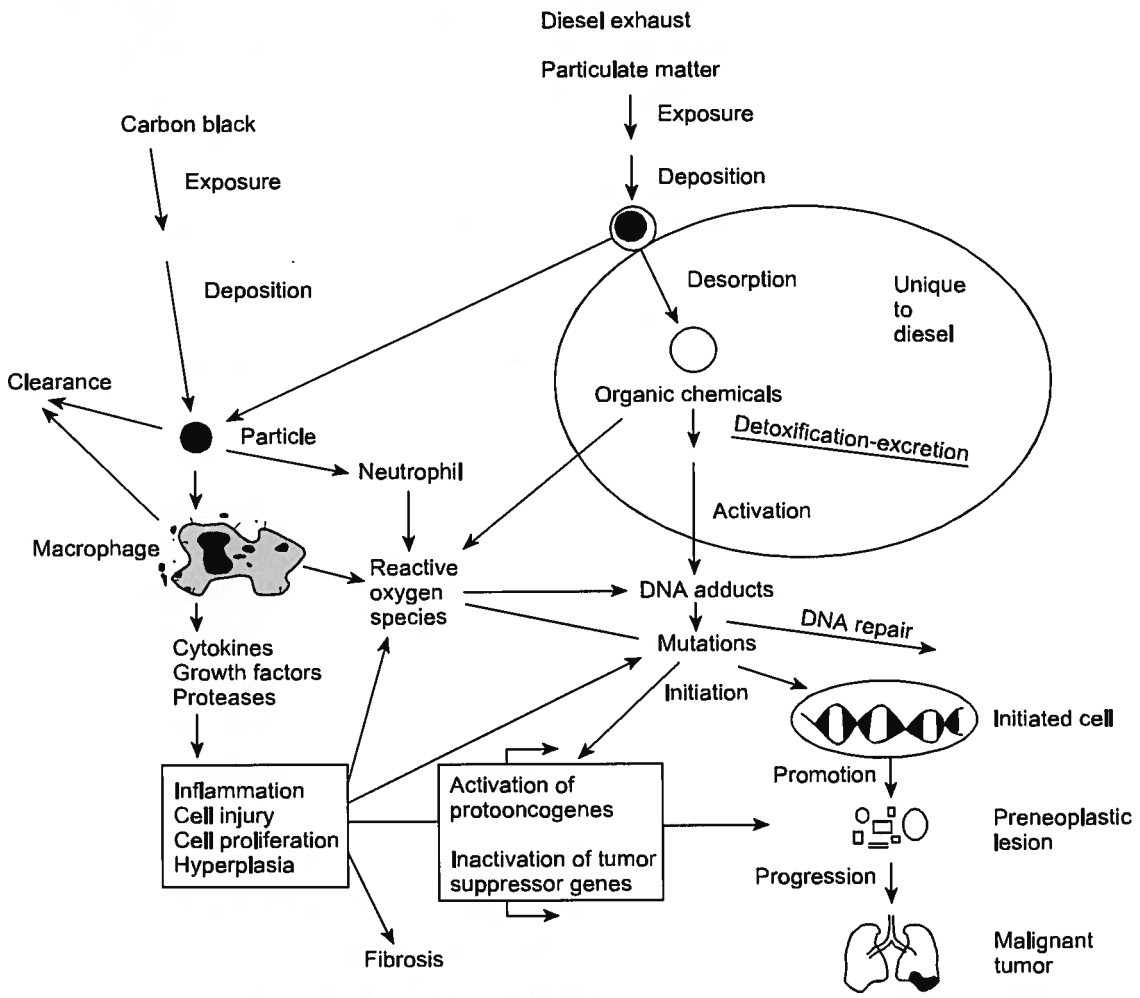
The induction of lung cancer in rats by large doses of carbon black via inhalation (Heinrich et al., 1995; Mauderly et al., 1991; Nikula et al., 1995) or intratracheal instillation (Kawabata et al., 1994; Pott et al., 1994; Dasenbrock et al., 1996) led to the development of the lung particle overload hypothesis. According to this hypothesis the induction of neoplasia by insoluble low- toxicity particles is associated with an inhibition of lung particle clearance and the involvement of persistent alveolar epithelial hyperplasia. Driscoll (1995), Driscoll et al. (1996), and Oberdörster and Yu (1990) outlined a proposed mechanism for the carcinogenicity of DE at high doses that emphasizes the role of phagocytic cells. Following exposure, phagocytosis of particles acts as a stimulant for oxidant production and inflammatory cytokine release by lung phagocytes. It was hypothesized that at high particle exposure concentrations the quantity of mediators released by particle-stimulated phagocytes exceeds the inflammatory defenses of the lung (e.g., antioxidants, oxidant-metabolizing enzymes, protease inhibitors, cytokine inhibitors), resulting in tissue injury and inflammation. With continued particle exposure and/or the persistence of excessive particle burdens, there then develops an environment of phagocytic activation, excessive mediator release-tissue injury and, consequently, more tissue injury, inflammation, and tissue release. This is accompanied by cell proliferation. As discussed in a review by Cohen and Ellwein (1991), conceptually, cell proliferation can increase the likelihood that any oxidant-induced or spontaneously occurring genetic damage becomes fixed in a dividing cell and is clonally expanded. The net result of chronic particle exposures sufficient to elicit inflammation and cell proliferation in the rat lung is an increased probability that the genetic changes necessary for neoplastic transformation will occur. A schematic of this hypothesis has been outlined by McClellan (1997) (see Figure 7-3). In support of this hypothesis, it was reported that concentrations of inhaled CB resulted in increased cytokine expression and inflammatory influx of neutrophils (Oberdörster et al., 1995), increased formation of 8-OhdG (Ichinose et al., 1997b), and increase in the yield of hprt mutants, an effect ameliorated by treatment with antioxidants (Driscoll, 1995; Driscoll et al., 1996). Metabolism of carcinogenic organics to active forms as well as the generation of reactive oxygen species from certain organic species are likely to contribute to the toxic and carcinogenic process.

At low exposure concentrations, the lung particle overload condition is not present and the overload-induced inflammatory effects are not present. Note, however, as discussed in Chapters 5 and 6, that other types of inflammation are present in the rat lung at exposures below those inducing lung particle overload. However, at low exposures, activation of organic carcinogens and generation of oxidants from the organic fraction can still be expected. Actual contribution depends upon elution/bioavailability and the effectiveness of antioxidants. Direct effects of ultrafine diesel particles taken up by epithelial cells are also likely to play a role.

Although high-dose induction of cancer is logically explained by this hypothesis, particle overload has not been clearly shown to induce lung cancer in other species. As noted in the quantitative chapter, the relevance of the rat pulmonary response is therefore problematic. The

rat pulmonary noncancer responses to DPM, however, have fairly clear interspecies and human parallels. In response to poorly soluble particles such as DPM, humans and rats both develop an alveolar macrophage response, accumulate particles in the interstitium, and show mild interstitial fibrosis (ILSI, 2000). Other species (mice, hamsters) also have shown similar noncancer pulmonary responses to DPM, but without accompanying cancer response. The rat response for noncancer pulmonary histopathology, however, seems to be more pronounced compared with humans or other species, i.e., rats appear to be more sensitive. Although many critical elements of interspecies comparison, such as the role of airway geometry and patterns of particle deposition, need further elucidation, this basic interspecies similarity and the possible greater sensitivity of pulmonary response seen after longer exposures at high doses make pulmonary histopathology in rats a valid basis for noncancer dose-response assessment.

Figure 7-3. Pathegenesis of lung disease in rats with chronic, high-level exposures to particles.



Source: Modified from McClellan, 1997.

7.4.6. Summary

Recent studies have shown rat lung tumor rates resulting from exposures to nearly organic-free carbon black (CB) particles at high concentrations to be similar to those observed for DE exposures, thus providing strong evidence for a particle overload mechanism for DE-induced pulmonary carcinogenesis in rats. Such a mechanism is also supported by the fact that carbon particles per se cause inflammatory responses and increased epithelial cell proliferation and that AM function may be compromised under conditions of particle overload.

The particle overload hypothesis appears sufficient to account for DE-induced lung cancer in rats. However, there is also biological plausibility for lung cancer induction in humans at concentrations insufficient to induce lung particle overload as seen in rats (Chapter 3, Section 3.4 and ILSI, 2000). The uptake of particles by epithelial cells at ambient or occupational exposure levels, DNA damage resulting from oxygen-free radicals generated from organic molecules, and the gradual in situ extraction and activation of procarcinogens associated with the diesel particles may play a role in this response and provide a basis for the plausibility. The slower particle clearance rates in humans (up to a year or more) may result in greater extraction of organics. This is supported by reports of increased DNA adducts in humans occupationally exposed to DE at concentrations unlikely to induce lung particle overload. Although these modes of action can be expected to function at lung overload conditions also, they are likely to be overwhelmed by inflammatory associated effects.

The evidence to date indicates that caution must be exercised in extrapolating observations made in animal models to humans when assessing the potential for DE-induced pulmonary carcinogenesis. The carcinogenic response and the formation of DNA adducts in rats exposed to DE and other particles at high exposure concentrations may be species-specific and not DPM specific. The likelihood that different modes of action predominate at high and low doses, such as lung particle overload, also renders high-dose extrapolation to lower ambient concentrations uncertain.

7.5. WEIGHT-OF-EVIDENCE EVALUATION FOR POTENTIAL HUMAN CARCINOGENICITY

A carcinogenicity weight-of-evidence evaluation is a synthesis of all pertinent information addressing the question of how likely an agent is to be a human carcinogen. EPA's 1986 Guidelines for Carcinogen Risk Assessment (U.S. EPA, 1986) provide a classification system for the characterization of the overall weight of evidence for potential human carcinogenicity based on human evidence, animal evidence, and other supportive data. This system includes Group A: *Human Carcinogen*; Group B: *Probable Human Carcinogen*; Group C: *Possible Human Carcinogen*; Group D: *Not Classifiable as to Human Carcinogenicity*; and Group E: *Evidence for Noncarcinogenicity to Humans*.

As part of the guidelines development and updating process, the Agency has developed revisions to the 1986 guidelines to take into account knowledge gained in recent years about the carcinogenic processes. With regard to the weight-of-evidence evaluation for potential human carcinogenicity, EPA's 1996 Proposed Guidelines for Carcinogen Risk Assessment (U.S. EPA, 1996b) and the subsequent revised external review draft (U.S. EPA, 1999) emphasize the need for characterizing cancer hazard, in addition to hazard identification. To express the weight of evidence for potential human carcinogenicity, EPA's proposed 1996 and 1999 guidelines utilize a hazard narrative in place of the 1986 A-E classification system. In order to provide some measure of consistency in using the 1996 and 1999 draft guidelines, standard hazard descriptors are used as part of the hazard narrative. The revised guidelines also stress the importance of considering the mode(s) of action information for making an inference about potential cancer hazard beyond the range of observation, typically encountered at levels of exposure in the general environment. "Mode of action" refers to a series of key biological events and processes that are critical to the development of cancer. This is contrasted with "mechanisms of action," which is defined as a more detailed description of the complete sequence of biological events at the molecular level that must occur to produce a carcinogenic response.

The sections to follow evaluate and weigh the individual lines of evidence and combine all evidence to make an informed judgment about the carcinogenicity hazard of DE. A conclusion in accordance with EPA's 1986 classification system (U.S. EPA, 1986) is provided, as well as a hazard narrative along with appropriate hazard descriptors according to EPA's Proposed Guidelines (U.S. EPA, 1996b, 1999). These sections draw on information reviewed in Chapters 2, 3, 4, and 7.

7.5.1. Human Evidence

Twenty-two epidemiologic studies about the carcinogenicity of workers exposed to DE in various occupations are reviewed in Section 7.2. Exposure to DE has typically been inferred based on job classification within an industry. Increased lung cancer risk, although not always statistically significant, has been observed in 8 out of 10 cohort and 10 of 12 case-control studies within several industries, including railroad workers, truck drivers, heavy equipment operators, and professional drivers. The increased lung cancer relative risks generally range from 1.2 to 1.5, though a few studies show relative risks as high as 2.6. Statistically significant increases in pooled relative risk estimates (1.33 to 1.47) from two independent meta-analyses further support a positive relationship between DE exposure and lung cancer in a variety of DE-exposed occupations.

The generally small increased lung cancer relative risk (less than 2) observed in the epidemiologic studies and meta-analyses potentially weakens the evidence of causality. When a relative risk is less than 2, if confounders (e.g., smoking, asbestos exposure) are having an effect on the observed risk increases, it could be enough to account for the increased risk. With the

strongest risk factor for lung cancer being smoking, there is a concern that smoking effects may be influencing the magnitude of the observed increased relative risks. However, in studies for which the effects of smoking were accounted for, increased relative risks for lung cancer prevailed. Though some studies did not have information on smoking, significant confounding by smoking is unlikely because the comparison populations were from the same socioeconomic class. Moreover, when the meta-analysis focused only on the smoking-controlled studies, the relative risks tended to increase.

As evaluated in Section 7.2.4.5, application of the criteria for causality (including the biological plausibility) leads to the conclusion that the increased risks observed in available epidemiologic studies are consistent with a causal association between exposure to DE and occurrence of lung cancer. Overall, the human evidence for potential carcinogenicity for DE is judged to be strong, but less than sufficient for DE to be considered as a human carcinogen because of exposure uncertainties (lack of historical exposure data for workers exposed to DE) and an inability to reach a fully and direct accounting for all possible confounders.

7.5.2. Animal Evidence

DE and its organic constituents, both in the gaseous and particle phase, have been extensively tested for carcinogenicity in many experimental studies using several animal species and with different modes of administration.

Several well-conducted lifetime rat inhalation studies have consistently demonstrated that chronic inhalation exposure to sufficiently high concentrations of DE produced dose-related increases in lung tumors (benign and malignant). However, the lung cancer responses in rats from high-concentration exposures appear to be mediated by impairment of lung clearance mechanisms through particle overload, resulting in persistent chronic inflammation and subsequent pathologic and neoplastic changes in the lung. Overload conditions are not expected to occur in humans as a result of environmental or most occupational exposures to DE. Thus, the rat lung tumor response is not considered relevant to an evaluation of the potential for a human environmental exposure-related hazard (Section 7.4).

The chronic inhalation studies of DE in mice showed equivocal results, whereas negative findings were consistently seen in hamsters. The gaseous phase of DE (filtered exhaust without particulate fraction) was found not to be carcinogenic in rats, mice, or hamsters.

In several intratracheal instillation studies, diesel particulate matter (DPM), carbon black, and the organic DPM extracts which were virtually devoid of PAHs, have been found to produce increased lung tumors in rats. When directly implanted into the rat lung, DPM condensate containing mainly four- to seven-ring PAHs induced increases in lung tumors. In several dermal studies in mice, DPM extracts have also been shown to cause skin tumors and sarcomas in mice following subcutaneous injection.

Available data and hypotheses suggest that both the carbon core and the adsorbed organics have potential roles in inducing lung tumors in the rat, although their relative contribution to the carcinogenic response remains to be determined.

The consistent findings of carcinogenic activity by DPM and the organic extracts of DPM in noninhalation studies (intratracheal instillation, lung implantation, skin painting) contribute to the overall evidence for a human hazard potential for DE. The lack of a tumor response from traditional animal inhalation studies in other rodent species is noted. Without understanding the mode(s) of action of DE's carcinogenicity in humans it is difficult to assess the meaning of nonpositive results from the mouse and hamster inhalation bioassays, and the unusable results from the rat, while having other evidence of carcinogenic potential and plausibility.

It should be noted that the animal studies used DE from engines available in the 1980s, and that present-day engine emissions have different characteristics (e.g., higher elemental carbon content and lesser amounts of adsorbed organics on the carbon particles), with uncertain impact on the outcome of the experimental studies. The same point can be made for the occupational epidemiologic studies.

7.5.3. Other Key Data

Other key data are judged to be supportive of potential carcinogenicity of DE. As discussed in Chapter 2, DE is a complex mixture of hundreds of constituents in either gaseous phase or particle phase. Although present in small amounts, several organic compounds in the gaseous phase (e.g. PAHs, formaldehyde, acetaldehyde, benzene, 1,3-butadiene) are known to exhibit mutagenic and/or carcinogenic activities. PAHs and PAH derivatives, including nitro-PAHs, present on the diesel particle are also known to be mutagenic and carcinogenic. As reviewed in Chapter 4, DPM and DPM organic extracts have been shown to induce gene mutations in a variety of bacteria and mammalian cell test systems. In addition, DE, DPM and DPM extracts have been found to cause chromosomal aberrations, aneuploidy, and sister chromatid exchange in both in vivo and in vitro tests.

There is also suggestive evidence for the bioavailability of the organics from DE (Chapter 3, Section3.5). Elevated levels of DNA adducts in lymphocytes have been reported in workers exposed to DE. In addition, animal studies showed that some of the radiolabeled organic compounds are eluted from DE particles following deposition in the lungs.

7.5.4. Mode of Action

As discussed in Section 7.4, the modes of action of DE-induced carcinogenicity in humans is not understood. It can be suggested that one or multiple modes of action may be involved. These may include: (a) mutagenic and genotoxic events (e.g., direct and indirect effects on DNA and effects on chromosomes) by organic compounds in the gaseous and particle

phases; (b) indirect DNA damage via the production of reactive oxygen species (ROS) induced by particle-associated organics; and (c) particle-induced chronic inflammatory response leading to oxidative DNA damage through the release of cytokines, ROS, etc., and an increase in cell proliferation.

The particulate phase or whole DE exposure, as measured by DPM, appears to have the greatest observable contribution to the carcinogenic effects, and both the particle core and the associated organic compounds have demonstrated carcinogenic properties, although a role for the gas-phase components cannot be ruled out. The carcinogenic activity of DE may also be related to the small size of the particles. Moreover, the relative contribution of the possible mode(s) of action may be different at different exposure levels. For example, available evidence from rat studies indicates the importance of the role of the DPM in mediating lung tumor response at high exposure levels. Thus, the role of the adsorbed organic compounds may take on increasing importance at lower exposure levels.

7.5.5. Characterization of Overall Weight of Evidence: EPA's 1986 Guidelines for Carcinogen Risk Assessment

The totality of evidence supports the conclusion that DE is a *probable human carcinogen (Group B1)*. This conclusion is based on:

- "Limited"evidence (i.e., strong but less than sufficient evidence for "known human carcinogen"), for a causal association between DE exposure and increased risk of lung cancer among workers in different occupations;
- Evidence of carcinogenicity of DPM in rats and mice by noninhalation routes of exposure (intratracheal instillation, lung implantation, skin painting, and subcutaneous injection); and
- Extensive supporting data including the demonstrated mutagenic and/or chromosomal effects of DE and its organic constituents, suggestive evidence for the bioavailability of the organics from DE, and knowledge of the known mutagenic and/or carcinogenic activity of a number of individual organic compounds present on the particles (e.g,. PAH and derivatives) and in the DE gases (e.g., benzene, 1,3-butadiene, and aldehydes).

7.5.6. Weight-of-Evidence Hazard Narrative: EPA's Proposed Guidelines for Carcinogen Risk Assessment (1996b, 1999)

The combined evidence supports the conclusion that DE is *likely to be carcinogenic to humans* by inhalation and that this hazard applies to environmental exposure conditions. The spectrum of evidence and the inferences drawn provide a substantial case for this hazard potential. The weight of evidence of human carcinogenicity is based on:

- Strong but less than sufficient epidemiologic evidence for a causal association between DE exposure and increased risk of lung cancer among workers in different occupations;
- Evidence of carcinogenicity of DPM in rats and mice by noninhalation routes of exposure (intratracheal instillation, lung implantation, skin painting, and subcutaneous injection); and
- Extensive supporting data including the demonstrated mutagenic and/or chromosomal effects of DE and its organic constituents, suggestive evidence for the local and systemic bioavailability of the organics from DE, and knowledge of the known mutagenic and/or carcinogenic activity of a number of individual organic compounds present on the particles (e.g., PAH and derivatives) and in the DE gases (e.g., benzene, 1,3 butadiene, and aldehydes).

The weight-of-evidence for the lung cancer hazard is considered strong, even though inferences and uncertainties are involved. Major uncertainties include:

- There is scientific debate about the significance of the occupational epidemiologic evidence for a causal association between occupational exposure and increased lung cancer risk. Some experts view the evidence as weak given that most of the relative risk increases are <2.0, whereas others consider the evidence as more than adequate and compelling. With relatively low relative risks (<2.0), the effects of possible confounding exposures or other factors could play a significant role in the risk increases. For example, there is specific concern about whether the effects of smoking, a known cause of lung cancer, has been adequately or fully accounted for in the key studies. In more general terms, the lack of historical exposure data to retrospectively validate estimated DE exposure levels is also a limitation.
- A lack of knowledge about the mode(s) of action of DE lung cancer in humans results in the use of a number of default risk assessment assumptions which, while justifiable by evidence or policy choice, introduce uncertainty. To date, available evidence for the role of DPM, both the adsorbed organics and the carbon core

particle, has been shown only for high exposure conditions in the rat lung. The tumor inducing mode-of-action in the rat lung appears to depend on particle overloading of the lung and subsequent pathology. This sequence is judged not to be relevant for assessing the hazard to humans exposed in the ambient environment. There is virtually no information about the relative role of DE constituents in mediating the carcinogenic effects at lower experimental exposure levels, though hypotheses exist.

While a major uncertainty relates to the incomplete understanding of DE's mode(s) of action for the induction of lung cancer in humans, available data and hypotheses suggest that DE-induced lung carcinogenicity may be mediated by mutagenic and nonmutagenic events from both the particles and the associated organic compounds, although a role for the organics in the gaseous phase cannot be ruled out. Given that there is some evidence for a mutagenic mode of action, a cancer hazard is presumed at environmental exposure levels. This is consistent with EPA's science policy position, which assumes a nonthreshold effect for carcinogens in the absence of definitive data demonstrating a nonlinear or threshold mechanism. It should also be noted that there are not orders of magnitude differences between lower level occupational and higher end environmental exposure levels, in fact, there appears to be exposure overlap. This observation means that an extrapolation of the occupational hazard to lower environmental exposure levels is minimal, and thus, the conclusion of an environmental hazard is supported. Given these circumstances, linear low-dose extrapolation also would be an appropriate default choice in dose-response assessment that is focused on environmental levels of exposure (Chapter 8, Section 8.2). Because of insufficient information, the human carcinogenic potential of DE by oral and dermal exposures cannot be determined.

7.6. EVALUATIONS BY OTHER ORGANIZATIONS

Several organizations have reviewed the relevant data and evaluated the potential human carcinogenicity of DE or its particulate component. The conclusions reached by these organizations are generally comparable to the evaluation made in this assessment using EPA's Carcinogen Risk Assessment Guidelines. A summary of available evaluations conducted by other organizations is provided in Table 7-9.

7.7. CONCLUSION

It is concluded that environmental exposure to DE may present a lung cancer hazard to humans. The particulate phase appears to have the greatest contribution to the carcinogenic effect, both the particle core and the associated organic compounds have demonstrated

Table 7-9. Evaluations of DE as to human carcinogenic potential

Organization	Human data	Animal data	Overall evaluation
NIOSH (1988)	Limited	Confirmatory	Potential occupational carcinogen
IARC (1989)	Limited	Sufficient	Probably carcinogenic to humans
IPCS (1996)	N/A[a]	N/A	Probably carcinogenic to humans
California EPA (1998)	"Consistent evidence for a causal association"	"Demonstrated carcinogenicity"	DPM as a "toxic air contaminant" (California Air Resources Board)
NTP (2000)	"Elevated lung cancer in occupationally exposed groups"	"Supporting animal and mechanistic data"	DPM-Reasonably anticipated to be a carcinogen

[a]Not applicable.

carcinogenic properties, although a role for the DE gas-phase components cannot be ruled out. Using either EPA's 1986 Guidelines for Carcinogen Risk Assessment (U.S. EPA, 1986) or the proposed revisions (U.S. EPA, 1996b, 1999), DE is judged to be a probable human carcinogen, or likely to be carcinogenic to humans by inhalation, respectively. The weight of evidence for potential human carcinogenicity for DE is considered strong, even though inferences are involved in the overall assessment. Major uncertainties of the hazard assessment include the following unresolved issues:

- There has been a considerable scientific debate about the significance of the available human evidence for a causal association between occupational exposure and increased lung cancer risk. Some experts view the evidence as weak given that most of the relative risk increases are <2.0 whereas others consider the evidence as more than adequate and compelling. Additionally, there is debate about whether the effects of smoking have been adequately accounted for in key studies, as well as the lack of historical DE exposure data to retrospectively validate estimated DE exposure levels for the available studies.
- A lack of knowledge about the mode(s) of action for DE lung cancer in humans results in the use of a number of default risk assessment assumptions which, while justifiable by evidence or policy choice, introduce uncertainty. To date, available evidence for the role of DPM, both the adsorbed organics and the carbon core particle, has been shown only for high-exposure conditions in the rat lung. The

tumor-inducing mode of action in the rat lung appears to depend on particle overloading of the lung but this is judged to be not relevant for assessing the human hazard of ambient exposures. There is virtually no information about the relative role of DE constituents in mediating carcinogenic effects at lower experimental or environmental exposure levels. Furthermore, there is only a limited understanding regarding the relationship between DPM particle size and carcinogenicity.

- DE is present in ambient PM (e.g., $PM_{2.5}$ or PM_{10}); however, a cancer hazard for ambient PM has not been identified, as of 1996 (EPA 1996b). An updated evaluation is expected in 2002.

Additional research is needed to address these issues to reduce the uncertainty associated with the potential cancer hazard of exposure to DE.

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8. DOSE-RESPONSE ASSESSMENT: CARCINOGENIC EFFECTS

8.1. INTRODUCTION

Dose-response assessment for carcinogenicity defines the relationship between the exposure/dose of an agent and the degree of carcinogenic response, and evaluates potential cancer risks to humans at exposure/dose levels of interest. Most often, the exposure/dose response of interest is well below the range of observation. As a result, dose-response assessment usually entails an extrapolation from the generally high exposures in studies on humans or laboratory animals to the exposure levels expected from human contact with the agent in the environment. It also includes considerations of the scientific validity of these extrapolations based on available knowledge about the underlying mechanisms or modes of carcinogenic action. The complete sequence of biological events that must occur to produce an adverse effect is defined as "mechanism of action." In cases where only partial information is available, the term "mode of action" is used to refer to the mechanisms for key events that are judged to be sufficient to inform about the shape of the dose-response curve beyond the range of observation.

This chapter evaluates the available exposure/dose-response data and discusses extrapolation issues in estimating the cancer risk of environmental exposure to diesel engine exhaust (DE). It concludes that available data are inadequate to confidently derive a cancer unit risk estimate for DE or its component, diesel particulate matter (DPM). Unit risk is one possible output from a dose-response assessment and is defined as the estimated upper-bound cancer risk at a specific exposure or dose from a continuous average lifetime exposure to a carcinogen (in this case, cancer risk per $\mu g/m^3$ of DPM). In lieu of unit-risk-based quantitative risk estimates, this chapter provides a perspective about potential risk at environmental levels. Subsequent sections of this chapter discuss issues related to dose-response evaluation of human cancer risk for DE exposure, including the target tumor site and underlying mode of action, suitable measures of dose, approaches to low-dose extrapolation, and appropriate data to be used in the dose-response analysis. This is followed by a simple analysis of the possible degree and extent of risk from environmental exposure to DE.

Appendix C provides a summary review of dose-response assessments conducted to date by other organizations and investigators. These risk estimations were performed on the basis of either epidemiologic and/or experimental data. As concluded in Section 8.5, EPA finds that available epidemiologic data are too uncertain to confidently derive a unit risk estimate for DE-induced lung cancer, and that rat data are not suitable for estimating human risk. Nevertheless, a review of dose-response evaluations is provided in the appendix for historical context.

8.2. MODE OF ACTION AND DOSE-RESPONSE APPROACH

According to EPA's 1996 Proposed Guidelines for Carcinogen Risk Assessment (U.S. EPA, 1996), dose-response assessment is performed in two steps: assessment of observed data to derive a point of departure, followed by extrapolation to lower exposures to the extent necessary. Human data are always preferred over animal data, if available, as their use obviates the need for extrapolation across species. Mode-of-action information is important to dose-response evaluation, as it informs about the relevance of animal data to assessment of human hazard and risk, the shape of the dose-response curve at low doses, and the most appropriate measure(s) of exposure/dose and response.

If there are sufficient quantitative data (humans and/or animals) and adequate understanding of the carcinogenic process, the preferred approach is to use a biologically based model for both the range of observation and extrapolation below that range. Otherwise, as a default procedure, a standard mathematical model is used to curve-fit the observed dose-response data to obtain a point of departure, which is the lower 95% confidence limit of the lowest exposure/dose that is associated with a selected magnitude of excesses of cancer risk in human or animal studies. Default approaches for low-dose extrapolation should be consistent with the current understanding of the mode(s) of action. These include approaches that assume linearity or nonlinearity, or both. Linear extrapolation is used when there is insufficient understanding of the modes of action, or the mode-of-action information indicates that the dose-response curve at low dose is, or is expected to be, linear. Linear extrapolation involves the calculation of the slope of the line drawn from the point of departure to zero exposure or dose (i.e., above background). When there is sufficient evidence for a nonlinear mode of action but not enough data to construct a biologically based model for the relationship, a margin of exposure is used as a default approach. A margin-of-exposure analysis compares the point of departure (i.e., the lowest exposure associated with some cancer risk) with the dose associated with the environmental exposure(s) of interest and determines whether or not the exposure margins are adequate. Both default approaches may be used for a tumor response if it is mediated by linear and nonlinear modes of action. The dose-response approaches considered in this chapter follow the principles of EPA's guidelines for carcinogen risk assessment (U.S. EPA, 1986, 1996, 1999).

As reviewed in Chapter 7, there is substantial evidence from combined human and experimental evidence that DE is likely to pose a cancer hazard to humans at anticipated levels of environmental exposure. The critical target organ is the lung. Evidence exists for a causal relationship between risk for lung cancer and occupational exposure to DE in certain occupational workers such as railroad workers, truck drivers, heavy equipment operators, transit workers, etc.

The mechanism(s) by which DE induces lung cancer in humans has not been established. As discussed in Chapter 7, Section 7.4, several modes of action have been postulated on the basis of available mechanistic studies, including direct DNA effects (gene mutations) by the adsorbed organic compounds and the gaseous fractions, indirect DNA effects (e.g., chromosomal aberrations, sister chromatid exchange [SCE], micronuclei) by DE and DPM, oxidative DNA damage by DPM via release of reactive oxygen species (ROS), and particle-induced chronic inflammatory response leading to epithelial cell cytotoxicity and regenerative cell proliferation via release of cytokines, growth factors, and ROS. It is likely that a combination of modes of action contributes to the overall carcinogenic activity of DE, and that the relative contribution of the various modes of action may vary with different exposure levels.

In the absence of a full understanding of the relative roles of DE constituents in inducing lung cancer in humans, and because there is some evidence for a mutagenic mode of action, linear low-dose extrapolation is an appropriate and prudent default choice for modeling dose-response, and if needed, risk extrapolation from high to lower exposures (U.S. EPA, 1986, 1996, 1999). It also should be noted that there are not order of magnitude differences between lower levels of occupational and higher end environmental exposure estimates. In fact, there appears to be exposure overlap. This means that an extrapolation of the occupational hazard to lower environmental exposure levels is minimal. Other individuals and organizations have used either linear risk extrapolation models and/or mechanistically based models to estimate cancer risk from environmental exposure to DE (e.g., IPCS, 1996; Cal EPA, 1998; also see Appendix C). These were examined but not found to provide a compelling basis for unit risk derivation because of database uncertainty and/or recent understandings about the suitability of the rat data for modeling a dose-response at environmental levels of exposure.

For example, there are an observable series of events showing how DE causes lung tumors in the rat under high exposure experimental conditions. Prolonged exposure to high concentrations of a variety of poorly soluble particles including DPM (and its carbon core, devoid of organics) causes lung tumors in rats through a mode of action that involves impairment of lung clearance mechanisms (referred to as "lung overload response"), leading to persistent chronic inflammation, cell proliferation, metaplasia, and ultimately the development of lung tumors (ILSI, 2000). Because this mode of action is not expected to be operative at environmental exposure conditions, the rat lung tumor dose-response data are not considered suitable for predicting human risk at low environmental exposure concentrations.

8.3. USE OF EPIDEMIOLOGIC STUDIES FOR QUANTITATIVE RISK ASSESSMENT

As discussed above, human data are considered more appropriate than animal data in estimating environmental cancer risk for DE. Still, there are many uncertainties in using the

available epidemiologic studies that have quantitative exposure data to extrapolate the risk to the general population for ambient-level DE exposure.

8.3.1. Sources of Uncertainty

The greatest uncertainty in estimating DE-induced cancer risk from epidemiologic studies is the lack of knowledge of actual historical exposures for individual workers, particularly for the early years. Reconstruction of historic exposures is based on job exposure categories, industrial hygiene measurements, and assumptions made about exposure patterns.

Another related uncertainty is the choice of markers of exposure to DE. As discussed above, the modes of action for DE-induced lung cancer in humans are not fully understood, and thus the best measure of DE exposure is unknown. Various markers of DPM (e.g., respirable-sized particles, elemental carbon [EC]) have been used as dosimeters for DE. Though EC is more sensitive and more specific than respirable-sized particles, both are considered appropriate dosimeters. Related to the choice of dosimeter, having a relatively constant relationship between the organics (on the particle) and the particle mass would be consistent with a possible mode-of-action role for both the particle and organic components. However, evidence of such a constant historic relationship remains unclear. As discussed in Chapter 2 (Section 2.5.2), it appears that newer model on-road engine exhaust has a lesser quantity of organics adsorbed onto the particle compared to older model engines. On the other hand, with regard to DE in the ambient air, there is significant variation in the amounts of DPM organic components emitted because of aged vehicles in the on-road fleet, driving patterns, and the additional presence of nonroad DE (e.g., marine vessels and locomotives, which generally use older technology than on-road engines).

Another major uncertainty associated with many of the DE epidemiologic studies was the inability to fully control for smoking effects, resulting in possible errors in estimating relative risk increases. Changes in adjustments for smoking could result in considerable changes in relative risk, because smoking has a much larger effect on relative lung cancer risk than is likely for DE. It is difficult to effectively control for a smoking effect in a statistical analysis because cigarette smoke contains an array of biologically active compounds and affects multiple steps of carcinogenesis, thus probably making smokers more susceptible to DE-induced lung cancer than are nonsmokers. A statistical analysis would not be able to adjust for such an effect without having a detailed record of the smoking history of individuals.

A potential uncertainty involves the use of occupational worker data to extrapolate cancer hazard risk to the general population and sensitive subgroups. By sex, age, and general health status, workers are not fully representative of the general population. For example, there is virtually no information to determine whether infants and children or people in poor health

respond differently to DE exposure than do workers. Finally, the use of linear low-dose extrapolation may contribute to uncertainty in estimating environmental risks.

8.3.2. Evaluation of Key Epidemiologic Studies for Potential Use in Quantitative Risk Estimates

Among the available epidemiologic studies, only the railroad worker studies and the Teamster truck driver studies have reconstructed quantitative historical exposure data for possible use in deriving a unit risk estimate for DE-induced lung cancer. This section evaluates the strengths and limitations of these data and their suitability for dose-response analysis.

8.3.2.1. *Railroad Worker Studies*

Garshick and colleagues conducted both cohort and case-control studies of lung cancer mortalities among U.S. railroad workers registered with the U.S. Railroad Retirement Board (RRB).

In the cohort study (Garshick et al., 1988), lung cancer mortality was ascertained through 1980 in 55,407 railroad workers, age 40 through 64 in 1959, with at least 10 years of work in selected railroad jobs (39 job titles). The cohort was selected on the basis of job titles in 1959. Industrial hygiene evaluations and descriptions of job activities were used to classify jobs as exposed or unexposed to diesel emissions. Workers with recognized asbestos exposure were excluded from the job categories selected for study. However, a few jobs with some potential for asbestos exposure were included in the cohort. Each subject's work history was determined from a yearly job report filed by his employer with the RRB from 1959 until death or retirement. The year 1959 was chosen as the effective start of DE exposure for this study because by this time 95% of the locomotives in the United States were diesel powered. The author reported statistically significant relative risk increases of 1.57 for the 40-44 year age group and 1.34 for the 45-49 year age group, after exclusion of workers exposed to asbestos and controls for smoking. Age groups were determined by their ages in 1959.

A main strength of the cohort study is the large sample size (55,407), which allowed sufficient power to detect small risks. This study also permitted the exclusion of workers with potential past exposure to asbestos. The stability of job career paths in the cohort ensured that of the workers 40 to 64 years of age in 1959 classified as DE-exposed, 94% of the cases were still in DE-exposed jobs 20 years later.

The main limitation of the cohort study is the lack of quantitative data on exposure to DE. The number of years exposed to DE was used as a surrogate for dose. The dose, based on duration of employment, has inaccuracies because individuals were working on both steam and diesel locomotives during the transition period. It should be noted that the investigators included

only exposures after 1959; the duration of exposure prior to 1959 was not known. Other limitations of this study include its inability to examine the effect of years of exposure prior to 1959 and the less-than-optimal latency period for lung cancer expression. No adjustment for smoking was made in this study. For a detailed description of this study please refer to Chapter 7, Section 7.2.1.7.

Garshick and colleagues also conducted a case-control study of railroad workers who died of lung cancer between 1981 and 1982 (Garshick et al., 1987). The author reported statistically significant increased odds ratios (with asbestos exposure accounted for) of 1.41 (95% confidence interval [CI] = 1.06, 1.88) for the ≤64 year age group and 1.64 (95% CI = 1.18, 2.29) for the ≤64 year age group with ≥20 years of exposure when compared with the 0-4 year exposure group. The population base for this case-control study was approximately 650,000 active and retired male U.S. railroad workers with 10 years or more of railroad service who were born in 1900 or later. The cases were selected from deaths with primary lung cancer, which was the underlying cause of death in most cases. Each case was matched to two deceased controls whose dates of birth were within 2.5 years of the date of birth of the case and whose dates of death were within 31 days of the date of death noted in the case. Controls were selected randomly from workers who did not have cancer noted anywhere on their death certificates and who did not die of suicide or of accidental or unknown causes. A total of 1,256 cases and 2,385 controls were selected for the study. Among younger workers, approximately 60% had exposure to DE, whereas among older workers, only 47% were exposed to DE. DE exposure surrogates for workers were similar to those in the cohort study. Asbestos exposure was categorized on the basis of jobs held in 1959, or on the last job held if the subject retired before 1959. Smoking history information was obtained from the next of kin.

The strengths of the case-control study are consideration of confounding factors such as asbestos exposure and smoking; classification of DE exposures by job titles and industrial hygiene sampling; and exploration of interactions between smoking, asbestos exposure, and DE exposure. Major limitations of this study include (a) possible overestimation of cigarette consumption by surrogate respondents; (b) use of the Interstate Commerce Commission (ICC) job classification as a surrogate for exposure, which may have led to misclassification of DE exposure jobs with low intensity and intermittent exposure, such as railroad police and bus drivers, as unexposed; (c) lack of data on the contribution of unknown occupational or environmental exposures and passive smoking; and (d) a suboptimal latency period of 22 years, which may not be long enough to observe a full expression of lung cancer. For a detailed description of this study, please see Chapter 7, Section 7.2.2.4.

As a part of these epidemiologic studies, Woskie et al. (1988a) conducted an industrial hygiene survey in the early 1990s for selected jobs in four small northern railroads. DE

exposure was considered as a yes/no variable based on job in 1959 and estimated years of work in a diesel- exposed job as an index of exposure. Thirty-nine job titles were originally identified and were then collapsed into 13 job categories and, for some statistical analyses, into 5 categories (clerks, signal maintainers, engineers/firers, brakers/conductors/hostlers, and shop workers) (Woskie et al., 1988b; Hammond et al., 1988). As discussed below, these exposure estimations were used by Crump et al. (1991) and by Cal EPA (1998) for their dose-response analyses.

8.3.2.1.1. ***Potential for the data to be used for dose-response modeling.*** Both case-control and cohort studies can be used for dose-response analysis if exposure for each worker is available. Control of a smoking effect is important when lung cancer is the disease of interest. However, as discussed previously (see Section 8.3.1), one may not be able to control smoking completely in a dose-response analysis because of the lack of detailed records of the smoking history of individuals.

Garshick et al. (1988) reported a positive relationship of relative risk and duration of exposure by modeling age in 1959 as a covariate in an exposure-response analysis. The positive relationship disappeared when attained age was used instead of age in 1959, and a negative dose-response was observed (Crump et al., 1991). This negative dose-response continued to be upheld in a subsequent reanalysis (Crump, 1999). Garshick (letter from Garshick, Harvard Medical School, to Chao Chen, U.S. EPA, dated August 15, 1991) performed further analysis and reported that the relationship between years of exposure and risk of lung cancer, when adjusted for attained age and calendar year, was flat to negative depending upon which model was used. In contrast, California EPA (Cal EPA, 1998) found a positive dose-response by using age in 1959 but allowing for an interaction term of age and calendar year in the model.

Crump et al. (1991) also found, and Garshick (letter from Garshick, Harvard Medical School, to Chao Chen, U.S. EPA, dated August 15, 1991) confirmed, that in the years 1977-1980 the death ascertainment was not complete. About 20% to 70% of deaths were unaccounted for, depending upon the calendar year. Further analysis, based on job titles in 1959 and limited to deaths occurring through 1976, showed that the youngest workers still had the highest risk of dying of lung cancer.

Extensive statistical analyses were conducted by a panel convened by HEI (1999) to investigate the utility of the railroad worker cohort for use in dose-response based quantitative risk assessment. Seven models were used to test the data, and the models were formed by varying a number of covariates in different combinations. The covariates included employment duration, cumulative exposure with and without correction for background exposure, and three job categories: clerks and signalmen, train workers (which include engineers/firers/brakers/

conductors), and shop workers. The coefficient for each covariate in a model is used to calculate relative risk for the associated covariate. In summary, the panel found that effects of exposure as defined by an exposure-response curve were either flat or negative in all of the models. In these analyses, relative risk for each job category was assumed to be constant with respect to age. Further exploration of the data showed that the relative risk for train workers was not constant. The panel's statistical analyses also revealed the complexity of the data and difficulties of providing an adequate summary measure of effect, probably because calendar year and cumulative exposure are highly correlated, which makes it especially difficult to sort out their separate effects. The difficulty of providing an adequate measure of DE effect was further demonstrated in Table C.3 of the HEI report, in which negative or positive effects for cumulative exposure (with background exposure adjustment) were obtained depending on whether or not job category was included in the model. A similar review of the divergent views about the railroad worker dose response also can be found in Chapter 7, Section 7.2.1.7.

The diverging results about the presence or absence of exposure response for the railroad worker data have become a source of continuing debate about the suitability of these data for estimating DE cancer risk. Although it is difficult to identify the exact reason for the diverging findings, the "age effect" appears to be a main source of uncertainty because age, calendar year, and cumulative exposure are not mutually independent. Therefore, an ideal dose-response analysis would account for the ages when exposure to DE began and terminated, along with the attained age and other covariates for each person, using age-dependent exposure concentration rather than cumulative exposure over lifetime as a dosimeter. This analysis would be possible for the railroad workers if information were available on the ages when exposure began and terminated.

Given the equivocal evidence for positive exposure response, EPA has not derived a unit risk on the basis of the available railroad worker data. This determination should not be construed, however, to imply that the railroad worker studies contain no useful information on lung cancer risk from exposure to DE.

8.3.2.2. *Teamsters Union Trucking Industry Studies*

Steenland et al. (1990) conducted a case-control study of lung cancer deaths in the Central States Teamsters Union to determine the risk of lung cancer among different trucking industry occupations. The study found statistically significant increased odds ratios for lung cancer of 1.89 and 1.64, depending on years of employment. Cases comprised all deaths from lung cancer (1,288). The 1,452 controls comprised every sixth death from the entire file, excluding deaths from lung cancer, bladder cancer, and motor vehicle accidents. Individuals were required to have 20 years tenure in the union to be eligible to claim benefits.

Detailed information on work history and potential confounders such as smoking, diet, and asbestos exposure was obtained by questionnaire. On the basis of interview data and the 1980 census occupation and industry codes, subjects were classified either as nonexposed or as having held other jobs with potential DE exposure. The Teamsters Union work history file did not have information on whether men drove diesel or gasoline trucks, and the four principal occupations were long-haul drivers, short-haul or city drivers, truck mechanics, and dockworkers. Subjects were assigned the job category in which they had worked the longest.

The main strengths of the study are the availability of detailed records from the Teamsters Union, a relatively large sample size, availability of smoking data, and measurement of possible asbestos exposures. Some limitations of this study include possible misclassifications of exposure and smoking habits, as information was provided by next-of-kin and lack of sufficient latency to observe lung cancer excess.

Steenland et al. (1998) conducted an exposure-response analysis by supplementing the data from their earlier case-control study of lung cancer and truck drivers in the Teamsters Union with exposure estimates based on a 1990 industrial hygiene survey of EC exposure (Zaebst et al., 1991), a surrogate for DE in the trucking industry. Available data indicate that exposure to workers in the trucking industry in 1990 averaged 2-27 $\mu g/m^3$ of EC. The 1990 exposure information was used by Steenland as a baseline exposure measurement to reconstruct past exposure (in the period of 1949 to 1983) by assuming that the exposure for workers in different job categories is a function of highway mileages traveled by heavy-duty vehicles and efficiency of the engine over the years.

The industrial hygiene survey by Zaebst et al. (1991) of EC exposures in the trucking industry provided exposure estimates for each job category in 1990. The EC measurements were generally consistent with the epidemiologic results, in that mechanics were found to have the highest exposures and relative risk, followed by long-haul and short-haul drivers. Dockworkers who had the lowest exposures also had the lowest relative risks.

Past exposures were estimated assuming that they were a function of (a) the number of heavy-duty trucks on the road, (b) the particulate emissions (grams/mile) of diesel engines over time, and (c) leaks from truck exhaust systems for long-haul drivers. Estimates of past exposure to EC (as a marker for DE exposure) were made based on the assumption that average 1990 levels for a particular job category could be assigned to all subjects in that category, and that levels prior to 1990 were directly proportional to vehicle miles traveled by heavy-duty trucks and the estimated emission levels of diesel engines. For example, a 1975 exposure level was estimated by the following equation: 1975 level = 1990 level × (vehicle miles 1975/vehicle miles 1990) × (emissions 1975/emissions 1990). Once estimates of exposure for each year of work history were derived for each subject, analyses were conducted by cumulative level of estimated

carbon exposure. As with most epidemiologic studies, the endeavors to reconstruct exposures for epidemiologic studies are subject to uncertainties.

8.3.2.2.1. ***Potential for the data to be used for dose-response modeling.*** Steenland et al. (1998) analyzed their case-control data and showed a significant positive trend in lung cancer risk with increasing cumulative exposure to DE. The study by Steenland et al. (1998) could provide a valuable database for calculating unit risk for DE emissions. The strength of this data set is that the smoking histories of workers were obtained to the extent possible. Smoking is especially important in assessing the lung cancer risk due to DE exposure because smoking has much higher relative risk (or odds ratio) of lung cancer than does DE. In the Steenland et al. (1998) study, the overall (ever-smokers vs. nonsmokers) odds ratio for developing lung cancer from smoking is about 7.2, which is about fivefold larger than the 1.4 relative risk increase from a large synthesis of many DE epidemiologic studies. It is possible that a modest change of information on smoking and diesel exposure might alter the conclusion and risk estimate.

Another strength of the Teamster data for use in environmental risk assessment for the general population is that exposures of Teamsters are closer to ambient exposures than are those of railroad workers. The Teamsters Union truck driver case-control workers had cumulative exposure ranging from 19 to 2,440 $\mu g/m^3$-years of EC, with the median and 95th percentile, respectively, of 358 and 754 $\mu g/m^3$-years of EC. The median and 95th percentile of an environmentally equivalent exposure would be 3 and 6 $\mu g/m^3$, respectively.[1] These environmental equivalent exposures for the Teamsters Union truck drivers are close to the estimated ambient exposures of <1.0 $\mu g/m^3$ to 4.0 $\mu g/m^3$ (see Table 2-31).

Steenland et al. (1998) stated that their risk assessment is exploratory because it depends on estimates about unknown past exposures. An EPA reanalysis of DE exposure for this study is underway. With a revised exposure assessment, a reevaluation of the dose-response would be appropriate. In a recent review, HEI (1999) concluded that the Teamsters studies may be useful for quantitative risk assessment, but significant further evaluation and development are needed. Given the ongoing reanalysis of exposure, EPA will not, at this time, use the Steenland et al. (1998) occupational risk assessment findings to derive equivalent environmental parameters and cancer unit risk estimates.

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[1]The conversion assumes (a) DPM = 40% EC as reported by Steenland et al. (1998), (b) environmental equivalent exposure is approximately = 0.21 × occupational exposure, and (c) 70 $\mu g/m^3$-years is equivalent to a lifetime of exposure at 1 $\mu g/m^3$.

8.3.3. Conclusion

Even though available evidence supports a conclusion that DE is likely to be a human lung carcinogen, the conclusion of the dose-response evaluation is that the available data are not sufficient to confidently estimate a cancer unit risk or unit risk range. The absence of such a cancer unit risk for DE limits the ability to quantify, with confidence, the potential impact of the hazard on exposed populations. Two significant short-term activities are underway to improve the epidemiologic database for dose-response assessment: (1) a follow-up study to correct the undercounting of mortality in the Garshick et al. (1988) railroad worker study, and (2) an EPA-sponsored effort to improve the exposure estimates for Teamsters Union truck drivers (Steenland et al., 1998). EPA will monitor this ongoing research as well as the ongoing NCI-NIOSH study of nonmetal miners and the recently NCI-funded epidemiologic study of truck drivers. As these studies or other new data become publicly available, EPA will reconsider the merit of conducting additional dose-response analysis and unit risk derivation.

8.4. PERSPECTIVES ON CANCER RISK

Although the available data are considered inadequate to confidently estimate a cancer unit risk, this does not mean that there is no information about the possible cancer risk of DE. To examine the significance of the potential cancer hazard from environmental exposure to DE, all relevant epidemiologic and exposure data as well as simple risk assessment tools can be used. Such an approach does not produce confident estimates of cancer unit risk. Rather, these exploratory approaches provide a perspective on the possible magnitude of cancer risk and thus insight about the potential significance of the hazard. This section describes approaches and methods that are used to gauge the magnitude of possible cancer risk from ambient exposure to DE.

The first approach involves examining the differences between the levels of occupational and ambient environmental exposures, while assuming that cancer risk to DE is linearly proportional with cumulative lifetime exposure. Risks to the general public would be low in comparison to occupational risk if the differences in exposure are large (e.g., about three orders of magnitude or more). On the other hand, if the exposure differences are smaller (i.e., within one to two orders of magnitude), environmental risks become more of a concern as they approach the range of workers' risk observed in epidemiologic studies of past occupational exposures. This assumes that the carcinogenic potency of historical and current-day DE is not significantly different, a reasonable assumption, though not without uncertainty.

Table 8-1 shows occupational exposure estimates for some of the occupational groups where increased relative risks of lung cancer (e.g., meta-analyses) have been analyzed. Given that no statistical properties associated with these exposure estimates are known, their use here is

Table 8-1. DPM exposure margins (ratio of occupational ÷ environmental exposures)

Occupational group	Estimated occupational exposure/concentration ---------- Environmental equivalent [a]	Exposure margin ratio - average environmental exposure for 0.8 μg/m³ of environmental exposure[b]	Exposure margin ratio - high-end environmental exposure for 4.0 μg/m³ of environmental exposure[b]	Reference[c]
Public transit workers	15-98 μg/m³ ---------- 3-21 μg/m³	4-26	0.8-5	Birch and Cary, 1996
U.S. railroad workers	39-191 μg/m³ ---------- 8- 40 μg/m³	10-50	2-10	Woskie et al., 1988b
Fork Lift Operators	7-403 μg/m³ ---------- 1- 85 μg/m³	2-106	0.37-21	Groves and Cain, 2000[d]
High end boundary estimate	1200 μg/m³ ---------- 252 μg/m³	315	63	see text discussion in Section 8.4

[a] Equivalent environmental exposure = occupational exposure × 0.21, see Chapter 2, Section 2.4.3.1, some values are rounded.
[b] 0.8 μg/m³ = average 1990 nationwide on-road exposure estimate from HAPEM model; the companion rural estimate is 0.5 μg/m³, and 4 μg/m³ is
a high-end estimate. The 1996 nationwide average is 0.7 μg/m³, the companion rural estimate is 0.2 μg/m³; however, a high-end estimate is not available for 1996. See Chapter 2, Sections 2.4.3.2.1 and 2.4.3.2.2.
[c] See Table 2-27 for more details about Birch and Cary, Woskie.
[d] 403 μg/m³ is a 99 percentile estimate of EC/μg/m³, the DPM equivalent of the EC measurement can be estimated as DPM = EC x 0.62 to 1.31.

not intended to be precise or to match with specific epidemiologic data, but rather to provide a broad range of possible exposures in the workplace. The purpose is to identify a high- and low-end occupational exposure consistent with the occupational groups of interest and then to compare these to estimates of environmental exposure. Given the special interest in discerning the lower risk magnitude, especially to see if the lower risk might be above or below one in 1 million, a high-end exposure estimate would be used, and as discussed later, the occupational exposure can be arbitrarily increased (e.g., toward an extreme value) to ensure that a low end of risk is identified, consistent with the reported occupational risk increases. Environmental exposure data from on-road vehicle emissions are based on the 1990 nationwide exposure estimates from the HAPEM model (see Chapter 2, Section 2.4.3.2.1). Both average (0.8 μg/m³) and high-end exposures (4 μg/m³) are used.

In order to compare differences between occupational and environmental exposures, it is necessary to convert occupational exposure to continuous exposure (i.e., environmental equivalent exposure = 0.21 × occupational exposure, see Section 2.4.3.1). Accordingly, Table 8-1 shows equivalent environmental levels and the ratios of occupational to environmental

exposures, referred to as exposure margins (EMs). An EM of 1 or less indicates that environmental exposure is comparable to occupational exposure. An EM >1 means that the occupational equivalent exposure is greater than the benchmarked environmental exposure.

Table 8-1 shows that the EMs based on the average nationwide environmental exposure (0.8 $\mu g/m^3$) approach three orders of magnitude. EM's that range from 1 to 10 also can be viewed as showing that adjusted occupational exposures are relatively close to the ambient environmental levels that were chosen as benchmarks. This closeness sets the stage for less uncertainty in hazard and risk extrapolation from the occupational to environmental setting. It also raises a concern that risks to the general public could approach worker risks that were observed in the occupational epidemiologic studies. Table 8-1 is based upon DE exposure estimates from on-road sources only. With the addition of exposure from nonroad sources, the average nationwide-based EM ratios would be lower. For example, using 1996 exposure data for urban populations (Table 2-30), the exposure from on-road sources is 0.5 $\mu g/m^3$, whereas nonroad sources contribute 0.9 $\mu g/m^3$, for a total of 1.4 $\mu g/m^3$. Using this exposure value in place of the EM calculation of Table 8-1 (1990 estimate of 0.8) produces a nearly 43% reduction in the EM ratio. A comparison of EM changes for the high-end on-road plus nonroad exposure is not possible at the present time because the 1996 data have not yet been modeled to obtain a high-end value similar to the 1990 value of 4.0 $\mu g/m^3$.

A second approach to explore the possible cancer risk to the general population from environmental exposure to DE is more quantitative. One begins by examining the risk observed in DE-exposed workers and then making reasoned assumptions as to how these risks can be translated to environmental exposure conditions. Such an approach involves three major assumptions: (1) the excess lung cancer risk as shown in numerous epidemiologic studies and in two meta-analyses is indeed due to DE exposure, (2) the increased lung cancer risk over background is linearly proportional to the lifetime exposure to DE, and (3) the past DE exposure for workers has the same cancer-inducing potential as the current DE in ambient air. Any of these assumptions could have an impact on the possible environmental risk by either increasing or decreasing the risk estimates, including the possibility of a lower or zero risk at environmental levels.

As reviewed in Chapter 7, Section 7.2, numerous epidemiologic studies have shown increased lung cancer risks (i.e., some are deaths, some are cases) among workers in certain occupations. The relative risks or odds ratios range from 1.2 to 2.6. Two independent meta-analyses show smoking-adjusted relative risk increases of 1.35 (Bhatia et al., 1997) and 1.47 (Lipsett and Campleman, 1999). For this analysis, a relative risk of 1.4 is selected as a reasonable estimate. This risk means that the workers faced an extra risk 40% higher than the

5% background lifetime lung cancer risk in the U.S. population.[2] Thus, using the relationship [excess risk = (relative risk-1) × background risk], these DE-exposed workers would have an excess risk of 2% (10^{-2}) (i.e., to develop lung cancer) due to occupational exposure to DE [(1.4 - 1) × (0.05) = 0.02]. The validity of this interpretation depends on an important assumption: that the observed incremental risk of 40% was due to DE exposure alone and not to other unknown extraneous factors. It should be noted, however, that the conclusion about the risk perspective would not be changed even if the incremental risk of 40% were greatly reduced (e.g., to 20%); the conclusion would be changed only if almost all of the incremental risk were due to nondiesel factors.

Next, one would consider the EM (i.e., the EM ratio) between the occupational exposures and general-population environmental exposures. DPM concentrations in the workplace, used as a surrogate for worker exposure, are shown for three occupational worker groups in Table 8-1. These range from 7-403 $\mu g/m^3$ (with an equivalent continuous exposure of 1-85 $\mu g/m^3$). These worker groups are consistent with many of those cited in the meta-analyses. For this exploratory risk estimation approach, we want to intentionally adopt a high-end boundary exposure estimate that is unlikely to be exceeded, so that a lower bounding of the risk would be identified. An occupational boundary exposure of 1,200 $\mu g/m^3$ with its environmental equivalent estimated value of 252 $\mu g/m^3$ has been purposefully adopted to represent a high-end boundary estimate. This happens to be about three times the forklift operator value shown in Table 8-1, and clearly a high-end estimate when Table 2-27 is examined, exclusive of the estimates for miners which are not included in the meta-analyses. It should be noted once again that none of these estimates are intended to be precise.

Table 8-1 shows that the DPM exposure margin ratio between occupational and environmental exposure, using the nationwide average exposure value of 0.8 $\mu g/m^3$, may range from 2 to 315 when the boundary estimate is used, and range from 0.37-63 when 4.0 $\mu g/m^3$ is used as a high-end environmental benchmark exposure. Some of these extreme values will be used, as discussed in the next paragraph.

Risks from environmental exposure depend on the shape of the dose-response curve in the range between occupational and environmental exposures. If lifetime risks in this range were

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[2]The background rate of 0.05 is an approximated lifetime risk calculated by the method of lifetable analysis using age-specific lung cancer mortality data and probability of death in the age group taken from the National Health Statistics (HRS) monographs of Vital Statistics of the U.S. (Vol. 2, Part A, 1992). Similar values based on two rather crude approaches also can be obtained: (1) $59.8 \times 10^{-5} / 8.8 \times 10^{-3} = 6.8 \times 10^{-2}$ where 59.8×10^{-5} and 8.8×10^{-3} are, respectively, the crude estimates of lung cancer deaths (including intrathoracic organs, estimated to be less than 105 of the total cases) and total deaths for 1996 reported in Statistical Abstract of the U.S. (Bureau of the Census, 1998, 118th Edition), and (2) 156,900/270,000,000 × 76 = 0.045, where 156,900 is the projected lung cancer deaths for the year 2000 as reported in Cancer Statistics J of the American Cancer Society, Jan/Feb 2000), 270,000,000 is the current U.S. population, and 76 is the expected lifespan.

to fall proportionately with reduced exposure, and if one assumes that past occupational exposures were at the high-boundary end, then the risk from average environmental exposure could be between 10^{-5} and 10^{-4} ($0.02 \div 315 = 6 \times 10^{-5}$). On the other hand, if occupational exposures for different groups were lower, risks from environmental exposure would be higher. For example, if occupational concentrations or exposures were closer to 100 $\mu g/m^3$, a value that is represented in several data sets shown in Table 8-1 (with an equivalent environmental exposure of 21 $\mu g/m^3$ and a corresponding EM of 26), then risks from environmental exposure would approach 10^{-3} ($0.02 \div 26 = 8 \times 10^{-4}$). If lifetime risks were to fall more than proportionately, then risks would be lower. The latter two sources of dose-response uncertainty (i.e., the actual occupational exposures and the shape of the dose-response curve at low exposures) cannot be further defined with currently available information. Use of higher environmental exposures (>0.8 up to 4.0 $\mu g/m^3$) lowers the EM value and increases the estimated risk.

The magnitude of the estimated lifetime cancer risk derived from using a very high-end occupational-to-environmental exposure difference, establishes a reasonable basis to believe that the general population could face possible risks high enough to be of concern. This does not directly address the segments of the population that may be at highest risk: those who are additionally exposed to nonroad sources of DE and children who may be more sensitive to early-life DE exposure, if not in fact, a longer period of potential lifetime exposure.

The analyses presented above are not intended to be precise but are useful in gauging the possible risk range using simple risk exploration methods. Best scientific judgment guided the selection of assumptions and other elements of this analysis which are deemed reasonable and appropriate for identifying possible risks based on the information currently available. These analyses provide a sense of where an upper limit (or "upper bound") of the cancer risk may be. The simple methodologies used are generic and are valid for any increased relative risk data, however, they are not unique to the DE data. These analyses are subject to numerous uncertainties, particularly the lack of actual exposure information in the epidemiologic studies and uncertainties related to the three major underlying assumptions mentioned earlier. Any of these uncertainties could have an impact on the possible risk levels discussed above. Lower risks are possible and one cannot rule out zero risk. The risks could be zero because (a) some individuals within the population may have a high tolerance to exposure from DE and therefore not be susceptible to the cancer risk from environmental exposure, and (b) although evidence of this has not been seen, there could be a threshold of exposure below which there is no cancer risk.

The estimated possible risk ranges (10^{-5} to 10^{-3} as well as lower and zero risk) provide a perspective of the potential significance of the lung cancer hazard. This perspective should not

be viewed as a definitive quantitative characterization of risk. The development of risk estimates does not constitute endorsement of their validity as surrogates for cancer unit risk or their suitability for estimating numbers of cancer cases. Further research is needed to more accurately assess and characterize environmental cancer risks of DE.

8.5. SUMMARY AND DISCUSSION

There are numerous published quantitative dose-response assessments to estimate human cancer risk from exposure to DE that use epidemiologic and/or experimental animal data (see Appendix C). These dose-response assessments were considered but failed to present a fully sufficient basis for a confident derivation of a cancer unit risk. This is because of epidemiologic exposure-related database uncertainties and the recent understanding about the lack of relevance of the rat lung cancer response to environmentally exposed humans. The dose-response analysis in this chapter has focused on the feasibility of using the occupational epidemiologic data to develop dose-response relationships and extrapolating them to the presumably lower levels of environmental exposure. Typically, this would result in the derivation of an exposure/dose-specific cancer unit risk. In the absence of an understanding about the mode(s) of action for DE-induced lung cancer in humans, coupled with the consideration that DE contains many mutagenic and carcinogenic constituents, linear low-dose extrapolation is judged to be an appropriate default choice for dose-response analysis, should there be satisfactory data to perform such an analysis.

This chapter specifically evaluated the suitability of using the railroad worker studies (Garshick et al., 1987, 1988) and the Teamster Union truck driver studies (Steenland et al., 1990, 1998) for dose-response analysis. However, because of uncertainties about the exposure response for the railroad workers and exposure uncertainties for the truck drivers, a dose-response-based cancer unit risk estimate for DE is not developed from these data sets at this time.

In the absence of a unit risk to assess environmental cancer risk, some insight about the possible significance of the hazard can be drawn from the available epidemiologic data and exploratory risk evaluation techniques. A discussion of possible risk is presented in the form of a perspective on the possible magnitude of risk from environmental exposure. The perspective discussion notes the small exposure margins and possible overlap between some occupational and environmental exposure levels. This lessens the uncertainty of extrapolating the occupational hazard and observed risk into the environmental setting. Furthermore, based on a more quantitative approach involving the observed lung cancer from occupational exposures and the magnitude of occupational and environmental exposure differences, an exploratory risk analysis shows that environmental cancer risks possibly range from 10^{-5} to nearly 10^{-3}, while a

consideration of the numerous uncertainties and assumptions also indicates that lower risk is possible and zero risk cannot be ruled out. These risk findings are only general indicators of the potential significance of the lung cancer hazard and should not be viewed as a definitive quantitative characterization of risk or be used to estimate an exposure-specific population impact, i.e., estimating numbers of cancer deaths. Best scientific judgment guided the selection of assumptions and other elements of the analysis which are deemed reasonable and appropriate for identifying possible risks based on the information currently available. Further research is needed to more accurately assess and characterize environmental cancer risks of DE.

This exploratory risk analysis uses data collected from engines built prior to the mid-1990s. While engine exhaust emissions have been decreasing and exhaust composition has been changing in recent years, particularly for on-road engines, EPA believes that the insight gained from the risk perspective is pertinent to current on-road and nonroad engine use. New and cleaner engines will become available in response to environmental concerns and strict new regulations. As cleaner engines replace a substantial number of existing engines, the risk perspective will need to be reevaluated.

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9. CHARACTERIZATION OF POTENTIAL HUMAN HEALTH EFFECTS OF DIESEL EXHAUST: HAZARD AND DOSE-RESPONSE ASSESSMENTS

9.1. INTRODUCTION

Human health risk assessment entails the evaluation of all pertinent information on the hazardous nature of environmental agents, on the extent of human exposure to them, and on the characterization of the potential risk to an exposed population. The information is typically organized into four components: hazard assessment, dose-response assessment, exposure assessment, and risk characterization. This health assessment document focuses only on the hazard and dose-response assessment components. The overall objectives of this diesel engine exhaust (DE) assessment are:

- to identify and characterize the human health effects, i.e., hazards that may result from environmental exposure to DE;
- to determine whether there is a quantitative exposure/dose-response relationship for DE exposure and the health effect in the range of observation, and if sufficient data are available (1) for noncancer effects to derive estimates of exposure that are believed to be without appreciable risk, and (2) for carcinogenicity to derive an exposure/dose-specific cancer unit risk; and
- to summarize and integrate the findings of the assessment into a characterization and discuss the uncertainties.

This chapter summarizes and integrates the key findings about the nature and characteristics of environmental exposure to DE (Chapter 2), health hazard information (Chapters 3, 4, 5, and 7), and dose-response analyses (Chapters 6 and 8) that are relevant to the potential human health effects associated with current-day environmental exposure to DE. It also discusses the uncertainties associated with the key findings, including critical data and knowledge gaps, key assumptions, and EPA's science policy choices that are used to bridge the data and knowledge gaps.

This assessment is the Agency's first health assessment for DE emissions and was developed to provide information about the potential for DE-related environmental health hazards that could be used in evaluating regulatory initiatives under provisions of the Clean Air Act.

9.2. PHYSICAL AND CHEMICAL COMPOSITION OF DIESEL EXHAUST

As reviewed in Chapter 2, DE is a complex mixture of hundreds of constituents in gas or particle phases. Gaseous components of DE include carbon dioxide, oxygen, nitrogen, water vapor, carbon monoxide, nitrogen compounds, sulfur compounds, and low molecular-weight hydrocarbons and their derivatives. The particulate matter of DE, diesel particulate matter (DPM), is composed of elemental carbon (EC), adsorbed organic compounds, and small amounts of sulfate, nitrate, metals, trace elements, water, and unidentified compounds. Incomplete combustion of fuel hydrocarbons as well as engine oil and other fuel components such as sulfur leads to the formation of DPM. DPM is either directly emitted from diesel-powered engines (primary particulate matter) or is formed from the gaseous compounds emitted by a diesel engine (secondary particulate matter).

DE emissions vary in chemical composition and particle sizes among different engine types, fuel formulations, and within engine types according to operating conditions. As the emissions age in the environment they also change. There also have been changes in DE emissions over time as a result of changes in engine technology and fuel reformulation. The following sections identify and characterize the key components of DE that are of concern in possible health outcomes, and discuss the changes in the composition of DE over time. The latter information is critical for making a scientific judgment about the appropriateness of using epidemiologic and toxicologic findings from past DE exposures to assess hazard and risk from current-day environmental exposures. It should be noted that available animal studies are based on exhaust exposures from various model year on-road diesel engines since 1980, whereas many of the epidemiologic studies refer to exposures from on-road and nonroad diesel engines in use from the 1950s through the mid-1990s.

After emission from the tailpipe, DE undergoes dilution, chemical and physical transformations, and dispersion and transport into the atmosphere. After a day or so in the ambient environment, the exhaust mixture is said to be aging, a recognition of the atmospheric transformation processes, mostly focused on the organics present, though some particle size changes also may occur. The public health impact of DE mixture transformations is not clear, as some atmospheric processes alter chemical forms to a less toxic form whereas others seem to produce a chemical form with increased toxicity (Chapter 2, Section 2.3).

9.2.1. Diesel Exhaust Components of Possible Health Concern

The components of DE that are of health concern for this assessment are the particles (elemental carbon core), the organic compounds adsorbed to the particles, and the organic compounds present in the gas phase. The gaseous oxides of carbon, nitrogen, and sulfur are also

of public health interest and the relevant health considerations for these are reviewed separately in EPA's Ambient Air Quality Criteria Documents.

9.2.1.1. *Diesel Particles*

Approximately 80%-95% of DPM mass is in the fine particle size range (≤2.5 micrometers, ambient particulate matter [PM]), with a mean particle aerodynamic diameter of about 0.2 micrometers. Ultrafine particles (<0.1 micrometers), a smaller size component of the fine particles, average about 0.02 micrometers in aerodynamic diameter and account for about 1%-20% of the DPM mass and 50%-90% of the total number of particles in DPM (Chapter 2, Section 2.2.8.3).

Particle size is important for a number of reasons. Particles with aerodynamic diameters >2.5 micrometers (i.e., >$PM_{2.5}$) tend to be retained in the upper portions of the respiratory tract, whereas particles with diameters <2.5 micrometers (i.e., $PM_{2.5}$) are deposited in all areas, especially into the lower portions of the respiratory tract, including the deep lung. These fine and ultrafine particles have a very large surface area per gram mass (Chapter 2, Section 2.2.2), which enables them to adsorb and transport inorganic and organic compounds into the lung (Chapter 3, Section 3.3).

DPM is part of ambient particulate matter (PM). The EPA Emissions Trends Report (U.S. EPA, 2000) indicates that annual nationwide emissions of diesel $PM_{2.5}$ (on-road and nonroad) in 1998 were 77% of all mobile-source emissions in 1998, 23% of the total $PM_{2.5}$ inventory excluding natural and miscellaneous sources, and 6% if the natural and miscellaneous sources are included. Some geographic areas have a higher percentage of DPM in ambient $PM_{2.5}$ because of differences in the number and types of diesel engines present in the area (e.g., on-road engines as well as nonroad engines). For instance, in Manhattan, New York, on-road diesel PM was reported to contribute about 53% of ambient PM_{10} during 3 days in 1993, whereas 1996-1997 studies in the Phoenix and Denver areas showed diesel PM to be 10%-15% of total $PM_{2.5}$ mass (Chapter 2, Section 2.4.2.1).

DPM generally contains a high percentage of EC per unit mass, which can be used as a distinguishing feature from noncombustion sources of $PM_{2.5}$ and, to an extent, other combustion sources. The DPM EC content can range from more than 50% to approximately 75% of the DPM mass depending on age of engine, type of engine (heavy-duty versus light-duty), fuel characteristics, and driving conditions. The organic carbon portion of DPM can range approximately from 19% to 43%, though higher and lower values also have been reported. In comparison, gasoline engine exhaust generally has a reverse pattern of low EC content and a high percentage of organics on the particle mass (see Chapter 2, Table 2-13).

9.2.1.2. *Organic Compounds*

The organic compounds present in the gases and adsorbed onto the particles include a wide spectrum of compounds related to unburned diesel fuel, lube oil, low levels of partial combustion, and pyrolysis products (see Chapter 2, Table 2-19). The organic compounds present in the gaseous phase include alkanes, alkenes, aldehydes, monocyclic aromatic compounds, and polycyclic aromatic hydrocarbons (PAHs). Among the gaseous components of DE, the aldehydes are particularly important because of their potential carcinogenic effects and because they make up an important fraction of the gaseous emissions. Formaldehyde accounts for a majority of the aldehyde emissions (65%-80%) from diesel engines. Acetaldehyde and acrolein are the next most abundant aldehydes. Other gaseous components of DE that are notable for their carcinogenic effects include benzene, 1,3-butadiene, PAHs, and nitro-PAHs (including those with ≤4 rings and nitro-PAHs with 2 and 3 rings). A number of the gaseous compounds (e.g., aldehydes, alkanes, alkenes, NO_x, SO_x) also are known to induce respiratory tract irritation given sufficient exposure (see Chapter 2, Table 2-21). Very small amounts of dioxins have been measured in heavy-duty diesel truck exhaust. These emissions are estimated to represent about 1.2% of the 1995 national dioxin inventory; dioxin emissions from nonroad exhausts have not been estimated (Chapter 2, Section 2.2.7.2).

Organic substances adsorbed onto DPM include C_{14-35} hydrocarbon compounds, PAHs with ≥4 rings, and nitro-PAHs. PAHs and their derivatives comprise <1% of the DPM mass (Chapter 2, Section 2.2.8). Many of these hydrocarbons are known to have mutagenic and carcinogenic properties. California EPA (Cal EPA, 1998) identified at least 19 hydrocarbons present in DE that are known or suspected carcinogens, according to evaluations by the International Agency for Research on Cancer (IARC).

9.2.2. "Fresh" Versus "Aged" Diesel Exhaust

Newly emitted exhaust is termed "fresh," whereas exhaust that is more than 1 or 2 days old is referred to as "aged" because of alterations caused by sunlight and other chemical physical reactions that occur in the atmosphere. The overall toxicological consequence of DE aging is unclear because during aging some compounds in the DE mixture are altered to more toxic forms while others are made less toxic. For example, PAHs present in fresh emissions may be nitrated by atmospheric NO_3 to form nitro-PAHs, thus adding to the existing burden of toxic nitro-PAHs present in fresh exhaust. On the other hand, PAHs present in the gas phase can react with hydroxyl radicals present in the ambient air, leading to a reduced atmospheric lifetime of the original PAHs. Alkanes and alkenes may be converted to aldehydes, and oxides of nitrogen to nitric acid (Chapter 2, Section 2.3).

9.2.3. Changes in Diesel Exhaust Emissions and Composition Over Time

Chapter 2, with its Summary in Section 2.5, provides a full review of emissions trends and a complete characterization of the physical and chemical changes in DE over the years, taking into consideration the lack of consistent analytical and measurement techniques and the variability in emissions based on vehicle mix, driving cycles, engine deterioration, and other factors. Key findings and inferences relevant to the potential health effects of DE are discussed below.

As discussed in Chapter 2, Section 2.2.3, the EPA Emissions Trend Report estimates that DPM_{10} on-road emissions decreased 27% between 1980 and 1998. DPM emission factors (g/mile by model year) from new on-road diesel vehicles decreased on average by a factor of six from the mid-1970s to the mid-1990s. These significant reductions are largely attributable to reductions in three PM components: EC, organic carbon, and sulfate. Limited data are available to assess the changes in emission rates from locomotive, marine, or other nonroad diesel sources over time, although it is estimated that DPM_{10} (≤ 10 μm) emissions from nonroad diesel engines increased 17% between 1980 and 1998 (Chapter 2, Section 2.2.5).

Because of changes in engine technology and fuel composition, the chemical composition of DPM from on-road vehicles has also changed over time. The percentage of soluble organic material associated with DPM decreased by model year from the 1980s to the 1990s, and the proportion of EC is correspondingly higher. PAHs and nitro-PAHs are present in DPM from both new and older diesel engines. There are insufficient data to provide clear insight into the potential for changes in total PAH emissions over time or specific PAHs such as benzo[a]pyrene and 1-nitropyrene. It should be noted that the chemical composition of ambient DPM to which people are currently exposed is determined by a combination of exhaust from older and newer engines as well as on-road and nonroad applications of those engines. Consequently, the decrease in the soluble organic fraction of DPM by model year for on-road engines does not directly translate into a proportional decrease in DPM-associated organic material to which people are exposed. In addition, the contributions from high-emitting and/or smoking diesel engines have not been quantified (Chapter 2, Section 2.5.2).

Because of these uncertainties, the exposure impact of changes in DPM composition over time cannot be confidently characterized. Available data clearly indicate that toxicologically significant organic components of DE (e.g., PAHs, PAH derivatives, nitro-PAHs) were present in DPM and DE in the 1970s and are still present. Even though a significant fraction of ambient DPM (possibly more than 50%) is emitted by nonroad equipment, data are currently inadequate to characterize changes in the chemical composition of DPM from nonroad equipment over time. Given the variation in fuel, engine technology, and in-use operational factors over the years, caution should be exercised in presuming that a decrease in the amount of emissions or emission

constituents from older engines to present day in-use engines will result in a decrease in hazard/risk. In meeting the 2007 federal regulations for heavy-duty DE, the exhaust composition will be markedly changed with a consequence that health hazards are expected to be significantly reduced.

9.3. AMBIENT CONCENTRATIONS AND EXPOSURE TO DIESEL EXHAUST

Chapter 2, Section 2.4 provides information on occupational and environmental exposures to DE in order to provide a context for the hazard assessment and dose-response analysis. Highlights of the available information are discussed below.

DE is emitted from a variety of sources, both on-road (e.g., motor vehicles, construction equipment) and nonroad (e.g., farm equipment, railway locomotives, or marine uses). Environmental exposure to DE is generally higher in urban areas than in rural areas. The concentration of DE in the air will vary within any geographic area depending on the number and types of diesel engines in the area and the atmospheric patterns of dispersal. Some important factors that determine the difference between the ambient concentration of DE and the resultant exposure to an individual include the proximity of a person to the DE source and his/her pattern of activity which, for example, includes outdoor versus indoor activities as well as related breathing rates. Certain occupational populations (e.g., transportation and garage workers, heavy-equipment operators, and others who spend considerable time outdoors) can be exposed to much higher levels of DE than the general population. The amount or number of particles delivered and retained in the lung is one factor that could contribute to differential human susceptibility to DPM. For example, children have smaller lungs than adults and thus could have a higher lung burden of inhaled DPM per lung surface area if their activity pattern results in a high breathing frequency.

As DE is a complex mixture of many constituents, environmental concentration measurements and related human exposure is difficult to precisely measure. Even though levels of a number of DE constituents are generally known, it is difficult to quantify the portion that comes from DE since other types of emission sources also may emit the same constituent. Moreover, there is still incomplete knowledge about the relative roles of the relevant DE constituents in mediating the potential health effects of DE. Historically, exposure levels to DPM have been used as a surrogate marker/dosimeter for whole DE. Although uncertainty exists as to whether DPM mass (expressed as $\mu g/m^3$ of DPM) is the most appropriate dosimeter for health effect purposes, it is considered to be a reasonable choice until more definitive information is available about the mechanisms or mode(s) of toxicity action of DE.

Several techniques exist for estimating ambient concentrations of DPM, including chemical mass balance (CMB) source apportionment, dispersion modeling, and using EC as a

surrogate for DPM. DPM concentrations reported from CMB and dispersion modeling studies in the 1980s suggest that in urban and suburban areas (Phoenix and Southern California), the annual average DPM concentration ranged from 2 to 13 $\mu g/m^3$. In the 1990s, annual or seasonal average DPM concentrations in suburban or urban locations have ranged from 1.2 to 4.5 $\mu g/m^3$. DPM concentrations at a major bus stop in downtown Manhattan ranged from 13.2 to 46.7 $\mu g/m^3$ over a 3-day period in 1993. In nonurban and rural areas in the 1980s, DPM concentrations were reported to range from 1.4 to 5 $\mu g/m^3$. In the 1990s, nonurban air basins in California were reported to have DPM concentrations ranging from 0.2 to 2.6 $\mu g/m^3$ (Chapter 2, Section 2.4.2).

A comprehensive exposure assessment is not presented in this assessment, though EPA is developing this in an analysis called the National Air Toxics Assessment. Interim exposure estimation based on EPA's Hazardous Air Pollutant Exposure Model (HAPEM-MS3 model), for on-road sources only, suggests that in 1996 annual average DPM exposure in urban areas from only on-road engines was 0.7 $\mu g/m^3$, while in rural areas exposure was 0.3 $\mu g/m^3$. Among 10 urban areas, the 1996 annual average estimated exposure ranged from 0.5 to 1.2 $\mu g/m^3$. A high-end exposure estimate for 1996 is not yet available. Comparable 1990 exposure estimates for on-road sources ranged from 0.9 $\mu g/m^3$ for urban areas to 0.5 $\mu g/m^3$ for rural areas. In 1990 exposure estimates for the most highly exposed individuals (e.g., outdoor workers and children who spend large amounts of time outdoors) were estimated to be up to 4.0 $\mu g/m^3$ (Chapter 2, Section 2.4.3.2, Table 2-29). Nationwide level nonroad emission exposures are estimated to be nearly double those from on-road sources.

Estimates for occupational exposures to DE as DPM mass are generally higher than environmental exposures. Tables 2-27 and 2-28 provide historic exposure estimates for specific worker categories. For example, historic DPM exposure estimates range from 39–191 $\mu g/m^3$ for railroad workers, 4–748 $\mu g/m^3$ for firefighters, 7–98 $\mu g/m^3$ for public transit workers and airport crews, 5–61 $\mu g/m^3$ for mechanics and dock workers, and 2–7 $\mu g/m^3$ for long- and short-haul truck drivers. For a direct comparison of lifetime exposures between an occupational setting (8 hours per day, 5 days per week, for 45 years) and environmental exposure (continuous exposure for 70 years), the occupational estimates are converted to an equivalent environmental lifetime estimate,[1] which is also shown in Table 2-28. A conversion of EC-based measurements to total DPM also may be needed for some estimates. The estimated 70-year lifetime exposures equivalent to those for the occupational groups discussed above range from about 0.4–157 $\mu g/m^3$. These data indicate that some lower-end occupational estimates of DPM, when converted to environmental equivalents, overlap the range of estimated environmental exposures

[1]Environmental equivalent occupational exposure = 0.21 × occupational exposure.

to DPM from on-road emissions (national average in 1990 of 0.8 $\mu g/m^3$, with high-end exposures up to about 4 $\mu g/m^3$). The addition of nonroad emission exposures, when appropriate, makes the case for overlap of occupational and environmental exposure more prevalent.

9.4. HAZARD CHARACTERIZATION

The primary health effects of concern from environmental exposure to DE include effects associated with both acute and short-term exposures as well as chronic exposures. It is recognized that acute exposures may produce transitory physiological symptoms of varied severity as well as exacerbation of allergenic effects from acute and repeated exposures. On the basis of combined human and experimental evidence from chronic exposure studies, noncancer respiratory effects and lung cancer are observed.

The health effects data are based on DE from a variety of engines existing before the mid-1990s. There have been changes in the physical and chemical composition of some DE emissions (on-road vehicle emissions) over time, though there is no definitive information to show that the emission changes portend significant toxicological changes. The mode(s) of action for DE toxicity in humans is not understood, and hence knowledge is lacking about the role of exhaust mixture components in modulating the toxicity. Taken together, these considerations have lead to a judgment that the hazards identified from older technology-based exposures are applicable to current-day exposures. As new and cleaner diesel engines replace a substantial number of existing engines, the general applicability of the older data will need to be reevaluated.

As discussed in Chapter 6 (Section 6.4), it is also reasonable to expect that DPM, being a constituent of ambient fine PM ($PM_{2.5}$), would contribute to the wider spectrum of effects that have been associated with ambient $PM_{2.5}$. Community epidemiologic studies have shown that ambient $PM_{2.5}$ exposure is statistically associated with increased mortality (especially among people over 65 years of age with preexisting cardiopulmonary conditions) and morbidity as measured by increases in hospital admissions, respiratory symptom rates, decrements in lung function, and exacerbation of asthma, and possibly immunological effects in the respiratory system. There continues to be little epidemiologic evidence for an effect of ambient exposure to PM on cancer rates (U.S. EPA, 1996a,b), though U.S. EPA's Criteria Document for Ambient PM (expected to be released in 2002) will examine the question further.

9.4.1. Acute and Short-Term Exposures

The combined human and animal evidence indicates that DE can induce irritation to the eye, nose, and throat, as well as inflammatory responses in the airways and the lung following

acute and/or short-term exposure to high concentrations. There also is suggestive evidence for possible immunological and allergenic effects of DE.

9.4.1.1. *Acute Irritation*

DE contains various respiratory irritants in the gas phase and in the particulate phase (e.g., SO_x, NO_x, aldehydes). Acute exposure to DE has been associated with irritation of the eye, nose, and throat, respiratory symptoms (cough and phlegm), and neurophysiological symptoms such as headache, lightheadedness, nausea, vomiting, and numbness or tingling of the extremities. Such symptoms have been described mainly in reports of individuals exposed to DE in the workplace, or in clinical studies in humans exposed acutely to high concentrations of DE. Because of the general lack of validating exposure information in the reports, the role of DE in causing these effects is unknown. An exposure-response relationship for these acute irritation and respiratory symptoms has not been demonstrated (Chapter 5, Section 5.1.1.1).

9.4.1.2. *Respiratory Effects*

Available studies of occupational exposure to DE have not provided evidence for significant decrements of lung function in workers over a work shift or after a short-term exposure period. Short-term and subchronic inhalation studies of DE in animals (rats, mice, hamsters, cats, guinea pigs) showed inflammation of the airways and minimal or no lung function changes. These effects were associated with high DE exposures (up to 6 mg/m^3). Exposure-response relationships have not been established for these responses (Chapter 5, Sections 5.1.1, 5.1.2, and 5.1.3).

9.4.1.3. *Immunological Effects*

Recent human and animal studies show that acute DE exposure episodes can exacerbate immunological reactions to other allergens or initiate a DE-specific allergenic reaction. The effects seem to be associated with both the organic and carbon core fraction of DPM. In human subjects, intranasal administration of DPM has resulted in measurable increases of IgE antibody production and increased nasal mRNA for some proinflammatory cytokines. These types of responses also are markers typical of asthma, though for DE, evidence has not been produced in humans that DE exposure results in asthma. The ability of DPM to act as an adjuvant to other allergens also has been demonstrated in human subjects. For example, co-exposure to DPM and ragweed pollen was reported to significantly enhance the IgE antibody response and cytokine expression relative to ragweed pollen alone. Available animal studies also demonstrate the potential adjuvant effects of DPM with model allergens, e.g., in mouse studies the allergenic reaction to ovalbumin and Japanese cedar pollen (Chapter 5, Sections 5.1.1.1.3 and 5.1.1.1.4).

Additional research is needed to further characterize immunological effects of DE and to determine whether or not the immunological effects constitute a low-exposure hazard. This health endpoint is of considerable public health concern, given the increases in allergic hypersensitivity in the U.S. population (Chapter 5, Section 5.6.2.6).

9.4.2. Chronic Exposure

9.4.2.1. *Noncancer Effects*

Available long-term and cross-sectional human studies have provided evidence for an association between respiratory symptoms (cough and phlegm) and DE exposure, but there was no consistent effect on lung function. DE has been shown in many animal studies of several species to induce lung injury (chronic inflammation and histopathologic changes) following long-term inhalation exposure. DE also has been tested in laboratory animals for other health effects, but no significant effects have been found. Overall, available data lead to the conclusion of a potential chronic respiratory hazard to humans from long-term exposure to DE.

9.4.2.1.1. ***Respiratory effects.*** A few human studies in various diesel occupational settings suggest that DE exposure may impair pulmonary function, as evidenced by increases in respiratory symptoms and some reductions in baseline pulmonary function consistent with restrictive airway disease. Other studies found no particular effects. The methodologic limitations in available human studies limit their usefulness in drawing any firm conclusions about DE exposure and noncancer respiratory effects (Chapter 5, Section 5.1.1.2).

Available studies in animals, however, provide a large body of evidence demonstrating that prolonged inhalation exposure to high concentrations of DE can result in pulmonary injury. A number of long-term laboratory studies in rats, mice, hamsters, cats, and monkeys found varying degrees of adverse lung pathology including focal thickening of the alveolar walls, replacement of Type I alveolar cells by type II cells, and fibrosis. The rat is the most sensitive animal species to DE-induced pulmonary toxicity (Chapter 5, Sections 5.1.3 and 5.4).

Available mechanistic data, mainly in rats, indicates that the DPM fraction of DE is a controlling factor in the etiology of pulmonary toxicity, although a role for the adsorbed organic compounds on the particles and in the gaseous phase cannot be ruled out. The lung injury appears to be mediated by an invasion of alveolar macrophages that release chemotactic factors that attract neutrophils and additional alveolar macrophages, which in turn release mediators (e.g., cytokines, growth factors) and oxygen radicals. These mediators result in persistent inflammation, cytotoxicity, impaired phagocytosis, clearance of particles, and eventually deposition of collagen by activated fibroblasts. This mode of action seems to be operative for a variety of poorly soluble particles in addition to DPM (ILSI, 2000). Because long-term exposure

to DE has been shown to induce exposure-dependent chronic respiratory effects in a wide range of animal species, and the mode of action is deemed relevant to humans, there is a sufficient scientific basis to support a conclusion that humans also could be at hazard for these effects under a chronic exposure condition.

9.4.2.1.2. ***Other noncancer effects.*** The negative results from available studies in several animal species (rats, mice, hamsters, rabbits, monkeys) indicate that DE is not likely to pose a reproductive or developmental hazard to humans. There has been some evidence from animal studies indicating possible neurological and behavioral effects, as well as liver effects. These effects, however, are seen at exposures higher than the respiratory effects. Overall, there is insufficient evidence to conclude that a low-exposure hazard exists for these endpoints (Chapter 5, Section 5.1.3.3).

9.4.2.2. ***Carcinogenic Effects***

Many epidemiologic and toxicologic studies have been conducted to examine the potential for DE to cause or contribute to the development of cancer in humans and animals, respectively. In addition, there are some mode-of-action studies that seek to provide an improved understanding about the underlying carcinogenic process and thus contribute to a better understanding of the likelihood of hazard to humans. The available evidence indicates that chronic inhalation of DE is likely to pose a lung cancer hazard to humans. There is insufficient information for an evaluation of the potential cancer hazard of DE by oral and dermal routes of exposure.

9.4.2.2.1. ***Epidemiologic studies.*** Twenty-two epidemiologic studies about the carcinogenicity of workers exposed to DE in various occupations are reviewed in Chapter 7, Section 7.2. Exposure to DE has typically been inferred on the basis of job classification within an industry, with cumulative exposure based on duration of employment or age. Increased lung cancer risk, although not always statistically significant, has been observed in 8 out of 10 cohort studies and 10 of 12 case-control studies within several industries, including railroad workers, truck drivers, heavy-equipment operators, farm tractor operators, and professional diesel vehicle drivers. The increased lung cancer relative risks generally range from 1.2 to 1.5, although a few studies show relative risks as high as 2.6. Statistically significant increases in relative risk, 1.33 to 1.47, are also shown in two independent meta-analyses. The meta-analyses demonstrate the effect of pooling many studies and in this case show the positive relationship between DE exposure and lung cancer across a variety of DE-exposed occupations.

The generally small increases in lung cancer relative risk (1.2 to 1.5, i.e., less than 2) observed in the epidemiologic studies potentially weakens the evidence of causality. This is because with a relative risk of less than 2, if confounders (e.g., smoking, asbestos exposure) were having an effect on the observed risk increases, then it could be enough to account for the increased risk. With the strongest risk factor for lung cancer being smoking, there is a lingering uncertainty as to whether smoking effects may be influencing the magnitude of the observed increased relative risks, in spite of the fact that in key studies the investigating epidemiologists assert that they have effectively controlled for smoking. In studies in which the effects of smoking were controlled, increased relative risks for lung cancer prevailed. While some studies did not have information on smoking, confounding by smoking is judged unlikely to be significant if the comparison populations were from the same socioeconomic class.

As evaluated in Chapter 7 (Section 7.2.4.5), application of the criteria for causality provides a rational basis to conclude that the increased risks observed in available epidemiologic studies are consistent with a causal association between exposure to DE and occurrence of lung cancer. Overall, the human evidence for potential carcinogenicity for DE is judged to be strong but less than sufficient to satisfy the criteria for a "known" human carcinogen because of exposure uncertainties (lack of historical exposure of workers to DE) and residual uncertainty as to whether all confounders have been satisfactorily accounted for. The epidemiologic evidence is inconclusive for DE being associated with other forms of cancer.

9.4.2.2.2. ***Animal studies.*** DE and its organic constituents, both in the gaseous and particle phase, have been extensively tested for carcinogenicity in many experimental studies using several animal species and with different modes of administration. Several well-conducted studies have consistently demonstrated that chronic inhalation exposure to sufficiently high concentrations of DE produced dose-related increases in lung tumors (benign and malignant) in rats. In contrast, chronic inhalation studies of DE in mice showed equivocal results, whereas negative findings were consistently seen in hamsters. The gaseous phase of DE (filtered exhaust without particulate fraction), was found not to be carcinogenic in rats, mice, or hamsters. The available data indicate that among the traditional animal test species, the rat is the most sensitive species to DE. As reviewed in Chapter 7, Section 7.4, the lung cancer response in rats from high-concentration exposures to DE appears to be mediated by impairment of lung clearance mechanisms owing to particle overload, resulting in persistent chronic inflammation and subsequent pathologic and neoplastic changes (i.e., cancer) in the rat lung. Particle overload conditions in the human lung are not expected to occur as a result of environmental or most occupational exposures to DE. Thus, the increased lung tumors in the rat are not an appropriate

basis from which to judge the potential for a human hazard or perform a dose-response analysis to derive a cancer unit risk for humans.

In several intratracheal instillation studies, DPM, DPM organic extracts, and carbon black, which is virtually devoid of PAHs, have been found to produce increased lung tumors in rats. When directly implanted into the rat lung, DPM condensate containing mainly four- to seven-ring PAHs induced increases in lung tumors. DPM extracts also have been shown to cause skin tumors in several dermal studies in mice and sarcomas in mice following subcutaneous injection. Overall there are consistent findings of carcinogenic activity by the organic extracts of DPM in noninhalation studies (i.e., intratracheal instillation, lung implantation, skin painting). This contributes to the evidence for a potential human hazard.

9.4.2.2.3. ***Other key data.*** While not as extensive as the human and animal carcinogenicity data, other types of data are judged to be supportive of DE's potential carcinogenicity in humans. As mentioned previously, DE is a complex mixture of hundreds of constituents in either the gaseous phase or particle phase. Although present in small amounts, several organic compounds in the gaseous phase (e.g., PAHs, formaldehyde, acetaldehyde, benzene, 1,3-butadiene) are known to exhibit mutagenic and/or carcinogenic activities. PAHs and PAH derivatives, including nitro-PAHs present on the diesel particle, also are known to be mutagenic and carcinogenic. As reviewed in Chapter 4, DPM and DPM organic extracts have been shown to induce gene mutations in a variety of high-dose bacteria and mammalian cell test systems. DPM and DPM organic extracts also have been shown to induce chromosomal aberrations, aneuploidy, and sister chromatid exchange in both rodent and human in vitro tests.

There also is suggestive evidence for the bioavailability of organic compounds from the DE mixture. Elevated levels of DNA adducts in lymphocytes have been reported in workers exposed to DE. In addition, inhalation studies of animals using radio-labeled materials indicate some elution of organic compounds from DPM after deposition in the lung as measured by their presence in biological tissue and fluids (Chapter 3, Section 3.5).

9.4.2.2.4. ***Modes of carcinogenic action.*** The term "mode of action" refers to a series of key biological events and processes that are critical to the development of cancer. As discussed in Section 9.4.2.2.2, there is an understanding of the modes of action for the DE-induced lung tumors in the rat. However, the modes of action by which DE increases lung cancer risks in humans are unknown, and the evidence in rats is not applicable to environmentally exposed humans.

As discussed in Chapter 7, Section 7.4, it is hypothesized that multiple modes of action could be involved in mediating the carcinogenic effect of DE. These modes of action may

include: (a) mutagenic events (e.g., direct effects on DNA and effects on chromosomes) by organic compounds in the gas and particle phase, (b) indirect DNA damage via the production of reactive oxygen species (ROS) induced by particle-associated organics, and (c) particle-induced chronic inflammatory response leading to oxidative DNA damage through the release of cytokines, ROS, etc., and an increase in cell proliferation.

In rats, the particulate phase appears to have the greatest contribution to the carcinogenic effects, and both the particle core and the associated organic compounds have demonstrated carcinogenic properties in one or more test systems. While limited rat data and comparative potency calculations suggest that gas-phase components are not the primary factors in the development of lung cancer, a contributory role of the recognized toxic components cannot be dismissed. The relative importance of the various modes of action may be different at different exposure levels. Evidence from rat studies indicates the importance of the EC component of the DE particle in mediating lung tumor response at high exposure levels. As for the particle-absorbed organics, their inherent toxicity potential gives rise to a hypothesis that they may play a role in low or high exposures to DE.

9.4.2.2.5. ***Weight-of-evidence evaluation.*** Chapter 7, Section 7.5, provides an evaluation of the overall weight of evidence for human carcinogenicity in accordance with EPA's Guidelines for Carcinogen Risk Assessment (U.S. EPA, 1986, 1996a, 1999). The totality of evidence supports the conclusion that DE is a *probable human carcinogen (Group B1)* by inhalation exposure using the criteria in the 1986 guidelines. A cancer hazard narrative for DE also is provided in accordance with the revised draft 1996/1999 guidelines, which concludes that DE *is likely to be carcinogenic to humans* by inhalation from environmental exposures. The common bases for either conclusion include the following lines of evidence:

- strong but less than sufficient evidence for a causal association between DE exposure and increased lung cancer risk among workers in varied occupations where exposure to DE occurs;
- extensive supporting data including the demonstrated mutagenic and/or chromosomal effects of DE and its organic constituents, and knowledge of the known mutagenic and/or carcinogenic activity of a number of individual organic compounds present with particles and in the DE gases;
- evidence of carcinogenicity of DPM and the associated organic compounds in rats and mice by noninhalation routes of exposure; and
- suggestive evidence for the bioavailability of DE organics from DE in humans and animals.

A notable uncertainty in the characterization of the potential cancer hazard of DE at low levels of environmental exposure is the incomplete understanding of about its mode(s) of action for the induction of lung cancer in humans. Available data suggest that DE-induced lung carcinogenicity may be mediated by mutagenic and nonmutagenic events by both the particles and the associated organic compounds, and that a role for the organics in the gaseous phase cannot be ruled out. Given that there is some evidence for a mutagenic mode of action, a cancer hazard is presumed possible at environmental levels of exposure. This is consistent with EPA's science policy position that assumes a nonthreshold effect for carcinogens with a mutagenic component in the absence of definitive data demonstrating a threshold or nonlinear mechanism. Additional support for an environmental hazard also comes from a comparison of the estimated environmental levels to the estimated occupational exposure levels where risk is seen. Given that there is only a minimal margin between environmental and occupational exposure ranges, if not an overlap, the extrapolation of observable hazard from the occupational setting to the ambient environment is relatively confident. Because of insufficient information, the human carcinogenic potential of DE by oral and dermal exposures cannot be determined.

Several organizations previously have reviewed available relevant data and evaluated the potential human carcinogenicity of DE or the particulate component (DPM) of DE. Similar conclusions were reached by various organizations (see Table 7-9). For example, some organizations have concluded that DE is probably carcinogenic to humans (IARC, 1989; IPCS, 1996), or reasonably is anticipated to be a carcinogen (NTP, 2000).

Overall, the weight of evidence for potential human carcinogenicity for DE is considered strong, even though inferences are involved. Uncertainties are present, however, and include the following unresolved issues.

First, there has been a considerable scientific debate about the significance of the available human evidence for a causal association between occupational exposure and increased lung cancer risk. Some experts view the evidence as weak and/or inconsistent while others consider the evidence compelling. This is due to a lack of consensus about whether the effects of smoking and other potential confounders have been adequately accounted for in key studies, and the lack of agreed-upon historical DE exposure data for the available studies.

Second, while the mode of action for DE-induced lung tumors in rats from high exposure is sufficiently understood, the mode of action for the DE lung cancer risk in humans is not known. To date, available evidence for the role of both the adsorbed organics and the carbon core particle has only been shown under high-exposure experimental animal test conditions. There is virtually no information about the relative role of DE constituents in mediating carcinogenic effects at the low-exposure levels.

Additional research is needed to address these issues to reduce the uncertainty associated with the potential cancer hazard of exposure to DE.

The relevance of this hazard characterization to current ambient DE exposures hinges on recognizing that the health effects data are derived from engine technologies and fuels that existed in the past, and that some changes in the DE exhaust mixture have occurred and can be expected in the future. Although decreases in amount and changes in composition of DE emissions have occurred over time for on-road engines, a change is slow to manifest in the environment because, for example, vehicular fleet turnover is slow and the change is slow to dominate across an engine fleet. Available studies have not focused on the potential toxicological effect of the emission changes. There is no compelling evidence at present to show that past and present exhaust characteristics are so toxicologically dissimilar as to render the current use of the assessment's findings outdated.

9.5. DOSE-RESPONSE ASSESSMENT

In assessments of estimated human health risks, human data from environmental exposures are always preferred over animal data, if available, as their use obviates the need for extrapolation across species, e.g., from animals to humans. However, for most environmental agents, available health effects information is generally limited to occupational exposures in studies of humans (e.g., workers) or high experimental exposures to laboratory animals. For the agents with high-exposure data compared to environmental exposure levels of interest, dose-response assessment is performed in two steps: assessment of data in the observable range to derive a point of departure (which usually is the lowest exposure or dose that induces some, minimal, or no apparent effects), followed by extrapolation to lower exposures to the extent necessary. Extrapolation to low exposures is ideally based on the understanding of mode(s) of toxic action of the agent which allows the development and use of a mode of action specific exposure-response model. In the absence of sufficient data, default methods and models are used to extrapolate to the lower exposure levels.

For DE, there is sufficient evidence to conclude that acute or short-term inhalation exposure at relatively high levels can cause irritant effects to the eye, nose, and throat, respiratory symptoms, and neurophysiological symptoms such as headache, nausea, etc., however, no quantitative data are available to derive an estimate of human exposure that is not likely to elicit irritant and inflammatory effects in humans.

There is also sufficient evidence to support the conclusion that DE has the potential to cause cancer and noncancer effects of the lung from long-term inhalation exposure. Chapters 6 and 8 provide dose-response analyses related to the noncancer and cancer hazards to humans, respectively, from lifetime exposure to DE. A dose-response analysis to estimate the expected

response at environmental exposure levels has less uncertainty the closer the animal test or estimated human epidemiologic-related exposures are to the environmental levels of interest. With increasing exposure margins (EM), and thus a greater range of extrapolation, the uncertainty about the shape of the dose-response curve in the region of low-dose extrapolation increases and the possibility of a zero risk cannot be ruled out.

9.5.1. Evaluation of Risk for Noncancer Health Effects

As discussed previously (Section 9.4.2.1), the evidence for potential chronic noncancer health effects of DE is based primarily on findings from chronic animal inhalation studies showing a spectrum of dose-dependent chronic inflammation and histopathological changes in the lung in several animal species including rats, mice, hamsters, and monkeys. A limited number of epidemiologic investigations of workers exposed to DE have not provided consistently clear evidence of significant chronic respiratory effects associated with DE exposure. On the other hand, the relatively large epidemiologic database for ambient PM shows a clear relationship between respiratory effects and ambient fine PM that is partially composed of DPM. The specific role of DPM or any other source-related constituent of ambient PM in causing the observed respiratory effects has not been defined.

The approach taken in this assessment to estimate a level of DE in the air to which humans may be exposed throughout their lifetime without an appreciable risk of deleterious effects is to derive a reference concentration (RfC) for DE based on the consistent data for respiratory inflammation in the rat studies. This approach assumes that humans would respond to DE similarly to the tested animals under similar exposure conditions. An uncertainty of this approach stems from the circumstance that animal studies have used high DE exposures, and the animal results must be translated to humans as well as to lower exposure levels since the potential chronic health effects of DE in humans at environmental exposure levels cannot be ascertained from the available DE human data.

It also is relevant to recognize that DPM is a component of ambient fine PM and that there is a relative wealth of human effects data for ambient PM showing a similarity of certain adverse health effects for DPM and ambient fine PM. This allows one to reasonably expect that the $PM_{2.5}$ National Ambient Air Quality Standard (NAAQS) would provide a measure of protection from DPM, reflecting DPM's current and approximate proportion to $PM_{2.5}$. Ambient $PM_{2.5}$ has been shown to be statistically associated with increased mortality (especially among people over 65 years of age with preexisting cardiopulmonary conditions) and morbidity, as measured by increases in hospital admissions, respiratory symptom rates, and decrements in lung function with both long- and short-term changes in ambient $PM_{2.5}$ concentrations.

9.5.1.1. *Chronic Reference Concentrations for Diesel Exhaust*

An inhalation Reference Concentration (RfC) is based upon long-term data, i.e., chronic exposure, and can be derived from either human or animal data. An RfC is correctly defined as "an estimate of a continuous inhalation exposure to the human population, including sensitive subgroups, with uncertainty spanning perhaps an order of magnitude, that is likely to be without appreciable risks of deleterious noncancer effects during a lifetime." The RfC methodology assumes that there is an exposure threshold below which effects will not occur. The RfC is not a bright line; rather, as the long-term human exposure increases above the RfC, the margin of protection decreases.

With the absence of DE exposure-response data in humans, this assessment derives an RfC for DE based on dose-response data from four chronic inhalation studies in rats (Mauderly et al., 1987; Ishinishi et al., 1988; Heinrich et al., 1995; Nikula et al., 1995). All of these studies used DPM (expressed as $\mu g/m^3$) as a measure of DE exposure. The pulmonary effects, including inflamation and histopathologic lesions, were considered to be the critical noncancer effects. As shown in Table 6-2, the no-observable-adverse-effects levels (NOAELs), the lowest-observable-adverse-effects levels (LOAELs), and the adverse effects levels (AELs) for lung inflammation and histopathologic changes were identified for the first three studies. For the Nikula et al. study, lower 95% confidence estimates of the concentrations of DPM associated with a 10% incidence ($BMCL_{10}$) of chronic pulmonary inflammation and fibrosis were derived since NOAEL's were not observed. For all four studies, human equivalent concentrations (HECs) corresponding to the animal NOAEL, LOAEL, AEL, and $BMCL_{10}$ were then computed using a dosimetry model developed by Yu et al. (1991) as described in Chapter 6, Section 6.5.2, and Appendix A. The dosimetry model accounts for species differences (rat to human) in respiratory exchange rates, particle deposition efficiency, differences in particle clearance rates at high and low doses, and transport of particles to lymph nodes. The purpose is to identify the highest HEC value with no apparent effect, i.e., $NOAEL_{HEC}$.

The highest $NOAEL_{HEC}$ associated with no apparent effect is 144 $\mu g/m^3$ from the Ishinishi et al. (1988) study; this then becomes the point of departure for deriving an RfC. To obtain the RfC, this point of departure was divided by two types of uncertainty factors (UF): a factor of 3 recognizes interspecies (i.e., rat to human) extrapolation uncertainties, and a factor of 10 reflects uncertainties about interindividual human variation in sensitivity. An evaluation of the interspecies extrapolation issues for dosimeteric and pharmacodynamic equivalence between rats and humans showed that although some adjustments could be accounted for, there remained a residual uncertainty, and thus an uncertainty of 3 out of a possible factor of 10 is used. In the absence of mechanistic or specific data, a default value of 10 is considered appropriate to account for possible human variability in sensitivity, particularly for children and people with

preexisting respiratory conditions. The spectrum of the population that may have a greater susceptibility cannot be better characterized until there is additional knowledge about mode of action. The resulting RfC for DE is 5 $\mu g/m^3$ of DPM.

Overall, the confidence level in the RfC is considered medium in a range of low to high confidence. A principal uncertainty of the RfC analysis is the reliance on animal data to predict human risk. The critical effects, chronic inflammation, and pathologic changes, which are well characterized in four animal species, are considered relevant to humans. Collective evidence for all poorly soluble particles, including DPM, indicates that the rat is the most sensitive laboratory animal species tested to date. Although in general the rat is thought to be more sensitive to lung injury than humans to poorly soluble particles (ILSI, 2000), it is not clear that this is the case specifically for diesel. We must recall that DE is a mixture of not just carbon particles but also various organics, both on the particles and in gases. In addition, differences in particle deposition, retention, and clearance mechanisms have been largely but perhaps not completely addressed by the use of the rat-to-human dosimetry model. The use of rat data is not likely to grossly underestimate the human risk for pulmonary noncancer health effects. In terms of the potential for other critical health effects, there is growing evidence suggesting that DE can exacerbate allergenic effects to known sensitizers, while also evoking production of biochemical markers typically associated with asthma. Some work in this area indicates that humans may be as sensitive as rats and mice to the immunologic effects (Chapter 6, Section 6.3.4). This database is currently lacking key exposure-response data, but may in the future provide an alternative basis for RfC derivation. It also should be noted that the ambient PM health effects data show a broader array of adverse human health concerns (e.g., cardiovascular effects, as well as acute exposure effects). With DPM being a ubiquitous component of ambient PM, there is an uncertainty about the adequacy of the existing DE noncancer database to identify all of the pertinent DE-caused noncancer health hazards.

9.5.1.2. *Risks Based on Ambient $PM_{2.5}$*

As discussed in Chapter 6 (Section 6.4), in 1997 EPA established an annual NAAQS for $PM_{2.5}$, at a level of 15 $\mu g/m^3$ to provide protection against adverse health effects associated with both long- and short-term exposures to ambient fine PM. DPM is a typical constituent of ambient fine PM (generally about 10% of $PM_{2.5}$ with some examples up to 36%).[2] Given the

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[2]"A qualitative comparison of adverse effects of exposure to DPM and ambient fine PM shows that the respiratory system is adversely affected in both cases, though a wider spectrum of adverse effects has been identified for ambient fine PM. In contrast to the diesel PM database, there is a wealth of human data for fine PM noncancer effects which indicates that the health effects from fine PM do not have a discernable threshold at this time."

similarity of health concerns for respiratory inflammation and pulmonary health effects from both DPM and fine particles, it is reasonable to expect that DPM contributes to some of the health effects associated with $PM_{2.5}$. Current knowledge is insufficient, however, to describe the relative potencies of DPM and the other components of $PM_{2.5}$. As long as the percentage of DPM to total ambient $PM_{2.5}$ remains in similar proportion, protective levels for $PM_{2.5}$ would be expected to offer a measure of protection from effects associated with DPM.

9.5.1.3. *Conclusions*

This assessment estimates an exposure air level of DE (as measured by DPM) to which humans may be exposed throughout their lifetime without experiencing any adverse noncancer health effects. The approach taken applies the RfC method using data specific to DE to produce an RfC of 5 $\mu g/m^3$ of DPM on the basis of four chronic inhalation studies of DE in rats and a composite uncertainty factor of 30. In addition, this assessment also recognizes the relative wealth of data regarding health effects associated with ambient PM and presumes that a health protective level for $PM_{2.5}$ also would be expected to provide a measure of protection from DPM, a constituent part of $PM_{2.5}$. The $PM_{2.5}$ standard of 15 $\mu g/m^3$ as an annual average thus is expected to provide a measure of protection from DPM noncancer health effects, reflecting DPM's current approximate proportion to $PM_{2.5}$.

9.5.2. Evaluation of Cancer Risks

As discussed in Section 9.4.3, the combined weight of evidence indicates that DE has the potential to pose a cancer hazard to humans at anticipated levels of environmental exposure. The target organ of DE-induced carcinogenicity is the lung. Strong evidence exists for a causal relationship between risk for lung cancer and occupational exposure to DE in certain occupational workers such as railroad workers, truck drivers, heavy-equipment operators (e.g., shipyard, diesel farm equipment, and construction), and transit workers. The evidence, however, was less than sufficient to confidently characterize DE as carcinogenic to humans, and instead the assessment concludes that DE is likely to be a human carcinogen. It also has been shown unequivocally in several studies that DE can cause benign and malignant lung tumors in rats in a dose-related manner following chronic inhalation exposure to high concentrations; however, this response is not thought applicable to predict a hazard to humans exposed at lower environmental levels. The mechanism(s) by which DE would induce lung cancer in humans has not been established, but available data suggest that mutagenic and nonmutagenic modes of action are possible. Hence, for estimating DE cancer risk at low environmental exposures, linear low-dose extrapolation would be considered an appropriate default assumption, which is consistent with EPA's science policy position that in the absence of an understanding of modes of carcinogenic

action, a nonthreshold effect is to be presumed (U.S. EPA, 1986, 1996a). This same assumption has been used by other organizations/risk assessors who have previously used either linear risk extrapolation models or mechanistically based models to estimate cancer risk from environmental exposure to DE (e.g., WHO-IPCS, 1996; Cal EPA, 1998; also see Appendix C).

Dose-response assessment is based on either human or animal data, although human data are always preferred if available. Several quantitative assessments have been conducted by organizations and investigators on the basis of both occupational data and rat data (see Appendix C). However, more recent evidence indicates that DE causes tumors in the rat lung via a mode of action that involves impairment of lung clearance mechanisms (referred to as "lung overload response") associated with high exposures. This lung overload response is not expected in humans exposed to environmental levels (nor is it expected to occur in many occupational exposures), and thus the rat lung tumor dose-response data are not considered suitable for predicting human risk at low environmental exposures. Given that the rat data are not appropriate for estimating cancer risk to humans, this assessment focuses on using the occupational epidemiologic data for estimating environmental risk of DE to humans.

Even though occupational data are considered most relevant for use in dose-response assessment, uncertainties exist, including the following issues:

- the use of DPM (expressed as $\mu g/m^3$) as a surrogate dosimeter for DE exposure, given that the relative roles of various constituents in mediating carcinogenic effects and the mode of carcinogenic action are still unknown;
- the representativeness of occupational populations for the general population and vulnerable subgroups, including infants and children and individuals with preexisting diseases, particularly respiratory conditions;
- the lack of actual DE exposure data for workers in the available epidemiologic studies;
- possible confounders (smoking and asbestos exposure) that could contribute to the observed lung cancer risk in occupational studies of DE if the control for these confounders is not adequate; and
- whether or not an exposure-response relationship for occupational lung cancer risk can be estimated for DE.

Chapter 8, Section 8.3, provides a discussion of these uncertainties, along with an evaluation of the suitability of available occupational studies for a derivation of a cancer unit risk estimate for DE. Unit risk is defined as the estimated upper-bound cancer risk at a specific exposure or dose

from a continuous average lifetime exposure of 70 years (in this case, cancer risk per $\mu g/m^3$ of DPM).

Among the occupational studies, the railroad worker studies (Garshick et al., 1987, 1988) and the Teamsters Union truck driver studies (Steenland et al., 1990, 1998) are considered to have the best available exposure data for possible use in establishing exposure-response relationships and deriving a cancer unit risk. There have been different views on the suitability of these studies for estimating environmental cancer risks (e.g., Cal EPA, 1998; HEI, 1995, 1999). Given the equivocal evidence for the presence or absence of an exposure-response relationship for the study of railroad workers, and exposure uncertainties for the study of truck drivers, it is judged that available data are too uncertain at this time for the development of a confident quantitative dose-response analysis and subsequent derivation of cancer unit risk for DE.

In the absence of a cancer unit risk to assess population cancer risk, this assessment provides a "perspective" about the possible magnitude of risk in the population from environmental exposure to DE. One approach to estimating the possible magnitude of risk involves simply noting that risks to the general public would be low in comparison with occupational risk if the differences in the lower environmental exposures compared to the higher occupational exposures are large. If the differences are small, the environmental risks would approach the workers' risk observed in studies of past occupational exposures. A comparison of environmental equivalent occupational and ambient environmental exposures showed that for certain occupations, there is a potential for overlap between environmental exposure and the estimated environmental equivalent occupational exposure, while in other cases the environmental exposures could be up to about 100-fold lower than the occupational levels (see Table 8-1). For the exposure overlap case, one can infer that the environmental risk could be the same as, or approach, the risk magnitudes observed in the occupational studies. In the 100-fold lower case, the environmental risk could be about 100-fold lower than the observed risk magnitudes in the occupational studies. Risks to the general public are of potential concern when a significant risk is seen in the occupational setting and the difference between occupational and ambient exposure may overlap or is relatively small (within one to two orders of magnitude).

A second approach, which is related to the first approach but more quantitative, is to estimate possible ranges of lung cancer risk from occupational exposures to DE, and then use a proportional relationship of exposure differences (e.g., EMs) to scale the occupational risk to the environmental exposure setting. Given the range of observed relative risks or odds ratios of lung cancer in a number of occupational studies, a relative risk increase of 1.4 was selected as a reasonable estimate of occupational risk for the purpose of this analysis. The relative risk of 1.4

means that the workers faced an extra risk that is 40% higher than the approximate 5% background lifetime lung cancer risk in the U.S. population. Using the relationship [*excess risk = (relative risk-1) × background risk*], 2% of these DE-exposed workers (i.e., 10^{-2} risk) would have been at risk (and developed lung cancer) attributable to occupational exposure to DE.

Using a nationwide average environmental exposure (0.8 $\mu g/m^3$ DPM), and assuming (a) the excess lung cancer risk from occupational exposure is about 10^{-2}; and (b) the past occupational exposures were no higher than about 1,200 $\mu g/m^3$ (equivalent to an environmental equivalent EM of 315, connoting a relatively large EM), the environmental cancer risk would fall between 10^{-4} and 10^{-5}. The selection of 1,200 $\mu g/m^3$ is a very high value intentionally selected to illustrate a high-end exposure boundary and thus a lower bounding of risk calculated by this exploratory approach. On the other hand, if occupational exposures for some groups were lower, for example, closer to 100 $\mu g/m^3$ (equivalent to an environmental equivalent EM of 26, connoting a smaller EM), the environmental risk would be higher and approach 10^{-3}. The selection of 100 $\mu g/m^3$ is purposefully toward the lower end of the reported occupational exposure range which spans 7–403 $\mu g/m^3$ in Table 8-1. The risk estimates are attended by numerous uncertainties; their inclusion in this document does not constitute Agency endorsement of their validity as a surrogate for cancer unit risk; the range of values is not useful for estimating numbers of cancer cases; and the range of possible risk from environmental exposures also could be lower and a zero risk cannot be ruled out.

These types of exploratory analyses are not intended to be precise or provide a definitive characterization of cancer risk but are useful in illustrating and gauging the possible range of risk based on applying reasonable judgment. The analyses provides a sense of where an upper limit (or "upper bound") of the risk may be. These analyses are subject to uncertainties, particularly the lack of actual exposure information for the occupational epidemiologic studies and the use of public-health-conservative risk assessment assumptions. The possible risks also could be lower and a zero risk cannot be ruled out because (a) some individuals in the population may have a high tolerance to exposure from DE and therefore not be susceptible to cancer from environmental exposure, and (b) although not reported, there could be a threshold of exposure below which there is no cancer risk. Given these circumstances, we refer to this risk analysis as a "perspective" on possible risks. Best scientific judgment guided the selection of assumptions and other elements of this analysis which are deemed reasonable and appropriate for identifying possible risks based on the information currently available. Further research is needed to more accurately assess and characterize environmental cancer risks from DE.

9.6. SUMMARY AND CONCLUSIONS

The available health effects data show that acute (short-term episodic exposure) and chronic (long-term) exposure to DE can pose hazards to humans and that environmental exposures, in some cases, may have a risk.

At relatively high acute exposures, DE can cause acute irritation to the eye and upper respiratory airways and symptoms of respiratory irritation which may be temporarily debilitating. Evidence also shows that DE has immunological toxicity that can induce allergic responses (some of which are also typical of asthma) and/or exacerbate existing respiratory allergies. While the hazard potential is important for these acute and short exposure-related effects, quantitative dose-response estimates for these effects could not be developed because of the lack of exposure-response information.

It is concluded that long-term exposure to low levels of DE poses a hazard for chronic inflammation and pathological changes in the human lung. A level of human lifetime exposure thought to be without appreciable risk for lung damage is estimated to be 5 $\mu g/m^3$ of DPM, this being a calculated RfC value for DE. Because DPM is a constituent of ambient $PM_{2.5}$ and there is some similarity in potential adverse effects from DE and $PM_{2.5}$, it is expected that a measure of protection from health effects associated with DE is provided by the 1997 annual $PM_{2.5}$ NAAQS, set at a level of 15 $\mu g/m^3$.

DE is considered to pose a human lung carcinogenicity hazard, which is expressed in a weight-of-evidence conclusion that DE is judged to be a "probable" human carcinogen, or is "likely to be carcinogenic in humans by inhalation" at environmental or higher exposure conditions. Because of uncertainty in the available exposure-response data, a cancer unit risk/cancer potency for DE has not been derived. One should note that the closeness of the high-end environmental exposures and low-end estimates of occupational exposure suggest less uncertainty in the extrapolation of hazard and possible risk to the environmental setting. Exploratory analyses using public health conservative assumptions provides a perspective on the possible range of lung cancer risk from environmental exposure to DE. Best scientific judgment guided the selection of assumptions and other elements of this analysis which are deemed reasonable and appropriate for identifying possible risks based on the information currently available. These analyses indicate that lifetime cancer risk may exceed 10^{-5} and could be as high as 10^{-3} or nearly so, though considering the assumptions used and the uncertainties, lower risk is possible and a zero risk cannot be ruled out. This range of values is attended by numerous uncertainties, the inclusion of the range in this assessment does not constitute Agency endorsement of their validity as surrogates for cancer unit risk values, and the range is not suitable for estimating numbers of cancer cases. These risk findings should not be viewed as a definitive characterization of risk.

Even though the evidence for potential human health hazards for DE is convincing and persuasive, uncertainties exist because of the use of assumptions to bridge data and knowledge gaps about human exposures to DE and the underlying mechanisms by which DE may cause the observed toxicities in humans and animals. A notable uncertainty of this assessment is how the physical and chemical nature of DE emissions has changed over the years because the toxicological and epidemiologic observations are based on older engines and their emissions, yet the desire is to focus on the potential health hazards related to exposure from present-day or future emissions. There have been changes in the physical and chemical composition of some DE emissions (on-road vehicle emissions) over time, though there is no definitive information to show that the emission changes portend significant toxicological changes. The mode(s) of action for DE toxicity in humans is not understood, and hence knowledge is lacking about the role of exhaust mixture components in modulating the toxicity. Taken together, these considerations have lead to a judgment that the hazards identified from older technology-based exposures are applicable to current-day exposures. As new and cleaner diesel engines replace a substantial number of existing engines, the general applicability of the conclusions in this assessment will need to be reevaluated.

Other uncertainties include the assumptions that health effects observed at high doses may be applicable to low doses, and that toxicologic findings in laboratory animals are predictive of human responses. Also, the available data are not sufficient to demonstrate the absence or presence of an exposure/dose-response threshold in humans for DE toxicity at environmental exposures. Again, this is due in part to the lack of understanding of how DE may cause adverse health effects in exposed humans and laboratory animals. Although there are hypotheses about the specific mechanisms by which DE might cause cancer and other toxicities, no specific biological pathways or specific constituents of DE have been firmly established as responsible for low-dose effects. The assumptions used in this assessment, i.e., the presence of a biological threshold for chronic respiratory effects based on cumulative dosage and the absence of a threshold for lung cancer stemming from subtle and irreversible effects, are considered prudent and reasonable default choices.

The characterization of health hazards and risks contained in this document assumes that the potential DE health hazards are relevant for long-term exposures, up to and including lifetime exposures, and would apply to a wide spectrum of individuals but not necessary those that would have significant differential susceptibility. There is no DE-specific information that provides direct insight into the question of differential susceptibility within the general human population or vulnerable subgroups, for example, children or the elderly. Although default approaches to account for interindividual variation have been included in the derivation of the noncancer effects RfC (i.e., use of an uncertainty factor of 10), this may or may not adequately

protect certain subgroups that could be more vulnerable. Differential susceptibility to DPM among individuals in the population would be due to differences in dosimetry (i.e., differences in retained particle mass or number in the lung) and/or differences in respiratory system tissue response sensitivity. From the dosimetry perspective, we understand that age, gender, and disease status can influence deposition in the lung and other areas of the respiratory tract (U.S. EPA, 1996b, Section 10.7.7). For example, given that DE chronic toxicity is focused on the respiratory system, vulnerable subgroups might include those individuals who predispose their lungs to increased particle retention (e.g., smoking, high particulate burdens from nondiesel sources) or those having existing respiratory or lung inflammation, repeated respiratory infections, or chronic bronchitis or asthma. For children, there is also the hypothesis of possible increased sensitivity to exposure, given the ongoing processes of development from birth to maturation, of the respiratory and immune systems.

Despite the uncertainties regarding intraspecies variability, the default approach of using an uncertainty factor of 10 in the derivation of the noncancer effects RfC to account for possible interindividual variation in the toxic response to DE exposure is appropriate and reasonable given the lack of DE-specific data.

Variation in DE exposure is another source of uncertainty. Because of variation in human activity patterns and their proximity to DE sources of emissions, different population subgroups could potentially receive higher or lower exposure to DE. The highest exposed are clearly occupational subgroups whose job brings them very close to DE sources, such as diesel engine vehicle drivers and workers, diesel powered machinery operators, some underground miners, etc. High exposures in the general population would be to those living very near or having time outdoors in proximity to DE sources as well as those engaged in activities that cause high breathing rates where DE is present. Accordingly, where appropriate, analyses in this assessment have included possible high-end DE exposures in addition to the lower nationwide average exposure estimates.

Lastly, this assessment considers only potential heath effects from exposures to DE alone. DE exposure could be additive or synergistic to concurrent exposures to other air pollutants. For example, there is evidence that DPM that has been altered by being in the presence of ambient ozone significantly increases the rat lung inflammatory effect compared to DPM that was not subjected to ozone (Madden et al., 2000). This observation suggests a hypothesis that inflammation-related noncancer hazards of airborne DPM may be worsened by the increasing presence of ozone in the ambient air. Other concerns include the possible impacts for children and adults on the exacerbation of existing allergens resulting from DE exposure. However, in the absence of more definitive data demonstrating interactive effects

from combined exposures to DE and other pollutants, it is not possible to further address these issues at this time.

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Appendix A

Calculation of Human Equivalent Continuous Exposure Concentrations (HECs)

A.1. INTRODUCTION

As discussed in Chapter 3, the lung burden of diesel particulate matter (DPM) during exposure is determined by both the amount and site of particle deposition in the lung and, subsequently, by rates of translocation and clearance from the deposition sites. Mathematical models have often been used to complement experimental studies in estimating the lung burdens of inhaled particles in different species under different exposure conditions. This appendix presents a mathematical model that simulates the deposition and clearance of DPM in the lungs of rats and humans of Yu et al.(1991) also published as Yu and Yoon (1990).

Diesel particles are aggregates formed from primary spheres 15-30 nm in diameter. The aggregates are irregularly shaped and range in size from a few molecular diameters to tens of microns. The mass median aerodynamic diameter (MMAD) of the aggregates is typically 0.2 μm and is polydisperse with a geometric standard deviation of around 2.3. The organics adsorbed onto the aggregates normally account for 10% to 30% of the particle mass. However, the exact size distribution of DPM and the specific composition of the adsorbed organics depend upon many factors, including engine design, fuels used, engine operating conditions, and the thermodynamic process of exhaust. The physical and chemical characteristics of DPM have been reviewed extensively by Amann and Siegla (1982) and Schuetzle (1983).

Four mechanisms deposit DPM within the respiratory tract during exposure: impaction, sedimentation, interception, and diffusion. The contribution from each mechanism to deposition, however, depends upon lung structure and size, the breathing condition of the subject, and particle size distribution. Under normal breathing conditions, diffusion is the most dominant mechanism and the other three mechanisms play minor roles.

Once DPM is deposited in the respiratory tract, both the carbonaceous core and the adsorbed organics will be removed from the deposition sites by mechanical clearance, provided by mucociliary transport in the ciliated conducting airways as well as macrophage phagocytosis and migration in the nonciliated airways, and dissolution. As the carbonaceous core or soot of DPM is insoluble, it is removed from the lung primarily by mechanical clearance, whereas the adsorbed organics are removed principally by dissolution (Chapter 3).

A.2. PARTICLE MODEL

To develop a mathematical model that simulates the deposition and clearance of DPM in the lung, an appropriate model for diesel particles must be introduced. For the deposition study, an equivalent sphere model developed by Yu and Xu (1987) was used to simulate the dynamics and deposition of DPM in the respiratory tract by various mechanisms. For the clearance study, a diesel particle is assumed to be composed of three different material components according to their characteristic clearance rates: (1) a carbonaceous core of approximately 80% of the particle

mass; (2) absorbed organics of about 10% of particle mass, which are slowly cleared from the lung; and (3) adsorbed organics quickly cleared from the lung, accounting for the remaining 10% of particle mass. The presence of two discrete organic phases in the particle model is suggested by observations that the removal of particle-associated organics from the lung exhibits a biphasic clearance curve (Sun et al., 1984; Bond et al., 1986), as discussed in Chapter 3. This curve represents two major kinetic clearance phenomena: a fast- phase organic washout with a half-time of a few hours, and a slow phase with a half-time that is a few hundred times longer. The detailed components involved in each phase are not known. It is possible that the fast phase consists of organics that are leached out primarily by diffusion mechanisms while the slow phase might include any or all of the following components: (a) organics that are "loosened" before they are released, (b) organics that have become intercalated in the carbon core and whose release is thus impeded, (c) organics that are associated for longer periods of time because of hydrophobic interaction with other organic-phase materials, (d) organics that have been ingested by macrophages and as a result effectively remain in the lung for a longer period of time because of metabolism by the macrophage (metabolites formed may interact with other cellular components), and (e) organics that have directly acted on cellular components, such as the formation of covalent bonds with DNA and other biological macromolecules to form adducts.

The above distinction of the organic components is general and made to account for the biphasic clearance of DPM; it does not specifically imply the actual nature of the adsorbed organics. For aerosols made of pure organics, such as benzo(*a*)pyrene (BaP) and nitropyrene (NP) in the same size range of DPM, Sun et al. (1984) and Bond et al. (1986) observed a nearly monophasic clearance curve. This might be explained by the absence of intercalative phenomena (a) and of hydrophobic interaction imposed by a heterogeneous mixture of organics (b). The measurement of a pure organic might also neglect that quantity which has become intracellularly (c) or covalently bound (d).

A.3. COMPARTMENTAL LUNG MODEL

The model of Yu et al. (1991) comprises three principal compartments involved in deposition and clearance: tracheobronchial (T or TB), alveolar (A), and lung-associated lymph node (L), as shown in Figure A-1. The outside compartments blood (B) and GI tract (G) and nasopharyngeal or head (H) are also represented. The alveolar compartment in the model is obviously the most important for long-term retention studies. However, for short-term consideration, retentions in other lung compartments may also be significant. The presence of these lung compartments and the two outside compartments in the model therefore provides a complete description of all clearance processes involved.

In Figure A-1, $r_H^{(i)}$, $r_T^{(i)}$ and $r_A^{(i)}$ are, respectively, the mass deposition rates of DE material component i (i=1 [core], 2 [slowly cleared organics], and 3 [rapidly cleared organics]) in the head, tracheobronchial, and alveolar compartments; and $\lambda_{XY}^{(i)}$ represents the transport rate of material component i from any compartment X to any compartment Y. Let the mass fraction of material component i of a diesel particle be f_i. Then

$$r_H^{(i)} = f_i \, r_H \, , \tag{A-1}$$

$$r_T^{(i)} = f_i \, r_T \, , \tag{A-2}$$

$$r_A^{(i)} = f_i \, r_A \, , \tag{A-3}$$

where r_H, r_T, and r_A are, respectively, the total mass deposition rates of DPM in the H, T, and A compartments, determined from the equations:

$$r_H = c(TV)(RF)(DF)_H \, , \tag{A-4}$$

$$r_T = c(TV)(RF)(DF)_T \, , \tag{A-5}$$

$$r_A = c(TV)(RF)(DF)_A \, . \tag{A-6}$$

In Equations A-4 to A-6, c is the mass concentration of DPM in the air, TV is the tidal volume, RF is the respiratory frequency, and $(DF)_H$, $(DF)_T$, and $(DF)_A$ are, respectively, the deposition fractions of DPM in the H, T, and A compartments over a respiratory cycle. The

values of $(DF)_H$, $(DF)_T$, and $(DF)_A$, which vary with the particle size, breathing conditions, and lung architecture, were determined from the deposition model of Yu and Xu (1987).

The differential equations for $m_{XY}^{(i)}$, the mass of material component i in compartment X as a function of exposure time t, can be written as

Head (H)

$$\frac{dm_H^{(i)}}{dt} = r_H^{(i)} - \lambda_{HG}^{(i)} m_H^{(i)} - \lambda_{HB}^{(i)} m_H^{(i)} , \qquad \text{(A-7)}$$

Tracheobronchial (T)

$$\frac{dm_T^{(i)}}{dt} = r_T^{(i)} + \lambda_{AT}^{(i)} m_A^{(i)} - \lambda_{TG}^{(i)} m_T^{(i)} - \lambda_{TB}^{(i)} m_T^{(i)} , \qquad \text{(A-8)}$$

Alveolar (A)

$$\frac{dm_A^{(i)}}{dt} = r_A^{(i)} - \lambda_{AT}^{(i)} m_A^{(i)} - \lambda_{AL}^{(i)} m_A^{(i)} - \lambda_{AB}^{(i)} m_A^{(i)} , \qquad \text{(A-9)}$$

Lymph nodes (L)

$$\frac{dm_L^{(i)}}{dt} = \lambda_{AL}^{(i)} m_A^{(i)} - \lambda_{LB}^{(i)} m_L^{(i)} . \qquad \text{(A-10)}$$

Equation A-9 may also be written as

$$\frac{dm_A^{(i)}}{dt} = r_A^{(i)} - \lambda_A^{(i)} m_A^{(i)} , \qquad \text{(A-11)}$$

where

$$\lambda_A^{(i)} = \lambda_{AT}^{(i)} + \lambda_{AL}^{(i)} + \lambda_{AB}^{(i)} . \qquad \text{(A-12)}$$

is the total clearance rate of material component i from the alveolar compartment. In Equations A-7 to A-10, we have assumed vanishing material concentration in the blood compartment to calculate diffusion transport.

The total mass of the particle-associated organics in compartment X is the sum of $m_X^{(2)}$ and $m_X^{(3)}$ the total mass of DPM in compartment X is equal to

$$m_X = m_X^{(1)} + m_X^{(2)} + m_X^{(3)} \qquad \text{(A-13)}$$

The lung burdens of diesel soot (core) and organics are defined, respectively, as

$$m_{Lung}^{(1)} = m_T^{(1)} + m_A^{(1)} , \tag{A-14}$$

and

$$m_{Lung}^{(2)+(3)} = m_T^{(2)} + m_A^{(2)} + m_T^{(3)} + m_A^{(3)} . \tag{A-15}$$

Because the clearance of diesel soot from compartment T is much faster than from compartment A, $m_T^{(1)} < m_A^{(1)}$ a short time after exposure, Equation A-14 leads to

$$m_{Lung}^{(1)} \cong m_A^{(1)} . \tag{A-16}$$

Solution to Equations A-7 to A-10 can be obtained once all the transport rates $\lambda_{XY}^{(i)}$ are known. When $\lambda_{XY}^{(i)}$ are constant, which is the case in linear kinetics, Equations A-7 to A-10 will have a solution that increases with time at the beginning of exposure but eventually saturates and reaches a steady-state value. This is the classical retention model developed by the International Commission of Radiological Protection (ICRP, 1979). However, as discussed in Chapter 3, data have shown that when rats are exposed to DPM at high concentration for a prolonged period, long-termed clearance is impaired. This is the so-called overload effect, observed also for other insoluble particles. The overload effect cannot be predicted by the classical ICRP model. Soderholm (1981) and Strom et al. (1987, 1988) have proposed a model to simulate this effect by adding a separate sequestering compartment in the alveolar region. In the present approach, a single compartment for the alveolar region of the lung is used and the overload effect is accounted for by a set of variable transport rates $\lambda_{AT}^{(i)}$, $\lambda_{AL}^{(i)}$, and $\lambda_A^{(i)}$ which are functions of m_A. The transport rates $\lambda_A^{(i)}$ and $\lambda_{AL}^{(i)}$ in Equations A-7 to A-10 can be determined directly from experimental data on lung and lymph node burdens, and $\lambda_{AT}^{(i)}$ and $\lambda_{AB}^{(i)}$ from Equation A-12.

A.4. SOLUTIONS TO KINETIC EQUATIONS

Equation A-11 is a nonlinear differential equation of $m_A^{(i)}$ with known function of $\lambda_A^{(i)}$. For diesel soot, this equation becomes

$$\frac{dm_A^{(1)}}{dt} = r_A^{(1)} - \lambda_A^{(1)}(m_A)m_A^{(1)} \ . \qquad \text{(A-17)}$$

Because clearance of the particle-associated organics is much faster than diesel soot, $m_A^{(2)}$ and $m_A^{(3)}$ constitute only a very small fraction of the total particle mass (less than 1%) after a long exposure, and we may consider $\lambda_A^{(1)}$ as a function of $m_A^{(1)}$ alone. Equation A-17 is then reduced to a differential equation with $m_A^{(1)}$ the only dependent variable.

The general solution to Equation A-17 for constant $r_A^{(1)}$ at any time, t, can be obtained by the separation of variables to give

$$\int_0^{m_A^{(1)}} \frac{dm_A^{(1)}}{r_A^{(1)} - \lambda_A^{(1)} m_A^{(1)}} = t \ . \qquad \text{(A-18)}$$

If $r_A^{(1)}$ is an arbitrary function of t, Equation A-17 needs to be solved numerically such as by a Runge-Kutta method. Once $m_A^{(1)}$ is found, the other kinetic equations A-7 to A-10 for both diesel soot and the particle-associated organics can be solved readily, as they are linear equations. The solutions to these equations for constant $r_H^{(i)}$, $r_T^{(i)}$ and $r_A^{(i)}$ are given below:

Head (H)

$$m_H^{(i)} = r_H^{(i)}/\lambda_H^{(i)} + (m_{H0}^{(i)} - r_H^{(i)})/\lambda_H^{(i)}) \exp\ (-\lambda_H^{(i)}\ t) \qquad \text{(A-19)}$$

$$\textit{where} \quad \lambda_H^{(i)} = \lambda_{HG}^{(i)} + \lambda_{HB}^{(i)} \qquad \text{(A-20)}$$

Tracheobronchial (T)

$$m_T^{(i)} = \exp\,(-\lambda_T^{(i)}\ t\ ) \int_0^t (\ r_T^{(i)} + \lambda_{AT}^{(i)}\ \ m_A^{(i)}\ )\ \exp\,(\lambda_T^{(i)}\ t\ )\ dt + m_{T0}^{(i)} \qquad \text{(A-21)}$$

$$where\ \ \lambda_T^{(i)} = \lambda_{TG}^{(i)} + \lambda_{TB}^{(i)} \qquad \text{(A-22)}$$

Lymph nodes (L)

$$m_L^{(i)} = \exp(-\lambda_{LB}^{(i)}\ t) \int_0^t \lambda_{AL}^{(i)} m_A^{(i)} \exp(\lambda_{LB}^{(i)}\ t\ )\ dt + m_{L0}^{(i)}) \qquad \text{(A-23)}$$

In Equations A-19 to A-23, $m_{XO}^{(i)}$ represents the value of $m_X^{(i)}$ at t = 0.

In the sections to follow, the methods of determining $r_H^{(i)}$, $r_T^{(i)}$ and $r_A^{(i)}$, or $(DF)_H$, $(DF)_T$, and $(DF)_A$ $r_H^{(DF)}$, $r_T^{(DF)}$ and $r_A^{(DF)}$ as well as the values of $\lambda_{XY}^{(i)}$ in the compartmental lung model are presented.

A.5. DETERMINATION OF DEPOSITION FRACTIONS

The mathematical models for determining the deposition fractions of DPM in various regions of the respiratory tract have been developed by Yu and Xu (1986, 1987) and are adopted in this report. Yu and Xu consider DPM as a polydisperse aerosol with a specified mass median aerodynamic diameter (MMAD) and geometrical standard deviation σ_g. Each diesel particle is represented by a cluster-shaped aggregate within a spherical envelope of diameter d_e. The envelope diameter d_e is related to the aerodynamic diameter of the particle by the relation

$$\frac{d_e}{d_a} = \varphi^{-1/2}(\frac{C_a}{C_e})^{1/2)}(\frac{\zeta}{\zeta_o})^{1/2} \qquad \text{(A-24)}$$

where ζ is the bulk density of the particle in g/cm^3, ζ_0 = 1 g/cm^3; φ is the packing density, which is the ratio of the space actually occupied by primary particles in the envelope to the overall envelope volume; and C_x is the slip factor given by the expression:

$$C_x = 1 + 2\frac{\lambda}{d_x}\,[1.257 + 0.4\ \exp -(\frac{0.55d_x}{\lambda})] \qquad \text{(A-25)}$$

in which $\lambda \cong 8 \times 10^{-6}\text{cm}^3$ is the mean free path of air molecules at standard conditions. In the diesel particle model of Yu and Xu (1986), ζ has a value of 1.5 g/cm^3 and a φ value of 0.3 is chosen based upon the best experimental estimates. As a result, Equation A-24 gives d_e/d_a = 1.35. In determining the deposition fraction of DPM, d_e is used for diffusion and interception according to the particle model.

A.5.1. Deposition in the Head

Particle deposition in the naso- or oropharyngeal region is referred to as head or extrathoracic deposition. The amount of particles that enters the lung depends upon the breathing mode. Normally, more particles are collected via the nasal route than by the oral route because of the nasal hairs and the more complex air passages of the nose. Since the residence time of diesel particles in the head region during inhalation is very small (about 0.1 s for human adults at normal breathing), diffusional deposition is insignificant and the major deposition mechanism is impaction. The following empirical formulas derived by Yu et al. (1981) for human adults are adopted for deposition prediction of DPM:

For mouth breathing:

$$(DF)_{H,\ in} = 0,\ for\ d_a^2 \leq 3000 \qquad \text{(A-26)}$$

$$(DF)_{H,\ in} = -1.117 + 0.324\ \log(d_a^2 Q),\ for\ d_a^2 Q > 3000 \qquad \text{(A-27)}$$

$$(DF)_{H,\ ex} = 0, \qquad \text{(A-28)}$$

and for nose breathing:

$$(DF)_{H,\ in} = -0.014 + 0.023\ \log(d_a^2 Q),\ for\ d_a^2 Q \leq 337 \qquad \text{(A-29)}$$

$$(DF)_{H,\ in} = -0.959 + 0.397\ \log(d_a^2 Q),\ for\ d_a^2 Q > 337 \qquad \text{(A-30)}$$

$$(DF)_{H,\ ex} = 0.003 + 0.033\ \log(d_a^2 Q),\ for\ d_a^2 Q \leq 215 \qquad \text{(A-31)}$$

$$(DF)_{H,\ ex} = -0.851 + 0.399\ \log(d_a^2 Q),\ for\ d_a^2 Q > 215 \qquad \text{(A-32)}$$

where $(DF)_H$ is the deposition efficiency in the head, the subscripts in and ex denote inspiration and expiration, respectively, d_a is the particle aerodynamic diameter in μm, and Q is the air flowrate in cm^3/sec.

Formulas to calculate deposition of diesel particles in the head region of children are derived from those for adults using the theory of similarity, which assumes that the air passage in the head region is geometrically similar for all ages and that the deposition process is characterized by the Stokes number of the particle. Thus, the set of empirical equations from A-26 through A-32 are transformed into the following form:

For mouth breathing:

$$(DF)_{H,\ in} = 0,\ for\ d_a^2 Q \leq 3000 \qquad \text{(A-33)}$$

and for nose breathing:

$$(DF)_{H,\ in} = -1.117 + 0.972\ logK + 0.324\ \log(d_a^2 Q),\ for\ d_a^2 Q > 3000 \qquad \text{(A-34)}$$

$$(DF)_{H,\ ex} = 0. \qquad \text{(A-35)}$$

$$(DF)_{H,\ in} = -\ 0.014 + 0.690\ \log\ K + 0.023\ \log(d_a^2 Q),\ for\ d_a^2 Q \leq 337 \qquad \text{(A-36)}$$

$$(DF)_{H,\ in} = -0.959 + 1.191\ \log\ K + 0.397\ \log\ (d_a^2 Q),\ \text{for}\ d_a^2 Q > 337 \qquad \text{(A-37)}$$

$$(DF)_{H,\ ex} = 0.003 + 0.099\ \log\ K + 0.033\ \log(d_a^2 Q),\ \text{for}\ d_a^2 Q \leq 215 \qquad \text{(A-38)}$$

where K is the ratio of the linear dimension of the air passages in the head region of adults to that of children, which is assumed to be the same as the ratio of adult/child tracheal diameters.

$$(DF)_{H,\,ex} = 0.851 + 1.197 \log K + 0.399 \log(d_a^2 Q), \text{ for } d_a^2 Q > 215 \qquad \text{(A-39)}$$

For rats, the following empirical equations are used for deposition prediction of DPM in the nose:

$$(DF)_{H,\,in} = (DF)_{H,\,ex} = 0.046 + 0.009 \log(d_a^2 Q), \text{ for } d_a^2 Q \leq 13.33 \qquad \text{(A-40)}$$

A.5.2. Deposition in the Tracheobronchial and Alveolar Regions

The deposition model adopted for DPM is the one previously developed for monodisperse (Yu, 1978) and polydisperse spherical aerosols (Diu and Yu, 1983). In the model,

$$(DF)_{H,\,in} = (DF)_{H,\,ex} = -0.522 + 0.514 \log(d_a^2 Q), \text{ for } d_a^2 Q > 13.33 \qquad \text{(A-41)}$$

the branching airways are viewed as a chamber model shaped like a trumpet (Figure A-2). The cross-sectional area of the chamber varies with airway depth, x, measured from the beginning of the trachea. At the last portion of the trumpet, additional cross-sectional area is present to account for the alveolar volume per unit length of the airways. Inhaled diesel particles that escape capture in the head during inspiration will enter the trachea and subsequently the bronchial airways (compartment T) and alveolar spaces (compartment A).

Assuming that the airways expand and contract uniformly during breathing, the equation for the conservation of particles takes the form:

$$\beta(A_1 + A_2)\frac{\partial c}{\partial x} + Q\frac{\partial c}{\partial x} = -Qc\eta \qquad \text{(A-42)}$$

where c is the mean particle concentration at a given x and time t; A_1 and A_2 are, respectively, the summed cross-sectional area (or volume per unit length) of the airways and alveoli at rest; η is the particle uptake efficiency per unit length of the airway; β is an expansion factor, given by:

$$\beta = 1 + \frac{V_t}{V_l} \qquad \text{(A-43)}$$

and Q is the air flow rate, varying with x and t according to the relation

$$\frac{Q}{Q_o} = 1 - \frac{V_x}{V_l} \tag{A-44}$$

where Q_0 is the air flow rate at x = 0. In Equations A-43 and A-44, V_t is the volume of new air in the lungs and V_x and V_ℓ are, respectively, the accumulated airway volume from x = 0 to x, and total airway volume at rest.

Equation A-42 is solved using the method of characteristics with appropriate initial and boundary conditions. The amount of particles deposited between location x_1 and x_2 from time t_1 to t_2 can then be found from the expression

$$DF = \int_{t_1}^{t_2} \int_{x_1}^{x_2} Qc\eta \, dx dt \tag{A-45}$$

For diesel particles, η is the sum of those due to the individual deposition mechanisms described above, i.e.,

where η_I, η_S, η_P, and η_D are, respectively, the deposition efficiencies per unit length of the

$$\eta = \eta_I + \eta_S + \eta_P + \eta_D \tag{A-46}$$

airway due to impaction, sedimentation, interception, and diffusion. On the basis of the particle model described above, the expressions for η_I, η_S, η_P, and η_D are obtained in the following form:

$$\eta_I = \frac{0.768}{L}(St)\theta. \tag{A-47}$$

$$\eta_S = \frac{2}{\pi L}[2\epsilon \sqrt{1 - \epsilon^{(2/3)}} - \epsilon^{1/3}\sqrt{1 - \epsilon^{2/3}} + \sin^{-1} \epsilon^{1/3}] \tag{A-48}$$

$$\eta_P = \frac{4}{3\pi L}(\Gamma - \frac{\Gamma^3}{32}) \tag{A-49}$$

$$\eta_D = \frac{1}{L}[1-0.819\exp(-14.63\Delta) - 0.0976\exp(-89.22\Delta) - 0.0325\exp(-228\Delta) - 0.0509\exp(-125\Delta^{2/3})] \quad \text{(A-50)}$$

$$\eta_D = \frac{4}{L}\Delta^{1/2}(1 - 0.444\Delta^{1/2}) \quad \text{(A-51)}$$

for Reynolds numbers of the flow smaller than 2000, and for Reynolds numbers greater than or equal to 2000, where $ST=d_a^2u/(18\mu R)$ is the particle Stokes number, $\theta = L/(8R)$, $\epsilon = 3\mu u_s L/(32uR)$, $\Gamma = d_c/R$, and $\Delta = DL/(4R^2u)$. In the above definitions u is the air velocity in the airway; μ is the air viscosity; L and R are, respectively, the length and radius of the airway; $u_s = C_a d_a^2/(18\mu)$ is the particle settling velocity; and $D = C_c kT(3\pi\mu d_a)$ is the diffusion coefficient with k denoting the Boltzmann constant and T the absolute temperature. In the deposition model, it is also assumed that η_I and $\eta_P = 0$ for expiration, while η_D and η_S have the same expressions for both inspiration and expiration.

During the pause, only diffusion and sedimentation are present. The combined deposition efficiency in the airway, E, is equal to:

$$E = 1 - (1 - E_S)(1 - E_D) . \quad \text{(A-52)}$$

where E_D and E_S are, respectively, the deposition efficiencies due to the individual mechanisms of diffusion and sedimentation over the pause period. The expression for E_D and E_S are given by

$$E_D = 1 - \sum_{i=1}^{3} \frac{4}{\alpha_i} \exp(-\alpha_i^2\tau_D)(1 - \sum_{i=1}^{3} \frac{4}{\alpha_i^2}) \exp\left[- \frac{4\tau_D^{1/2}}{\pi^{1/2}(1 - \sum_{i=1}^{3} \frac{4}{\alpha_i^2})} \right] \quad \text{(A-53)}$$

where $\tau_D = D\tau/R^2$ in which τ is the pause time and α_1, α_2, and α_3 are the first three roots of the equation:

$$J_o(\alpha) = 0 . \quad \text{(A-54)}$$

in which J_o is the Bessel function of the zero$_{th}$ order, and:

$$E_S = 1.1094\tau_S - 0.1604\tau_S^2, \; for \; 0 < \tau_S \leq 1. \quad \text{(A-55)}$$

and

$$E_S = 1 - 0.0069\tau_S^{-1} - 0.0859\tau_S^{-2} - 0.0582\tau_S^{-3}, \quad \textit{for } \tau_S > 1, \tag{A-56}$$

where $\tau_S = u_S\tau/2R$.

The values of $(DF)_T$ and $(DF)_A$ over a breathing cycle are calculated by superimposing DF for inspiration, deposition efficiency E during pause, and DF for expiration in the tracheobronchial airways and alveolar space. It is assumed that the breathing cycle consists of a constant flow inspiration, a pause, and a constant flow expiration, each with a respective duration fraction of 0.435, 0.05, and 0.515 of a breathing period.

A.5.3. Lung Models

Lung architecture affects particle deposition in several ways: the linear dimension of the airway is related to the distance the particle travels before it contacts the airway surface; the air flow velocity by which the particles are transported is determined by the cross-section of the airway for a given volumetric flowrate; and flow characteristics in the airways are influenced by the airway diameter and branching patterns. Thus, theoretical prediction of particle deposition depends, to a large extent, on the lung model chosen.

A.5.3.1. *Lung Model for Rats*

Morphometric data on the lung airways of rats were reported by Schum and Yeh (1979). Table A-1 shows the lung model data for Long Evans rats with a total lung capacity of 13.784 cm^3. Application of this model to Fischer rats is accomplished by assuming that the rat has the same lung structure regardless of its strain and that the total lung capacity is proportional to the body weight. In addition, it is also assumed that the lung volume at rest is about 40% of the total lung capacity and that any linear dimension of the lung is proportional to the cubic root of the lung volume.

A.5.3.2. *Lung Model for Human Adults*

The lung model of mature human adults used in the deposition calculation of DPM is the symmetric lung model developed by Weibel (1963). In Weibel's model, the airways are assumed to be a dichotomous branching system with 24 generations. Beginning with the 18th generation, increasing numbers of alveoli are present on the wall of the airways, and the last three generations are completely aleveolated. Thus, the alveolar region in this model consists of

all the airways in the last seven generations. Table A-2 presents the morphometric data of the airways of Weibel's model adjusted to a total lung volume of 3000 cm^3.

A.5.3.3. ***Lung Model for Children***

The lung model for children in the diesel study was developed by Yu and Xu (1987) on the basis of available morphometric measurements. The model assumes a lung structure with dichotomous branching of airways, and it matches Weibel's model for a subject when evaluated at the age of 25 years, the age at which the lung is considered to be mature. The number and size of airways as functions of age t (years) are determined by the following equations.

A.5.3.3.1. ***Number of airways and alveoli.*** The number of airways $N_i(t)$ at generation i for age t is given by

$$N_i(t) = 2^i, \qquad \text{for } 0 \le i \le 20 \tag{A-57}$$

$$\begin{cases} N_{21}(t) = N_r(t), \\ N_{22}(t) = N_{23}(t) = 0. \end{cases} \qquad \text{for } N_r(t) \le 2^{21} \tag{A-58}$$

$$\begin{cases} N_{21}(t) = 2^{21}, \\ N_{22}(t) = N_r(t) - 2^{21}, \\ N_{23}(t) = 0, \end{cases} \qquad \text{for } 2^{21} < N_r(t) \le 2^{22} \tag{A-59}$$

$$\begin{cases} N_{21}(t) = 2^{21}, \\ N_{22}(t) = 2^{22}, \\ N_{23}(t) = N_r(t) - 2^{21} - 2^{22} \end{cases} \qquad \text{for } N_r(t) > 2^{21} + 2^{22}, \tag{A-60}$$

where $N_r(t)$ is the total number of airways in the last three airway generations. The empirical equation for N_r which best fits the available data is

Thus, $N_r(t)$ increases from approximately 1.5 million at birth to 15 million at 8 years of age and

$$N_r(t) = \begin{cases} 2.036 \times 10^7(1 - 0.926e^{-0.15}t), & t \le 8 \\ 1.468 \times 10^7, & t > 8 \end{cases} \tag{A-61}$$

remains nearly constant thereafter. Equations A-58 to A-60 also imply that in the last three

generations, the airways in the subsequent generation begin to appear only when those in the preceding generation have completed development.

The number of alveoli as a function of age can be represented by the following equation according to the observed data:

$$N_A(t) = 2.985 \times 10^8(1 - 0.919e^{-0.45t}) \qquad \text{(A-62)}$$

The number of alveoli distributed in the unciliated airways at the airway generation level is determined by assuming that alveolization of airways takes place sequentially in a proximal direction. For each generation, alveolization is considered to be complete when the number of alveoli in that generation reaches the number determined by Weibel's model.

A.5.3.3.2. ***Airway size.*** Four sets of data are used to determine airway size during postnatal growth: (a) total lung volume as a function of age; (b) airway size as given by Weibel's model; (c) the growth pattern of the bronchial airways; and (d) variation in alveolar size with age. From these data, it is found that the lung volume, LV(t) at age t, normalized to Weibel's model at 4800 cm^3 for an adult (25 years old), follows the equation

$$LV(t) = 0.959 \times 10^5(1 - 0.998e^{-0.002t}) \quad (cm^3). \qquad \text{(A-63)}$$

The growth patterns of the bronchial airways are determined by the following equations

$$D_i(t) - D_{iw} = \alpha_i[H(t) - H(25)], \qquad \text{(A-64)}$$

$$L_i(t) - L_{iw} = \beta_i[H(t) - H(25)], \qquad \text{(A-65)}$$

where $D_i(t)$ and $L_i(t)$ are, respectively, the airway diameter and length at generation i and age t, D_{iw} and L_{iw} the corresponding values for Weibel's model, α_i and β_i are coefficients given by

$$\alpha_i = 3.26 \times 10^{-2}\exp[-1.183\ (i+1)^{0.5}] \qquad \text{(A-66)}$$

$$\beta_i = 1.05 \times 10^{-6} \exp\ [10.1]\ (i+1)^{-0.2}] \qquad \text{(A-67)}$$

and H(t) is the body height, which varies with age t in the form

$$H(t) = 1.82 \times 10^2(1 - 0.725e^{-0.14t})\ (cm). \tag{A-68}$$

For the growth patterns of the airways in the alveolar region, it is assumed that

$$\frac{D_i}{D_{iw}} = \frac{L_i}{L_{iw}} = \frac{D_a}{D_{aw}} = f(t), \qquad for\ 17 \le i \le 23 \tag{A-69}$$

where D_a is the diameter of an alveolus at age t, D_{aw} = 0.0288 cm is the alveolar diameter for adults in accordance with Weibel's model, and f(t) is a function determined from

$$f(t) = \sqrt[3]{\frac{\{LV(t) - \sum_{i=0}^{16} \frac{\pi}{4} D_i^2(t)\ L_i(t) N_i(t)\}}{\{\sum_{i=17}^{23} \frac{\pi}{4} D_{iw}^2 L_{iw} N_i(t) + \frac{5\pi}{36} D_{aw}^3 N_A(t)\}}} \tag{A-70}$$

A.6. TRANSPORT RATES

The values of transport rates $\lambda_{XY}^{(i)}$ for rats have been derived from the experimental data of clearance for diesel soot (Chan et al., 1981; Strom et al., 1987, 1988) and for the particle-associated organics (Sun et al., 1984; Bond et al., 1986; Yu et al., 1991). These values are used in the present model of lung burden calculation and are listed below:

$$\lambda_{HG}^{(i)} = 1.73\ (i = 1,2,3) \tag{A-71}$$

$$\lambda_{HB}^{(1)} = \lambda_{TB}^{(1)} = \lambda_{LB}^{(1)} = \lambda_{AB}^{(i)} = 0.00018 \tag{A-72}$$

$$\lambda_{HB}^{(2)} = \lambda_{TB}^{(2)} = \lambda_{LB}^{(2)} = \lambda_{AB}^{(2)} = 0.0129 \tag{A-73}$$

$$\lambda_{HB}^{(3)} = \lambda_{TB}^{(3)} = \lambda_{LB}^{(3)} = \lambda_{AB}^{(3)} = 12.55 \tag{A-74}$$

$$\lambda_{TG}^{(i)} = 0.693 \qquad (i = 1,2,3) \tag{A-75}$$

$$\lambda_{AL}^{(1)} = 0.00068\ [1 - \exp(-0.046 m_A^{1.62})] \tag{A-76}$$

$$\lambda_{AL}^{(i)} = \frac{1}{4}\lambda_{AB}^{(i)} \qquad (i = 2,3) \tag{A-77}$$

$$\lambda_{AT}^{(i)} = 0.012\ \exp(-0.11 m_A^{1.76}) + 0.00068\ \exp(-0.046 m_A^{1.62}) \quad (i = 1,2,3) \tag{A-78}$$

$$\lambda_A^{(1)} = \lambda_{AL}^{(1)} + \lambda_{AT}^{(1)} + \lambda_{AB}^{(1)} = 0.012\ \exp(-0.11 m_A^{1.76}) + 0.00086 \tag{A-79}$$

$$\lambda_A^{(2)} = \lambda_{AL}^{(2)} + \lambda_{AT}^{(2)} + \lambda_{AB}^{(2)} = 0.012\ \exp(-0.11 m_A^{1.76}) + 0.00068\ \exp(-0.046 m_a^{1.62}) + 0.0161 \tag{A-80}$$

$$\lambda_A^{(3)} = \lambda_{AL}^{(3)} + \lambda_{AT}^{(3)} + \lambda_{AB}^{(3)} = 0.012\ \exp(-0.11 m_A^{1.76}) + 0.00068\ \exp(-0.046 m_A^{1.62}) + 15.7 \tag{A-81}$$

where $\lambda_{XY}^{(i)}$ is the unit of day^{-1}, and $m_A \cong m_A^{(1)}$ is the particle burden (in mg) in the alveolar compartment.

Experimental data on the deposition and clearance of DPM in humans are not available. To estimate the lung burden of DPM for human exposure, it is necessary to extrapolate the transport rates $\lambda_{XY}^{(i)}$ from rats to humans. For organics, it is assumed that the transport rates are the same for rats and humans. This assumption is based upon the observation of Schanker et al. (1986) that the lung clearance of inhaled lipophilic compounds appears to depend only on their lipid/water partition coefficients and is independent of species. In contrast, the transport rates of diesel soot in humans should be different from those of rats, since the alveolar clearance rate, λ_A,

of insoluble particles at low lung burdens for human adults is approximately seven times that of rats (Bailey et al., 1982).

No data are available on the change of the alveolar clearance rate of insoluble particles in humans due to excessive lung burdens. It is seen from Equation A-79 that $\lambda_A^{(1)}$ for rats can be written in the form

$$\lambda_A^{(1)} = a \exp(-bm_A^c) + d \tag{A-82}$$

where a, b, c, and d are constants. The right-hand side of Equation A-82 consists of two terms, representing, respectively, macrophage-mediated mechanical clearance and clearance by dissolution. The first term depends upon the lung burden, whereas the second term does not. To extrapolate this relationship to humans, we assume that the dissolution clearance term is independent of species and that the mechanical clearance term for humans varies in the same proportion as in rats under the same unit surface particulate dose. This assumption results in the following expression for $\lambda_A^{(1)}$ in humans

$$\lambda_A^{(1)} = \frac{a}{P} \exp[-b(m_A/S)^c] + d \tag{A-83}$$

where P is a constant derived from the human/rat ratio of the alveolar clearance rate at low lung burdens and S is the ratio of the pulmonary surface area between humans and rats. Equation A-83 implies that rats and humans have equivalent amounts of biological response in the lung to the same specific surface dose of inhaled DPM.

From the data of Bailey et al. (1982), a value of $\lambda_A^{(1)} = 0.00169$ day^{-1} is obtained for humans at low lung burdens leading to P = 14.4. A value for S of 148 is reported from the data of the anatomical lung model of Schum and Yeh (1979) for rats and Weibel's model for human adults. For humans less than 25 years old, the model assumes the same value for P, but S is computed from the data of the lung model for young humans (Yu and Xu 1987). The value of S for different ages is shown in Table A-3.

The equations for other transport rates that have a lung-burden-dependent component are extrapolated from rats to humans in a similar manner. The following lists the values of $\lambda_{XY}^{(i)}$ (in day^{-1}) for humans used in the present model calculation:

$$\lambda_{HG}^{(1)} = 1.73 \quad (i = 1,2,3) \tag{A-84}$$

$$\lambda_{HB}^{(1)} = \lambda_{TB}^{(1)} = \lambda_{LB}^{(1)} = \lambda_{AB}^{(1)} = 0.00018 \tag{A-85}$$

$$\lambda_{HB}^{(2)} = \lambda_{TB}^{(2)} = \lambda_{LB}^{(2)} = \lambda_{AB}^{(2)} = 0.0129 \tag{A-86}$$

$$\lambda_{HB}^{(3)} = \lambda_{TB}^{(3)} = \lambda_{LB}^{(3)} = \lambda_{AB}^{(3)} = 12.55 \tag{A-87}$$

$$\lambda_{TG}^{(i)} = 0.693 \qquad (i = 1,2,3) \tag{A-88}$$

$$\lambda_{AL}^{(1)} = 0.00068\ \{1 - 0.0694\ \exp[-0.046(m_A/S)^{1.62}]\} \tag{A-89}$$

$$\lambda_{AL}^{(i)} = \frac{1}{4}\lambda_{AB}^{(i)} \qquad (i = 2,\ 3) \tag{A-90}$$

$$\lambda_{AT}^{(i)} = 0.0694\ \{0.012\ \exp[-0.11(m_A/S)^{1.76}] + 0.00068\ \exp[-0.046(m_A/S)^{1.76}]\}\ (i = 1,\ 2,\ 3) \tag{A-91}$$

$$\lambda_{A}^{(1)} = \lambda_{AL}^{(1)} + \lambda_{AB}^{(1)} + \lambda_{AT}^{(1)} = 0.0694\ \{0.012\ \exp[-0.11(m_A/S)^{1.76}]\} + 0.00086 \tag{A-92}$$

$$\lambda_{A}^{(2)} = \lambda_{AL}^{(2)} + \lambda_{AT}^{(2)} + \lambda_{AB}^{(2)} = 0.0694\{0.012\ \exp[-0.11(m_A/A)^{1.76}] + \tag{A-93}$$

$$0.00068\ \exp[-0.046(m_A/S)^{1.76}]\} + 0.016 \tag{A-94}$$

A.7. RESULTS

A.7.1. Simulation of Rat Experiments

To test the accuracy of the model, simulation results are obtained on the retention of DPM in the rat lung and compared with the data of lung burden and lymph node burden obtained by Strom et al. (1988). A particle size of 0.19 μm MMAD and a standard geometric deviation, σ_g, of 2.3 (as used in Strom's experiment) are used in the calculation.

The respiratory parameters for rats are based on their weight and calculated using the following correlations of minute volume, respiratory frequency, and growth curve data.

$$\text{Minute volume} = 0.9W\ (\text{cm}^3/\text{min}) \tag{A-95}$$

$$\text{Respiratory frequency} = 475W^{-0.3}\ (1/\text{min}) \tag{A-96}$$

where W is the body weight (in grams) as determined from the equation

$$W = 5+537T/(100+T),\ \text{for } T \geq 56 \text{ days} \tag{A-97}$$

in which T is the age of the rat measured in days.

Equation A-95 was obtained from the data of Mauderly (1986) for rats ranging in age from 3 mo to 2 years old; Equation A-96 was obtained from the data of Strom et al. (1988); and Equation A-97 was determined from the best fit of the experimental deposition data. Figures A-3 and A-4 show the calculated lung burden of diesel soot ($m_A^{(1)} + m_D^{(1)}$) and lymph node burden, respectively, for the experiment by Strom et al. (1988) using animals exposed to DPM at 6 mg/m^3 for 1, 3, 6, and 12 weeks; exposure in all cases was 7 days/week and 20 h daily. The solid lines represent the calculated accumulation of particles during the continuous exposure phase and the dashed lines indicate calculated post-exposure retention. The agreement between the calculated and the experimental data for both lung and lymph node burdens during and after the exposure periods was very good.

Comparison of the model calculation and the retention data of particle-associated BaP in rats obtained by Sun et al. (1984) is shown in Figure A-5. The calculated retention is shown by the solid line. The experiment of Sun et al. consisted of a 30-min exposure to diesel particles coated with [^3H] benzo[a]pyrene *([^3H] - BaP)* at a concentration of 4 to 6 μg/m^3 of air and followed by a post-exposure period of over 25 days. The fast and slow phase of *([^3H] - BaP)* clearance half-times were found to be 0.03 day and 18 days, respectively. These correspond to $\lambda_{AO}^{2} = 0.0385$ day^{-1} and $\lambda_{AO}^{(3)} = 23.1$ day^{-1} in our model, where $\lambda_{AO}^{(i)}$ is the value of $\lambda_{XY}^{(i)}$ at $m_A \rightarrow 0$. Figure A-5 shows that the calculated retention is in excellent agreement with the experimental data obtained by Sun et al. (1984).

A.7.2. Predicted Burdens in Humans

Selected results of lung burden predictions in humans are shown in Figures A-6 to A-9. The particle conditions used in the calculation are 0.2 μm MMAD with $\sigma_g = 2.3$, and the mass fractions of the rapidly and slowly cleared organics are each 10% $(f_1 = f_2 = 0.1)$. Figures A-6 and A-7 show, respectively, the lung burdens per unit concentration of diesel soot and the associated organics in human adults for different exposure patterns at two soot concentrations, 0.1 and 1 mg/m^3. The exposure patterns used in the calculation are (a) 24 h/day and 7 days week; (b) 12 h/day and 7 days/week; and (c) 8 h/day and 5 days/week, simulating environmental and occupational exposure conditions. The results show that the lung burdens of both diesel soot and the associated organics reached a steady-state value during exposure. Because of differences in the amount of particle intake, the steady-state lung burdens per unit concentration were highest for exposure pattern (a) and lowest for exposure pattern (b). Also, increasing soot concentration from 0.1 to 1 mg/m^3 increased the lung burden per unit concentration. However, the increase was not noticeable for exposure pattern (c). The dependence of lung burden on the soot concentration is caused by the reduction of the alveolar clearance rate at high lung burdens discussed above.

Figures A-8 and A-9 show the effect of age on lung burden, where the lung burdens per unit concentration per unit weight are plotted versus age. The data of lung weight at different ages are those reported by Snyder (1975). The exposure pattern used in the calculation is 24 h/day and 7 days/week for a period of 1 year at the two soot concentrations, 0.1 and 1 mg/m^3. The results show that, on a unit lung weight basis, the lung burdens of both soot and organics are functions of age, and the maximum lung burdens occur at approximately 5 years of age. Again, for any given age, the lung burden per unit concentration is slightly higher at 1 mg/m^3 than at 0.1 mg/m^3.

A.8. PARAMETRIC STUDY OF THE MODEL

The deposition and clearance model of DPM in humans, presented above, consists of a large number of parameters that characterize the size and composition of diesel particles, the structure and dimension of the respiratory tract, the ventilation conditions of the subject, and the clearance half-times of the diesel soot and the particle-associated organics. Any single or combined changes of these parameters from their normal values in the model would result in a change in the predicted lung burden. A parametric study has been conducted to investigate the effects of each individual parameter on calculated lung burden in human adults. The exposure pattern chosen for this study is 24 h/day and 7 days/week for a period of 10 years at a constant soot concentration of 0.1 mg/m^3. The following presents two important results from the parametric study.

A.8.1. Effect of Ventilation Conditions

The changes in lung burden due to variations in tidal volume and respiratory frequency are depicted in Figures A-10 and A-11. Increasing any one of these ventilation parameters increased the lung burden, but the increase was much smaller with respect to respiratory frequency than to tidal volume. This small increase in lung burden was a result of the decrease in deposition efficiency as respiratory frequency increased, despite a higher total amount of DPM inhaled. The mode of breathing has only a minor effect on lung burden because switching from nose breathing does not produce any appreciable change in the amount of particle intake into the lung (Yu and Xu, 1987). All lung burden results presented in this report are for nose breathing.

A.8.2. Effect of Transport Rates

Transport rates have an obvious effect on the retention of DPM in the lung after deposition. Because we are mainly concerned with the long-term clearance of diesel soot and the associated organics, only the effects of two transport rates, $\lambda_A^{(1)}$ and $\lambda_A^{(2)}$, are studied. Experimental data of $\lambda_A^{(1)}$ from various diesel studies in rats have shown that $\lambda_A^{(1)}$ can vary by a factor of two or higher. We use a multiple of 0.5 to 2 for the uncertainty in $\lambda_A^{(1)}$ and $\lambda_A^{(2)}$ to examine the effect on lung burden. Figures A-12 and A-13 show respectively, the lung burden results for diesel soot and the associated organics versus the multiples of $\lambda_A^{(1)}$ and $\lambda_A^{(2)}$ used in the calculation. As expected, increasing the multiple of $\lambda_A^{(1)}$ reduced the lung burden of diesel soot with practically no change in the organics burden (Figure A-12), while just the opposite occurred when the multiple of $\lambda_A^{(2)}$ was increased (Figure A-13).

A.9. OPERATIONAL DERIVATION OF HUMAN EQUIVALENT CONCENTRATIONS (HECs)

The model of Yu et al. (1991) is ordered into two parts; one part parameterized on the physiology and anatomy of a 300 g rat and the other part parameterized on the physiology and anatomy of a 25 year old human male. The sequence of steps taken to calculate the human equivalent continuous concentrations (the HECs), outlined in Table A-4, were as follows:

- The exposure scenario of the rats was entered into the rat portion of the model and the model ran to obtain the output of lung burden in mg DPM/ rat lung at the time of the sacrifice of the rats.
- The output of mg DPM/ rat lung was normalized to mg DPM/ cm^2 of rat lung tissue based on a total pulmonary surface area of 4090 cm^2.

- The normalized rat lung burdens were used to calculate the corresponding lung burden based on the pulmonary surface area of 627,000 cm^2. This operation yielded mg DPM / lung of a 25 year old human male.
- Various air concentrations were run in an iterative fashion with the human portion of the model under a continuous exposure scenario of 24 hrs/day, 7d/wk for 70 years with ventilatory parameters set at 0.926 L for tidal volume and 15 breaths per minute as the respiratory frequency to yield a total daily pulmonary volume of 20 m^3. This was continued until the output (mg DPM/lung) was matched to the mg DPM /human lung obtained from the normalized rat lung burden; the concentration from the model that matched this lung burden was termed the human equivalent continuous concentration, the HEC. The human modeling runs did not consider the preadult status of airway and alveoli number discussed above but rather were ran for 1 to 70 years with adult (25 years of age) parameters mentioned above.

These HEC values address kinetic issues of DPM deposition and retention in the lung by humans. As noted above, these values do not reflect the kinetic variability that may exist in the human population exposed to DPM which includes men and women, young and old. However, the limited parametric analysis of the model clearly shows variability of those parameters most determinative in humans (e.g., tidal volume, respiration rate, and rates of clearance of particles from the airways) were mirrored in the corresponding output of the model (lung burden of DPM). One interpretation of this parallel in parameter-output is that the variability in the physiological characteristics of humans reflects the variability in the model such that, for example, a small tidal volume would be reflected with a decreased lung burden of DPM. Variability among humans of these key parameters such as tidal volume do vary but within an order of magnitude. This would mean that the DPM dose received by different individuals in the population from the same concentration would indeed vary within the extremes of these determinative parameters.

Table A-1. Lung model for rats at total lung capacity

Generation number	Number of airways	Length (cm)	Diameter (cm)	Accumulative volume[a] (cm)
1	1	2.680	0.340	0.243
2	2	0.715	0.290	0.338
3	3	0.400	0.263	0.403
4	5	0.176	0.203	0.431
5	8	0.208	0.163	0.466
6	14	0.117	0.134	0.486
7	23	0.114	0.123	0.520
8	38	0.130	0.112	0.569
9	65	0.099	0.095	0.615
10	109	0.091	0.087	0.674
11	184	0.096	0.078	0.758
12	309	0.073	0.070	0.845
13	521	0.075	0.058	0.948
14	877	0.060	0.049	1.047
15	1,477	0.055	0.036	1.414
16[b]	2,487	0.035	0.020	1.185
17	4,974	0.029	0.017	1.254
18	9,948	0.025	0.016	1.375
19	19,896	0.022	0.015	1.595
21	39,792	0.020	0.014	2.003
22	79,584	0.019	0.014	2.607
25	318,336	0.017	0.014	7.554
24	636,672	0.017	0.014	13.784

[a]Including the attached alveoli volume (number of alveoli = 3×10^7, alveolar diameter = 0.0086 cm).
[b]Terminal bronchioles.

Table A-2. Lung model by Weibel (1963) adjusted to 3000 cm^3 lung volume

Generation number	Number of airways	Length (cm)	Diameter (cm)	Accumulative volume[a] (cm)
0	1	10.260	1.539	19.06
2	2	4.070	1.043	25.63
2	4	1.624	0.710	28.63
3	8	0.650	0.479	29.50
4	16	1.086	0.385	31.69
5	32	0.915	0.299	33.75
6	64	0.769	0.239	35.94
7	128	0.650	0.197	38.38
8	256	0.547	0.159	41.13
9	512	0.462	0.132	44.38
10	1,024	0.393	0.111	48.25
11	2,048	0.333	0.093	53.00
12	4,096	0.282	0.081	59.13
13	8,192	0.231	0.070	66.25
14	16,384	0.197	0.063	77.13
15	32,768	0.171	0.056	90.69
16[b]	65,536	0.141	0.051	109.25
17	131,072	0.121	0.046	139.31
18	262,144	0.100	0.043	190.60
19	524,283	0.085	0.040	288.16
20	1,048,579	0.071	0.038	512.94
21	2,097,152	0.060	0.037	925.04
22	4,194,304	0.050	0.035	1,694.16
23	8,388,608	0.043	0.035	3,000.00

Table A-3. Ratio of pulmonary surface areas between humansand rats as a function of human age

Age (year)	Surface area
0	4.99
1	17.3
2	27.6
3	36.7
4	44.7
5	51.9
6	58.5
7	64.6
8	70.4
9	76.0
10	81.4
11	86.6
12	91.6
13	96.4
14	101
15	106
16	110
27	115
28	119
19	123
20	128
21	132
22	136
23	140
24	144
25	148

Table A-4. Human equivalent continuous concentrations (HECs) calculated with the model of Yu et al. (1991) from long-term repeated exposure rat studies of DPM exposure

Study	Exposure conditions[a]	Rat exposure concs (mg/m^3)	mg DPM/ rat lung (modeled)[b]	mg DPM/cm^2 rat&human lung[b,c]	mg DPM/ human lung[c]	HEC (mg/m^3)[c]
Mauderly et al., 1987a	7 h/day, 5 days/wk, 130 wk[d]	0.35	0.28	6.85E-5	43	0.038
Mauderly et al., 1987a	7 h/day, 5 days/wk, 130 wk	3.47	20.23	4.95E-3	3101	1.375
Mauderly et al., 1987a	7 h/day, 5 days/wk, 130 wk	7.08	44.52	1.09E-2	6825	3.05
Ishinishi et al., 1988 (LD[e])	16 h/day, 6 days/wk, 130 wk	0.11	0.24	5.87E-5	37	0.032
Ishinishi et al., 1988 (LD)	16 h/day, 6 days/wk, 130 wk	0.41	1.00	2.45E-4	153	0.128
Ishinishi et al., 1988 (LD)	16 h/day, 6 days/wk, 130 wk	1.18	18.45	4.51E-3	2828	1.25
Ishinishi et al., 1988 (LD)	16 h/day, 6 days/wk, 130 wk	2.32	39.89	9.75E-3	6115	2.75
Ishinishi et al., 1988 (HD)	16 h/day, 6 days/wk, 130 wk	0.46	1.15	2.81E-4	176	0.144
Ishinishi et al., 1988 (HD)	16 h/day, 6 days/wk, 130 wk	0.96	12.94	3.16E-3	1984	0.883
Ishinishi et al., 1988 (HD)	16 h/day, 6 days/wk, 130 wk	1.84	31.22	7.63E-3	4786	2.15
Ishinishi et al., 1988 (HD)	16 h/day, 6 days/wk, 130 wk	3.72	64.67	1.58E-2	9914	4.4
Nikula et al., 1995	16 h/day, 5 days/wk, 100 wk	2.44	28.64	7.00E-3	4391	1.95
Nikula et al., 1995	16 h/day, 5 days/wk, 100 wk	6.3	76.15	1.86E-2	11674	5.1
Heinrich et al., 1995	18 h/day, 5 days/wk, 104 wk	0.84	3.83	9.4E-4	587	0.33
Heinrich et al., 1995	18 h/day, 5 days/wk, 104 wk	2.5	34.4	8.4E-3	5274	2.35
Heinrich et al., 1995	18 h/day, 5 days/wk, 104 wk	6.98	97.8	2.4E-2	14993	6.7

[a] These are entered into the program as hrs/day, days/week for the total number of weeks exposed and the last week of exposure before evaluation (as this would affect clearance). The parameters for the rat were based on a body weight which was set in the program at 300g.
[b] These values were obtained with the rat portion of the model and are noted as lung burden, in mg DPM /lung of a 300 g rat, at the final week of the exposure scenario. These outputs were then normalized to cm^2 of the rat lung, at 4090 cm^2 total (Xu and Yu, 1987).
[c] Preparatory to using the human portion of the model, the mg DPM/cm^2 value from above was used to project the mg DPM that would be present in the adult human lung based on a total lung surface area of 627,000 cm^2 (Xu and Yu, 1987). Various air concentrations were then entered into the human model as 70 years continuous exposure scenarios and ran iteratively until the output (in mg DPM / lung at age 70) matched this mg DPM/human lung, i.e., the total lung burden. This matching air concentration is, by definition, the human equivalent continuous concentration (HEC).
[d] weeks = (months of exposure) × 4.33.

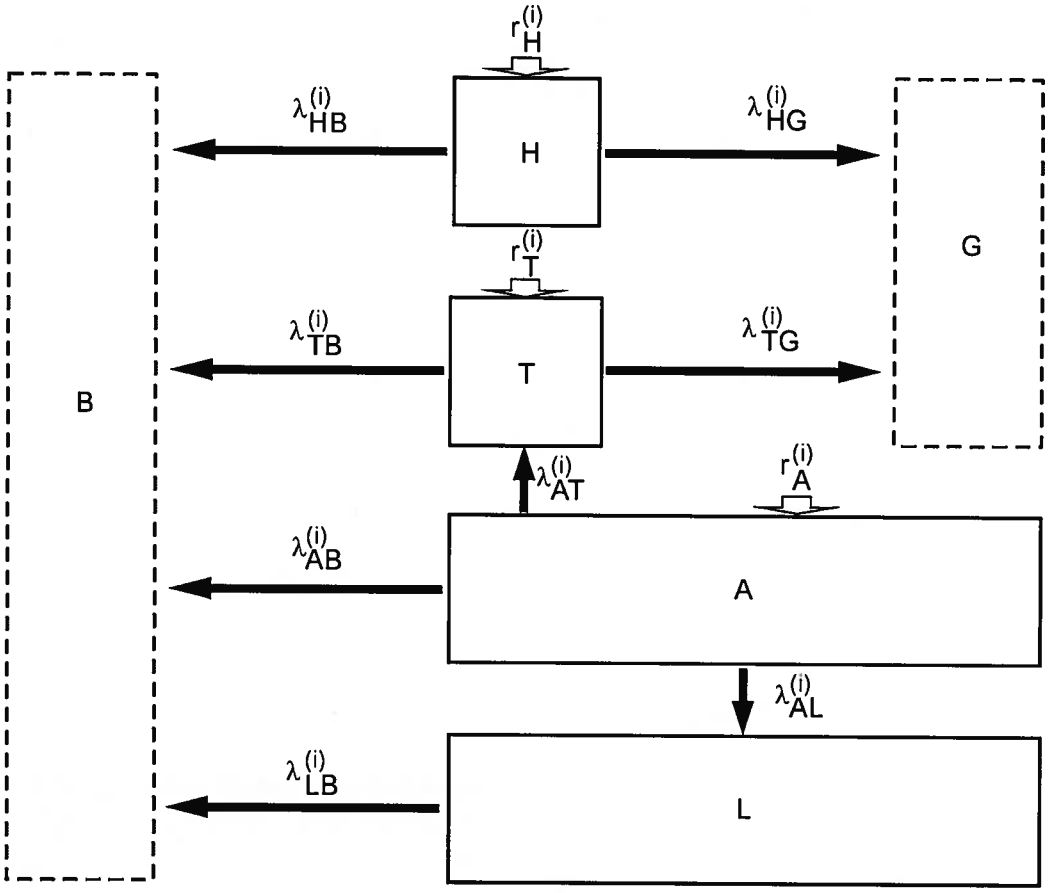

Figure A-1. Compartmental model of DPM retention.

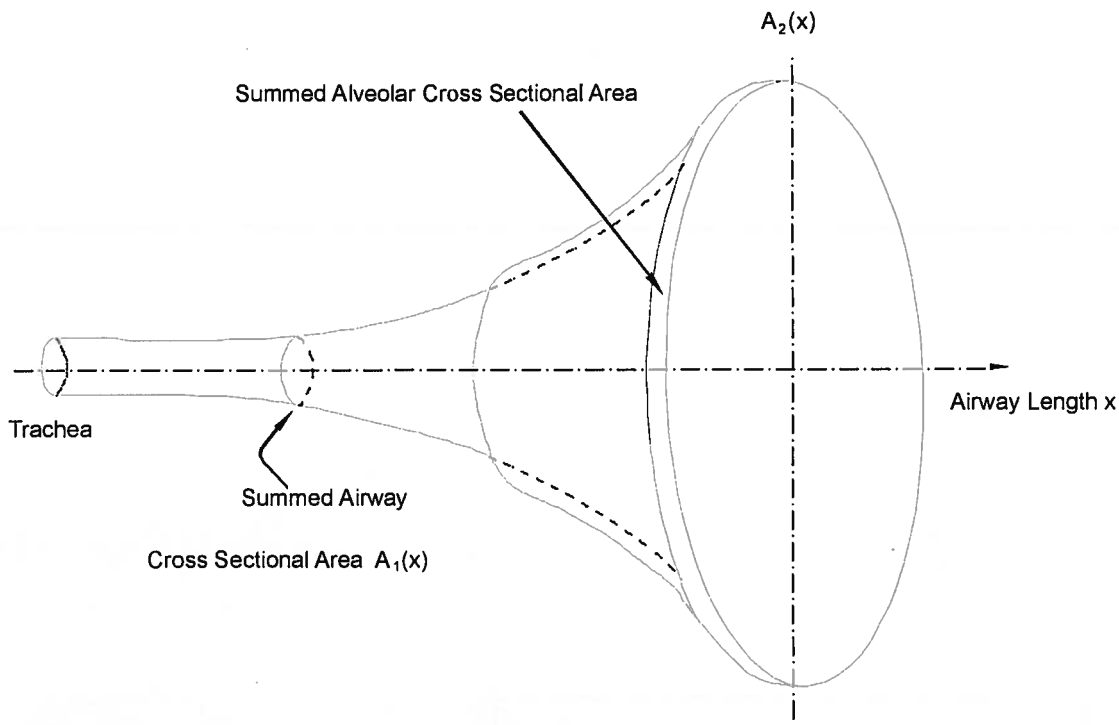

Figure A-2. Trumpet model of lung airways.

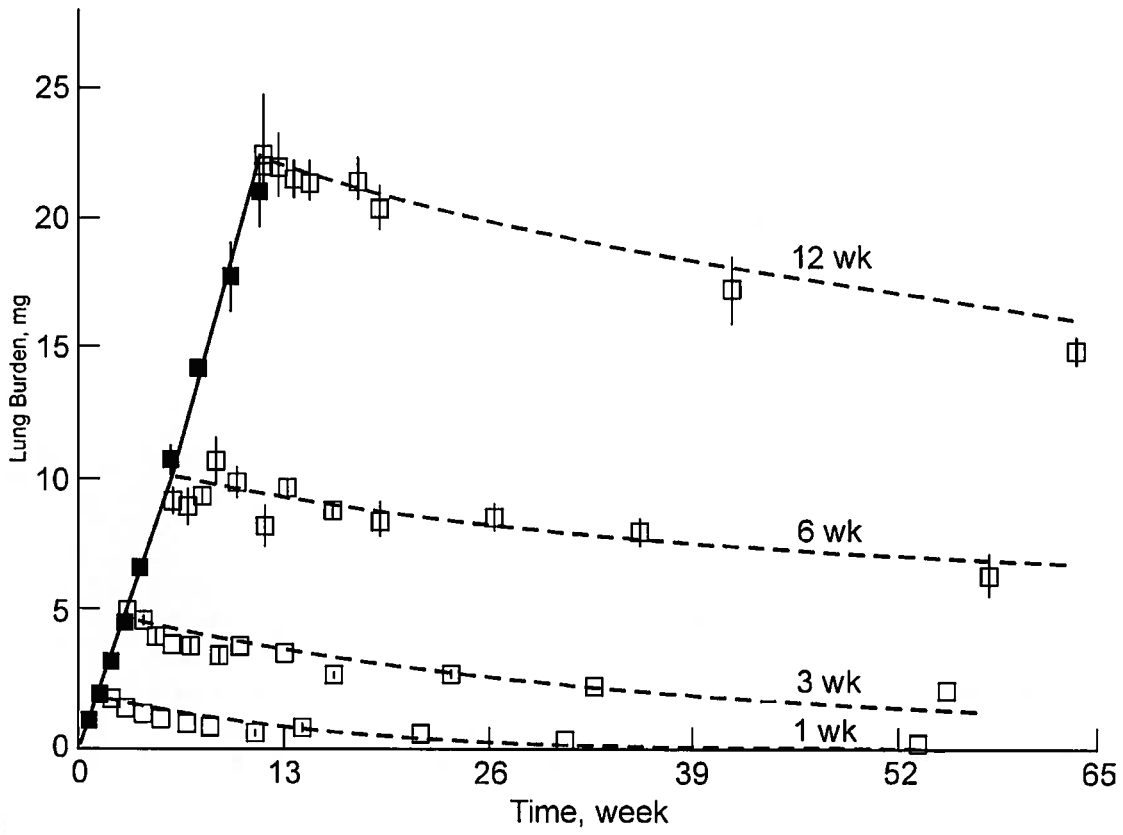

Figure A-3. The experimental and predicted lung burdens of rats to DPM at a solid and dashed concentration of 0.6 mg/m^3 for different exposure spans. Lines are, respectively, the predicted burdens during exposure and post-exposure. Particle characteristics and exposure pattern are explained in the text. The symbols represent the experimental data from Strom et al. (1988).

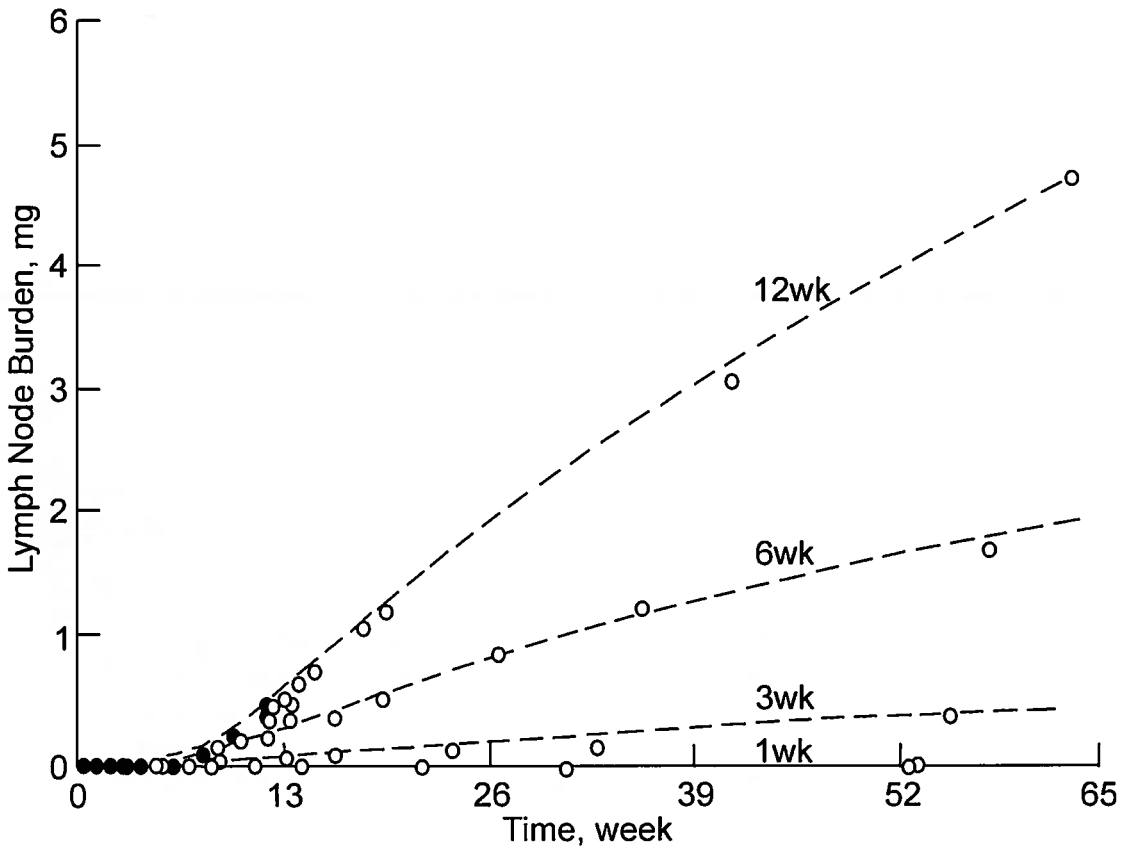

Figure A-4. Experimental and predicted lymph node burdens of rats exposed to CEPs at a concentration of 6.0 mg/m^3 for different exposure spans. The solid and dashed lines are, respectively, the predicted burdens during exposure and post-exposure. Particle characteristics and exposure pattern are explained in the text. The symbols represent the experimental data from Strom et al. (1988).

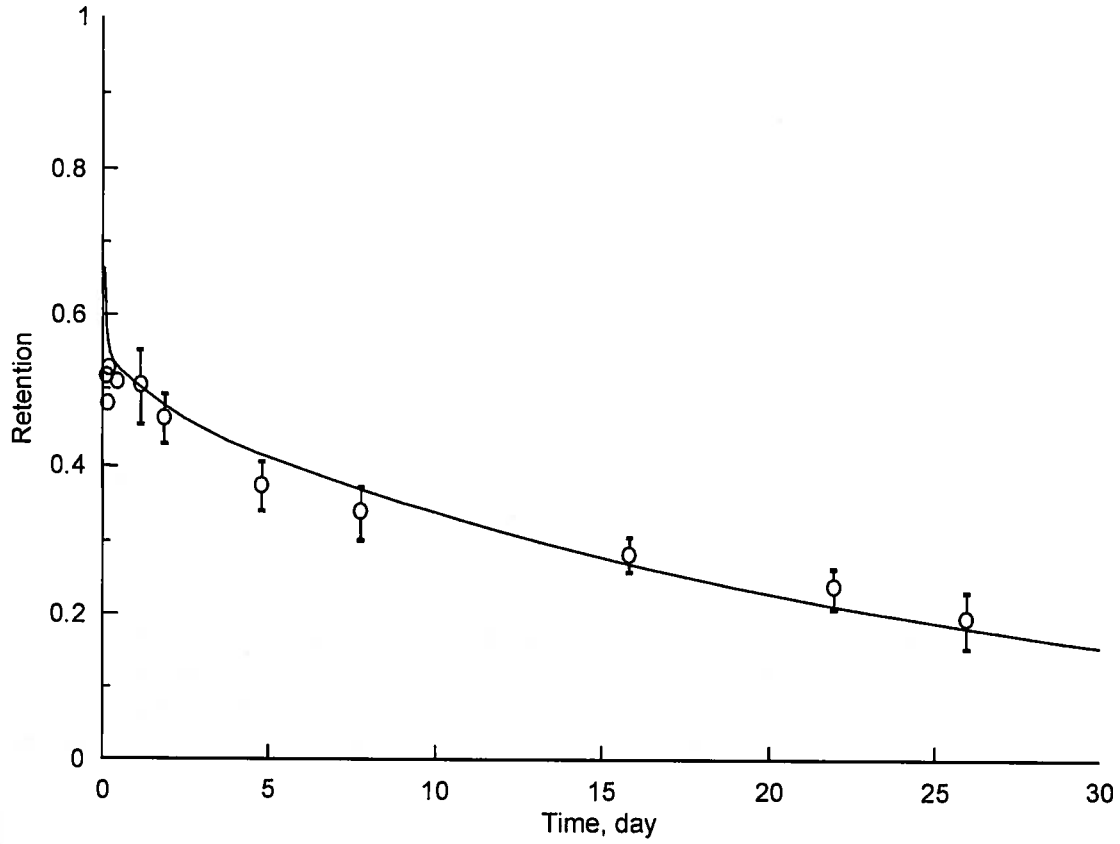

Figure A-5. Comparison between the calculated lung retention (solid line) and the experimental data obtained by Sun et al. (1984) for the particle-associated BaP in rats.

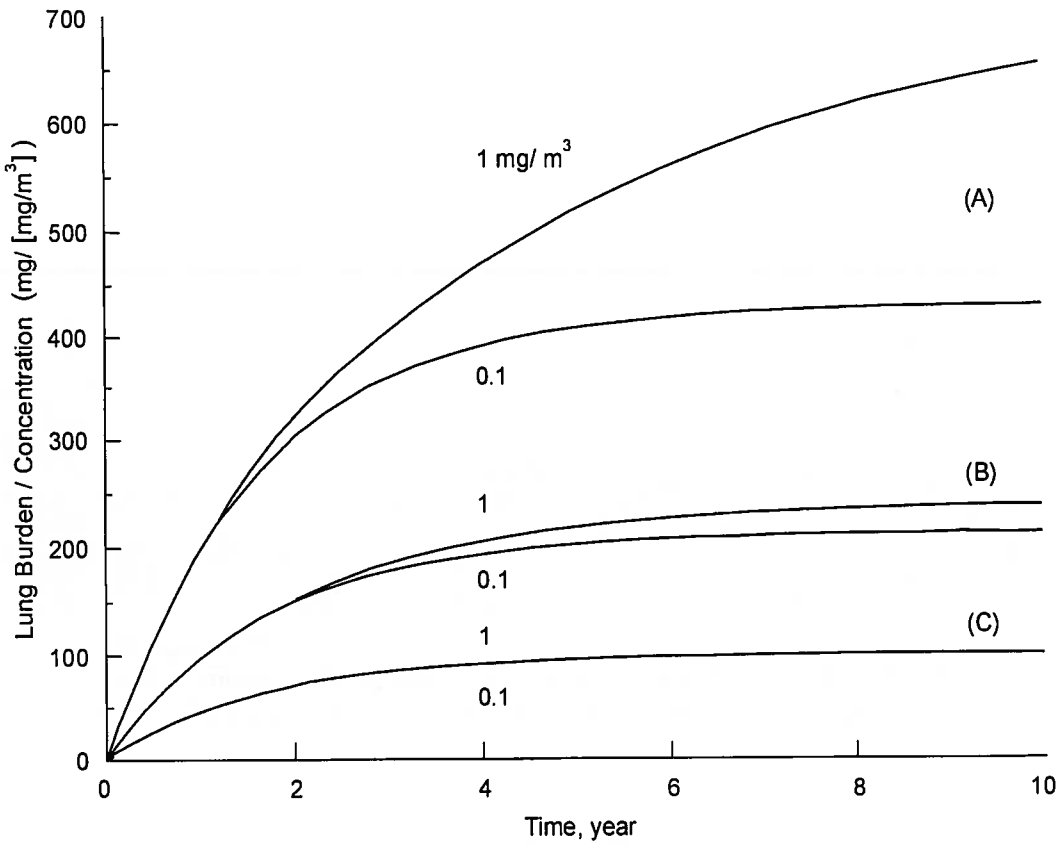

Figure A-6. Calculated lung burdens of diesel soot per unit exposure concentration in human adults exposed continuously to DPM at two different concentrations of 0.1 and 1.0 mg/m³. Exposure patterns are (a) 24 h/day and 7 days/week, (b) 12 h/day and 7 days/week, and (c) 8 h/day and 5 days/week.

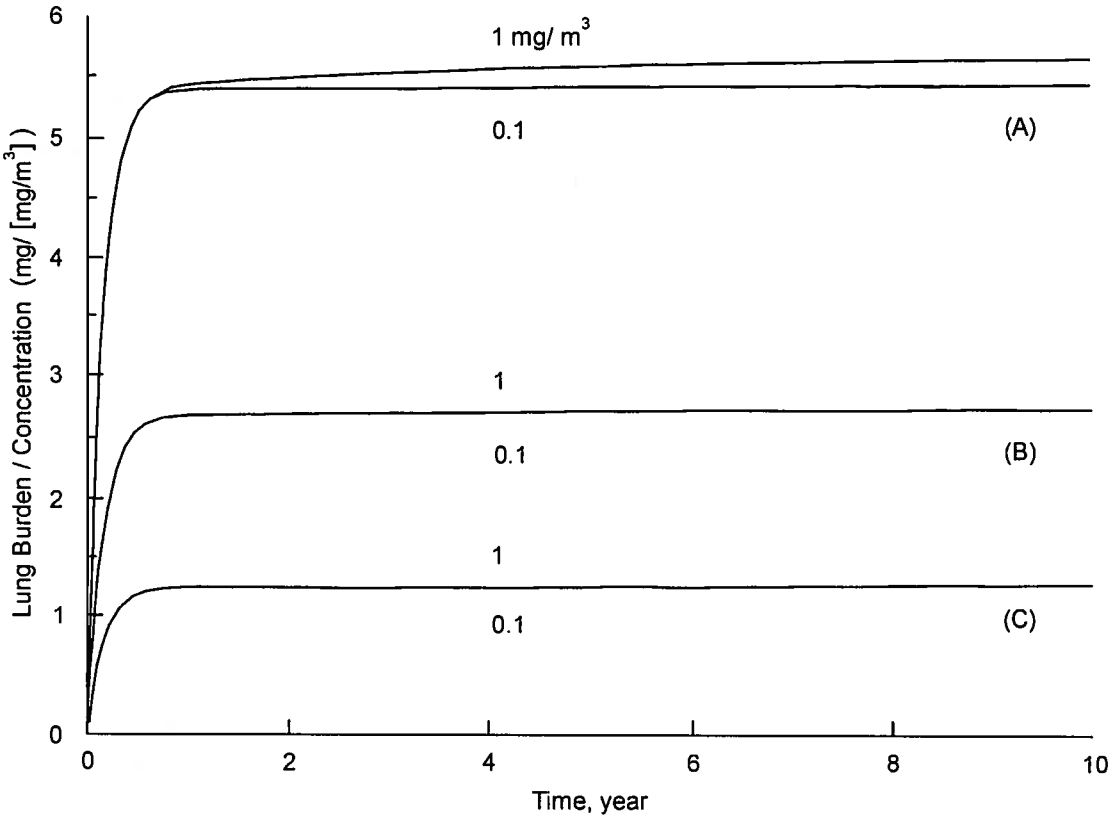

Figure A-7. Calculated lung burdens of the particle-associated organics per unit exposure concentration in human adults exposed continuously to DPM at two different concentrations of 0.1 and 1.0 mg/m^3. Exposure patterns are (a) 24 h/day and 7 days/week, (b) 12 h/day and 7 days/week, and (c) 8 h/day and 5 days/week.

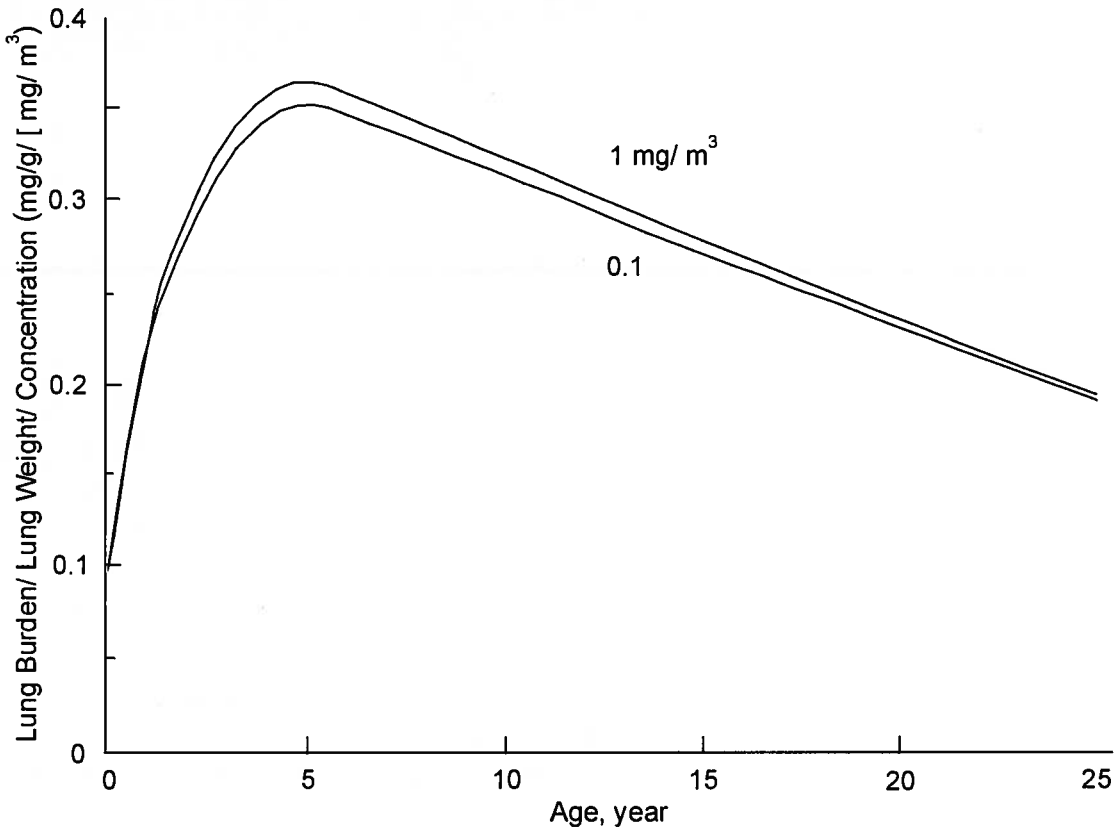

Figure A-8. Calculated lung burdens of diesel soot per gram of lung per unit exposure concentration in humans of different ages exposed continuously for 1 year to DPM of two different concentrations of 0.1 and 1.0 mg/m^3 for 7 days/week and 24 h daily.

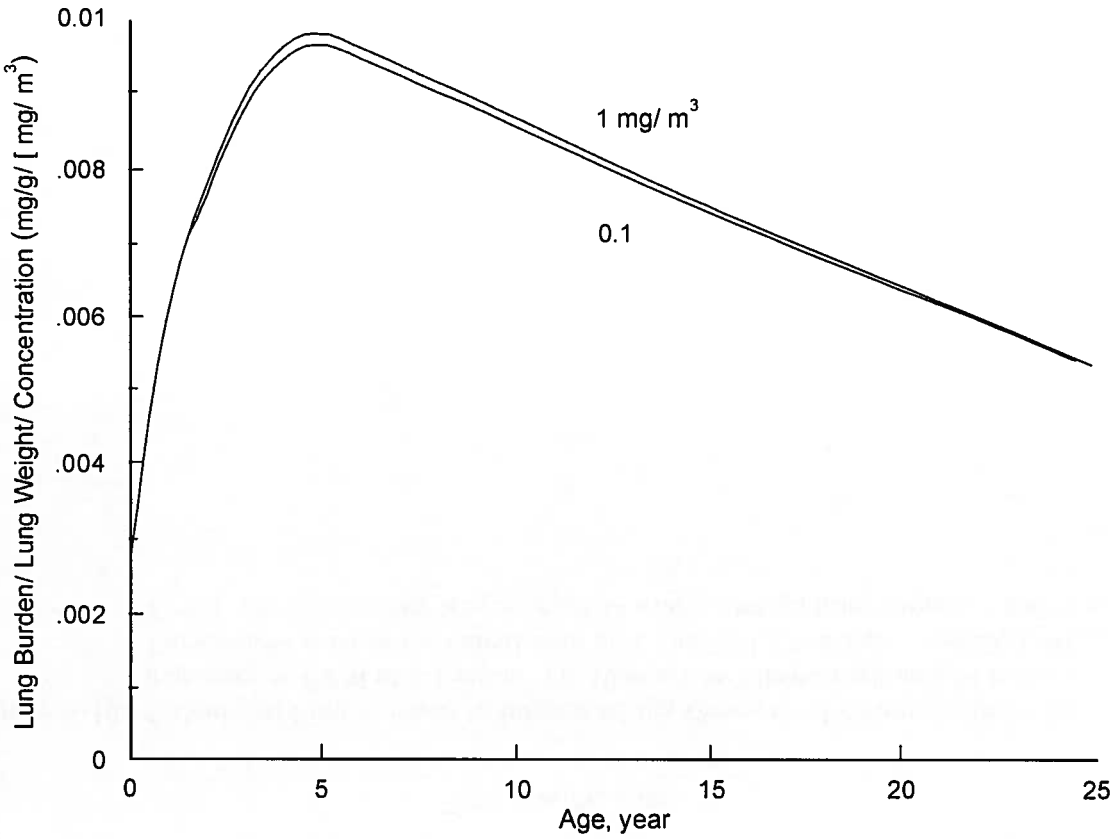

Figure A-9. Calculated burdens of the particle-associated organics per gram of lung per unit exposure concentration in humans of different ages exposed continuously for 1 year to DPM of two different concentrations of 0.1 and 1.0 mg/m^3 for 7 days/week and 24 h daily.

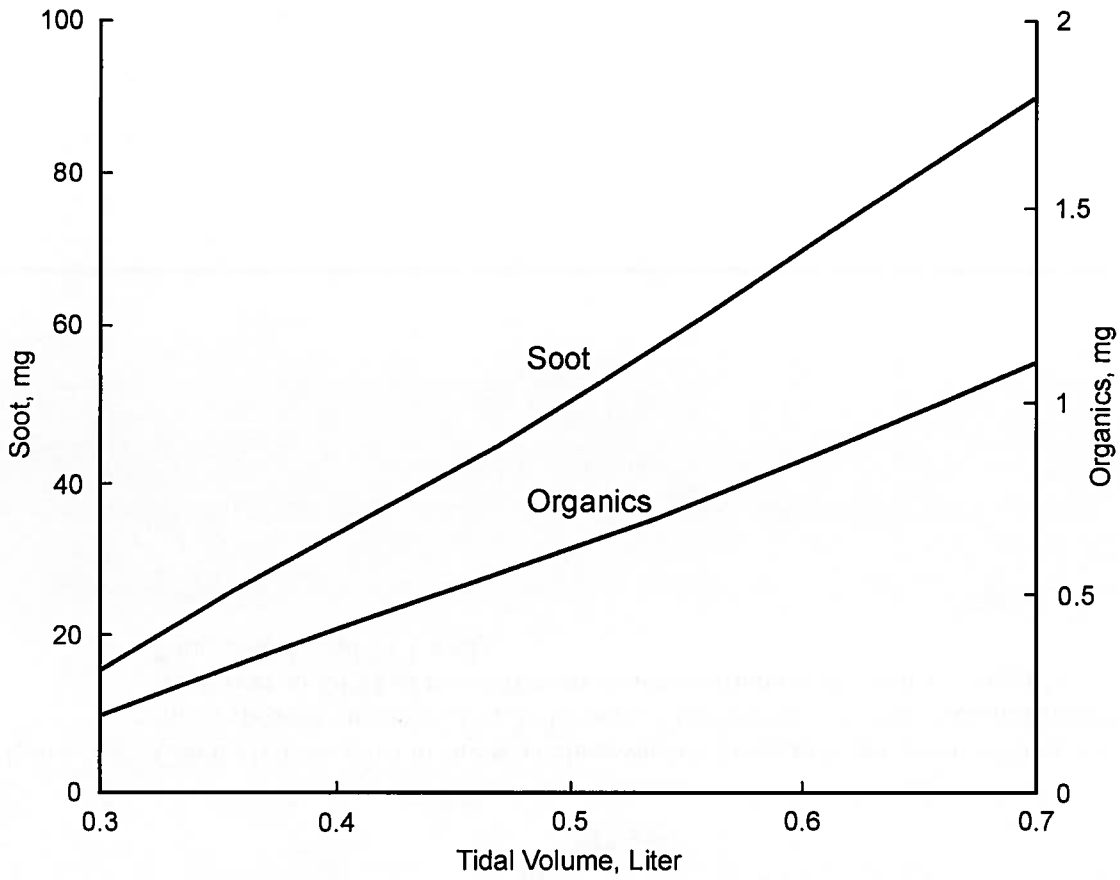

Figure A-10. Calculated lung burdens in human adults versus tidal volume in liters for exposure to DPM at 0.1 mg/m^3 for 10 years at 7 days/week and 24 h daily. Parameters used in the calculation are: (a) MMAD=0.2 µm, σ_g=2.3, f_2=0.1, f_3=0.1; (b) respiratory frequency = 14 min^{-1}; and (c) lung volume = 3000 cm^3.

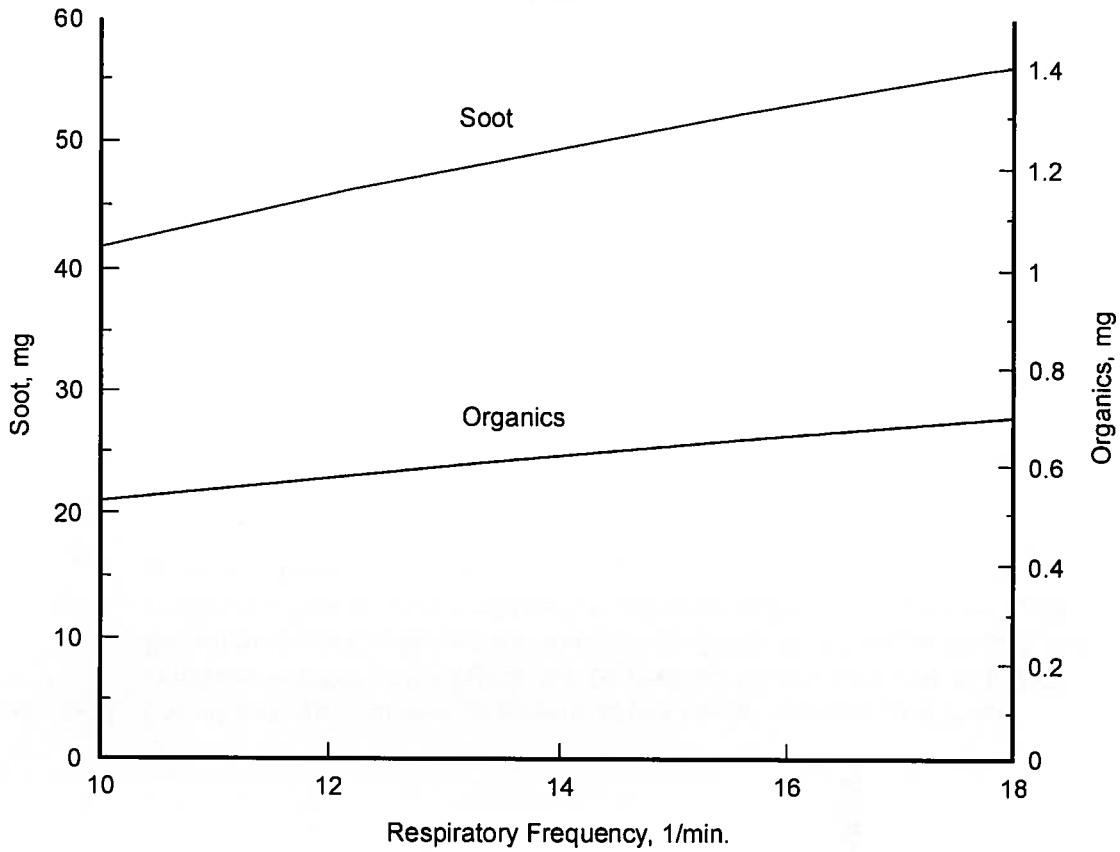

Figure A-11. Calculated lung burdens in human adults versus respiratory frequency in *bpm* for exposure to DPM at 0.1 mg/m^3 for 10 years at 7 days/week and 24 h daily. Parameters used in the calculation are: (a) MMAD=0.2 μm, σ_g=2.3, f_2=0.1, f_3=0.1; (b) tidal volume = 500 cm^3, and (c) lung volume = 3200 cm^3.

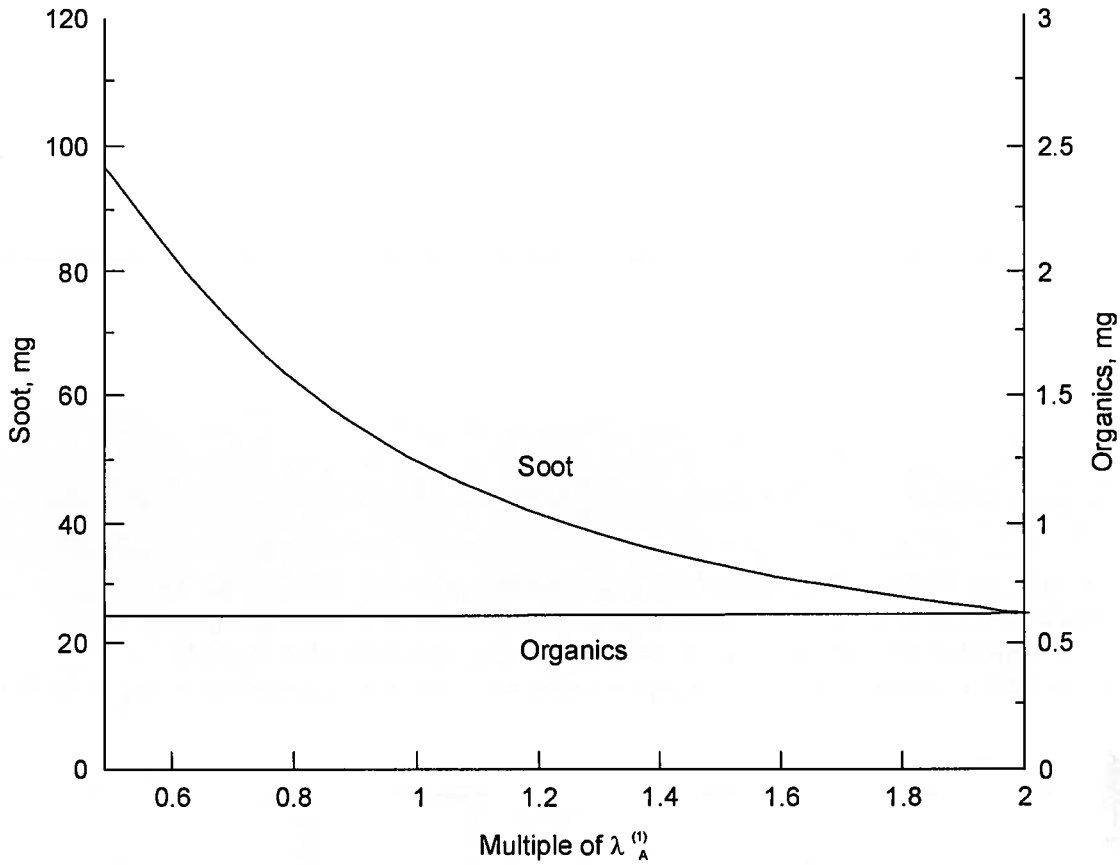

Figure A-12. Calculated lung burdens in human adults versus multiple of $\lambda_A^{(1)}$ for exposure to DPM at 0.1 mg/m$_3$ for 10 years at 7 days/week and 24 h daily. Parameters used in the calculation are: (a) MMAD=0.2 µm, σ_g=2.3, f_2=0.1, f_3=0.1; (b) tidal volume = 500 cm^3, respiratory frequency = 14 min^{-1}; and (c) lung volume = 3200 cm^3.

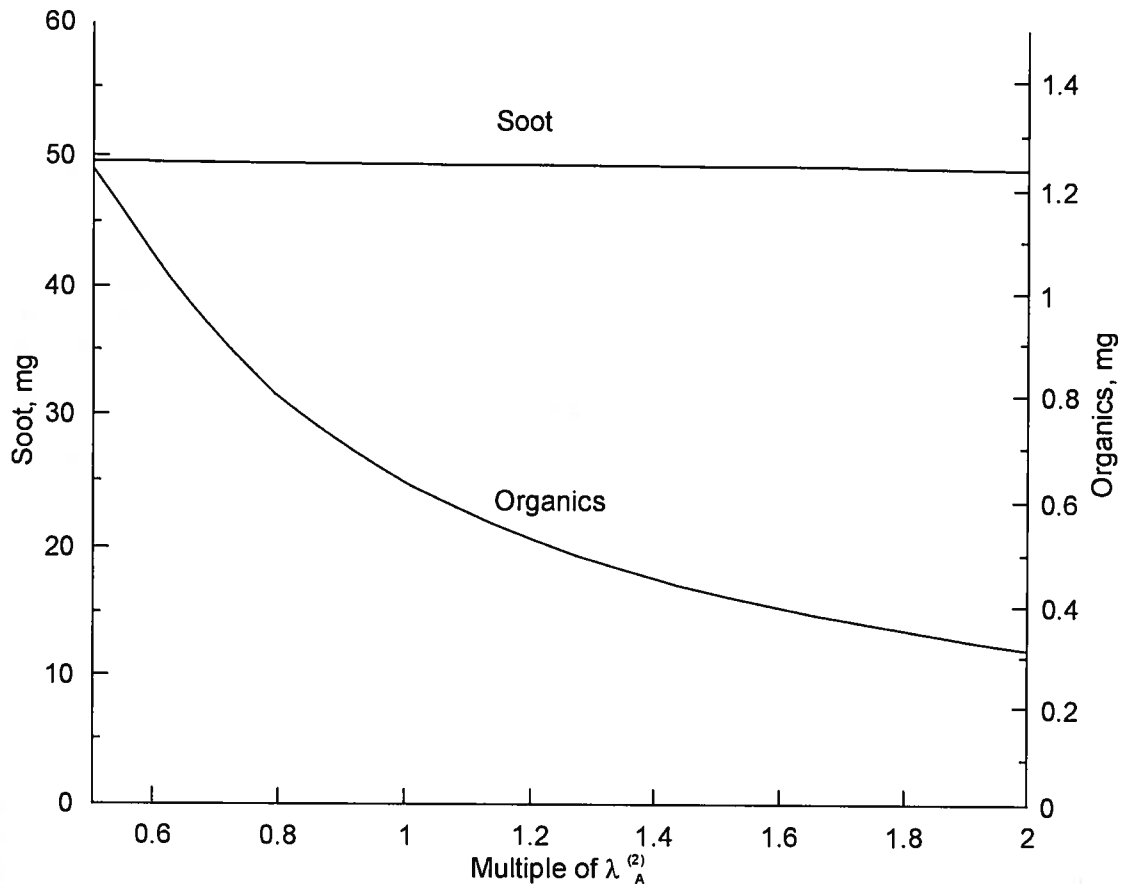

Figure A-13. Calculated lung burdens in human adults versus multiple of $\lambda_A^{(1)}$ for exposure to DPM at 0.1 mg/m^3 for 10 years at 7 days/week and 24 h daily. Parameters used in the calculation are: (a) MMAD=0.2 μm σ_g=2.3, f_2=0.1, f_3=0.1; (b) tidal volume = 500 cm^3, respiratory frequency = 14 min^{-1}; and (c) lung volume = 3200 cm^3.

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Appendix B

Benchmark Concentration Analysis of Diesel Data

B-1. INTRODUCTION TO BENCHMARK

The benchmark dose or benchmark concentration approach, hereafter referred to as the BMC approach, is an alternate to the N/LOAEL option for deriving effect levels. The BMC is currently undergoing extensive consideration by the Agency with promulgation of software and guidelines for application of this methodology (U.S. EPA, 2000). The BMC approach involves fitting a dose-response function to dose and effect information from a single study to derive the best fit of those data. This "best fit"is statistically termed the maximum likelihood estimate but is referred to in the benchmark terminology as the BMC curve. The curve defining the corresponding lower 95% confidence limit of this "best fit"estimate is termed the BMCL curve. This BMCL curve is used to predict the dose that will result in a level of response that is defined *a priori* as the benchmark response "x", $BMCL_x$. In the analyses below, for example, the benchmark response for a 10% increase in incidence[1] of chronic inflammation is defined as a $BMCL_{10}$; the corresponding 10% increase as determined from the BMC curve would be termed the BMC_{10}. This $BMCL_{10}$ would be derived by first using the data and the programs to determine the BMC and BMCL curves. The concentration corresponding to a 10% increase in incidence would then be determined directly from the BMCL. The $BMCL_{10}$ then would be used as the representative value for the effect level or point of departure in the dose-response assessment.

The latest version of the Agency Benchmark Dose Software (BMDS Version 1.2; U.S. EPA, 2000) was used to analyze data on chronic inflammation and pulmonary histopathology present in the chronic studies that were amenable to benchmark analysis. At this time, the Agency BMDS offers sixteen different models total that are appropriate for the analysis of dichotomous data (gamma, logistic, probit, Weibull, log-logistic, multistage, log-probit, quantal-linear, quantal-quadratic), continuous data (linear, polynomial, power, Hill) and nested developmental toxicology data (NLogistic, NCTR, Rai & Van Ryzin). Results from all models include a reiteration of the model formula and model run options chosen by the user, goodness-of-fit information, a graphical presentation for visual inspection and the concentration estimate for the response at the designated $BMCL_x$, as well as the corresponding BMC_x. More details on the modeling results are described and presented in the analysis on dichotomous data following.

The U.S. EPA benchmark dose (BMD/C) methods guidance has not been finalized at this time to provide definitive procedures and criteria (U.S. EPA 1995). Therefore, in this document provisional criteria for minimum data to perform a benchmark analysis are designated such that (1) complete quantitative information on the response of interest should be available (e.g.,

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[1]For increases in incidence "extra risk" is used which is response incidence (inc) normalized to the background (BG) incidence; response – BG/1-BG.

incidence as number affected / total, means with variability) and that (2) at least two exposure levels with responses that differ from those of the controls are provided, and (3) a benchmark response of 10% is employed such that outcomes are $BMCL_{10}$s. A response of 10% is at or near the limit of sensitivity in most long-term bioassays as determined from both the typical number of animals used in bioassays and a low spontaneous background rate (e.g., 0.1%) for a given effect (Haseman, 1984; Haseman et al., 1989).

B-2. DIESEL DATA FOR BENCHMARK ANALYSIS

Using the criteria set forth in Section B-1 and the information about the critical effects that have been identified (pulmonary inflammation, pulmonary histopathology including indicators of fibrotic changes such as increases in alveolar-capillary wall thickness) the following rat chronic studies identified in Chapter 6 were analyzed for information suitable for BMC analysis: Ishinishi et al. (1986, 1988), Mauderly et al. (1987a,b; 1988); Heinrich et al. (1986, 1995), and Nikula et al. (1995).

Results from this analysis yielded only a few data sets from a single study, that of Nikula et al. (1995), that could be used for BMC analysis. The basis for not including data from the other studies varied. Information on pulmonary histopathology in the studies of Ishinishi et al. (1986, 1988), for example, was supplied only in narrative form with no quantitative information given. A similar situation was found for those reports of the ITRI study; Wolff et al. (1987) reports on clearance alterations due to DPM exposure; Henderson et al. (1988) does give information on hydroxyproline but only in graphical form; the 1988 study of Mauderly et al. deals with pulmonary function as a function of DPM lung loading; the 1987a reference of Mauderly et al. discusses tumor prevalence only and the Mauderly 1987b reference reports on diesel exhaust in developing lung to a single exposure concentration of DPM with no dose-response information available. Those reports on the General Motor study contain extensive information relating not to the critical effects, but mostly to precursors of inflammation such as levels of polymorphonuclear neutrophils and lymphocytes in bronchoalveolar lavage from DPM exposed rats (Strom, 1984) and guinea pigs (Barnhart et al., 1981) as well as information on collagen biosynthesis (Misiorowski et al., 1980) all of which is presented in graphical rather than tabular form amenable for benchmark analysis. The information on noncancer histopathology reported by Heinrich et al. (1995) is in text form only and this author's 1986 study deals primarily with clearance and mortality. Nikula et al. (1995), however, do present extensive quantitative dose-response information (incidence / dichotomous data) on several measures of the critical effect including chronic inflamation (presence of focal aggregates of neutrophils), focal fibrosis with epithelial hyperplasia (nodular fibrosis rimmed by hyperplasia), and septal fibrosis (interstitial fibrosis within alveolar septa) although the study had but 2 exposure

concentrations both of which are different from the controls, a minimal number on which benchmark analysis should be performed.

B-3. BENCHMARK ANALYSIS OF DIESEL DATA

These data from Nikula et al. (1995) were extracted, HEC concentrations calculated using the model of Yu et al. (1991; Appendix A), and analyzed using all 9 applicable models for dichotomous data. Because the benchmark models were ran with the HEC, general from the model of Yu et al. (1991), the $BMCL_{10s}$ are also HECs. The results and data are presented in Table B-1. Results were evaluated based on the nature of the data set, visual inspection of the graphical output, and on the goodness-of-fit parameters, including p values and the AIC. When p values were generated for model fits, values for p that were less than 0.1 were considered to reflect a minimal fit to the data and were disqualified from further consideration. However, the small set of only 3 data points was often matched by the number of parameters fitted in several of the models such that the outcome of the model exactly fit the data and thus no p value is generated; these model fits are often referred to as being overparameterized, and are indicated as "NA" in Table B-1. Values for p that were less than 0.1 were considered to reflect a minimal fit to the data. The AIC (Akaike Information Coefficient; Akaike, 1973; Stone, 1998) is a parameter generated for the models in U.S. EPA (2000) that allows for a general comparison among models run on the same data set. The AIC is defined as $-2 \log L + 2 p$ where $\log L$ is the log likelihood of the fitted model, and p is the number of parameters estimated; smaller values indicate better fits.

The overall results of this mathematical analysis is reasonable in a biologically mechanistic sense in that chronic inflammation is more prevalent and apparently occurs at lower concentrations (i.e., has lower $BMCL_{10}$ values) than does focal fibrosis. The information on septal fibrosis were not interpretable as the data were not amenable (no or zero background and then total incidence) to any meaningful benchmark or other dose-response analysis. The most sensitive endpoint, chronic inflammation, is therefore the most sensitive benchmark concentration followed by focal fibrosis.

The choice for the most appropriate $BMCL_{10}$ from among the various modeled values for chronic inflammation requires analysis of both the statistical and graphical outputs of the data. The shape of the dose-response curve from information given in Chapter 6 (Table 6-2) gives evidence of considerable "S" character, e.g., several low HECs without any reported effects up to about 0.2 mg/m^3. The shape of the dose-response curves generated by several of the models, including gamma-hit, Weibull, multistage, and quantal linear were all a uniformly upward sloping arc from the origin (graphs not shown) with minimal evidence of any "S" character, a shape not concordant with the data array in Table 6.2. Models that did generate curves with "S"

character included log-logistic, logistic, probit, quantal-quadratic, and log-probit. Because of their concordance with this independent data array on dose-response, the latter outputs are further analyzes.

The results for both chronic inflammation and focal fibrosis for those models with outputs having appreciable "S" character suggest that females may be more sensitive than males for these endpoints as the incidences are higher and the $BMCL_{10}$ values are generally lower for females than for males. However, the model fits of the $BMCL_{10}$s to the chronic inflammation data segregated by sex were generally inadequate as judged from the p values (most being far less than 0.1) or from visual inspection of the fits to the data, several of which (e.g., log-logistic and log-probit) were lacking any appreciable "S" character. However, combining female and male data improved data fitting as judged by the increased p values to where nearly all were >0.1 and to where the visual fits were concordant with the independent information on dose-response. Too, most of the combined $BMCL_{10}$s were either intermediate between the female and male values or somewhat closer to the female values such that the combined $BMCL_{10}$ values were not much different from the females $BMCL_{10}$s.

From among the combined male and female model outputs in Table B-1, the logistic, probit, and quantal quadratic results were all excluded based on the high AIC value relative to the log-logistic and log-probit results. The log-logistic results were excluded based on the shape of the lower portion of the dose-response curve which was upward sloping near the origin (graph not shown) and not as concordant with the independent dose-response information in Table 6-2 as was the fit of the log-probit model (Figure B-1). This leaves the fit of the log-probit model as being most reflective of the information in Table 6-2. The $BMCL_{10}$ of the log-probit curve at 0.37 mg/m^3 remains and, by elimination, appears to be the most defensible choice from among the $BMCL_{10}$s arrayed in Table B-1. Figure B-1 shows the graphical representation of the log-probit model fit to the data and the origin of the $BMCL_{10}$. This graph also shows the relationship of the $BMCL_{10}$ of 0.37 mg/m^3 to the variability that exists around the control value and that the value of 0.37 mg/m^3 is not far removed from the outer range of this variability. The log-probit $BMCL_{10}$ for focal fibrosis (combined) of 1.3 mg/m^3 noted as being representative of this lesion from the BMC analysis in Table B-1.

Characterization of this benchmark value indicates that it may not be a suitable candidate for use as a point of departure for development of a dose-response assessment such as the RfC. An attribute of the benchmark method is that the response (such as the 10% as used here) is near the range of the actual experimental values, such that extrapolation is not far below the observed experimental range. However, due to the paucity of data points overall and lack of any values below an HEC of nearly 2 mg/m^3 in the Nikula et al. (1995) study, the extrapolation of this BMC to the 10% response level is considerable, the $BMLC_{10}$ of 0.37 mg/m^3 being > 5-fold below the

nearest observed value of 1.95 mg/m^3. Also, the high experimental exposures used in this study are in the range of those resulting in pulmonary overload conditions in rats and therefore in the range of the model assumptions of Yu et al. (1991) about this phenomenon in humans for calculation of the HECs (Chapter 3). The $BMCL_{10}$ of 0.37 mg/m^3 is considerably greater than other NOAELs in the DPM data base of 0.144 mg/m^3 and 0.128 mg/m^3 (Table 6-2 in Chapter 6), possibly indicating that these NOAELs represent actual incidence levels that are considerably less than10%; from the same log-probit model the corresponding $BMCL_{05}$ was 0.21 mg/m^3 (near the range of these NOAELs) and the corresponding $BMCL_{01}$ was 0.07 mg/m^3 (below the range of these NOAELs). These limitations on this $BMCL_{10}$ make it a less than optimal candidate for consideration as a point of departure in the development of dose-response assessments.

B-4. SUMMARY

The recently developed EPA Benchmark dose software (U.S. EPA, 2000) and preliminary guidance was utilized to analyze diesel data by the benchmark approach. Data from only one of the array of principal studies identified elsewhere (Chapter 6) was found to contain data amenable to benchmark analysis. The data from this study, that of Nikula et al. (1995) on pulmonary inflammation and histopathology, was extracted and analyzed as dichotomous data using all available models and designating a 10% response level such that $BMCL_{10}$s were calculated; as the models were ran with HECs, the $BMCL_{10s}$ were also HECs.

The analysis resulted in an array of $BMCL_{10}$s from 3 different effects in two sexes (both separate and combined) with 9 different models. These $BMCL_{10}$s were each considered from a perspective of biological relevance, known dose-response character, and from the individual fit to the data by the models from statistical parameters and visual judgments. The $BMCL_{10}$ that emerged after the above considerations was 0.37 mg/m^3 for the combined male plus female incidence of chronic active pulmonary inflammation. A $BMCL_{10}$ of 1.3 mg/m^3 for pulmonary focal fibrosis was also noted in this analysis. Characterization of these benchmark values indicates that neither may be a suitable candidate for use as a point of departure in development of a dose-response assessment such as the RfC but that they are concordant with other quantitative dose-response aspects of the DPM database.

Table B-1. BMC analysis of pathology incidence data in male and female F344 rats from the study of Nikula et al. (1995) using the different models available from U. S. EPA benchmark dose project (U.S. EPA, 2000) for dichotomous data based on 10% extra risk (i.e., a 10% increase relative to a total that has been adjusted for background) and no threshold term. The concentrations used in the analysis are human continuous equivalent concentrations (HECs) obtained from the interspecies extrapolation model of Yu et al. (1991). The table listings include the $BMCL_{10}$ (the benchmark response level of 10% obtained from the lower 95% limit of the benchmark curve in mg/m^3), the BMC_{10} (the corresponding estimate at 10% response from the best fit benchmark curve, also in mg/m^3), P = goodness-of-fit values. NA indicates a G-O-F value was not available, usually due to the lack of degrees of freedom. AIC = Akaike Information Coefficient (see U.S. EPA, 2000 and below) which may be used for model comparison on the same data set.

Effect (from Table 5 and 6, p 86, Nikula et al., 1995)	Inc @ 0 mg/m^3	Inc @ 1.95 mg/m^3 HEC	Inc @ 5.1 mg/m^3 HEC	$BMCL_{10}$ (BMC_{10}) log-logistic	$BMCL_{10}$ (BMC_{10}) log-probit	$BMCL_{10}$ (BMC_{10}) multi-stage	$BMCL_{10}$ (BMC_{10}) - Weibull	$BMCL_{10}$ (BMC_{10}) - gamma	$BMCL_{10}$ (BMC_{10}) - quantal linear	$BMCL_{10}$ (BMC_{10}) - probit	$BMCL_{10}$ (BMC_{10}) - logistic	$BMCL_{10}$ (BMC_{10}) quantal quadratic
Chronic active inflammation >18 mos, grades 1-3, male + female combined	5/177	59/162	118/174	0.32(0.64) P= NA AIC= 483	0.37(.70) P=NA AIC = 483	0.43(.49) P= 0.982 AIC= 481	0.43(.49) P= 0.982 AIC= 481	0.43(.49) P=0.98 AIC= 480	0.43(.49) P= .982 AIC= 481	1.06(1.19) P= 0.000 AIC= 499	1.12(1.26) P=0.000 AIC= 502	1.34(1.45) P= 0.000 AIC = 505
Chronic active inflammation >18 mos, grades 1-3 in males	1/86	19/81	54/85	0.67(1.16) P= NA AIC= 217	0.74(1.22) P = NA AIC = 217	0.56(.95) undefined AIC= 217	.56(1.04) P= NA AIC= 216	.56(1.09) P= NA AIC= 217	0.50(.61) P= 0.15 AIC= 216	1.31(1.55) P= 0.05 AIC= 219	0.67(1.16) P= NA AIC= 217	1.42(1.57) P= 0.055 AIC = 218
Chronic active inflammation >18 mos, grades 1-3 in females	4/91	40/81	64/89	0.18(0.26) P= NA AIC= 257	.016(.30) P = NA AIC = 257	0.33(.40) P= 0.173 AIC= 257	0.33(.40) P= 0.173 AIC= 257	0.33(.40) P= 0.17 AIC= 257	0.33(.40) P= 0.173 AIC= 257	0.83(.96) P= 0.0001 AIC= 272	0.85(1.0) P= 0.000 AIC= 273	1.21(1.35) P= 0.000 AIC = 279
Focal fibrosis with epithelial hyperplasia, grades 1-4 in males and females combined	0/177	18/162	63/174	1.25(1.8) P= 1.000 AIC= 345	1.3(1.8) P = 1.000 AIC = 345	1.21(1.8) P= 1.000 AIC= 345	1.21(1.8) P= 1.000 AIC= 345	1.21(1.8) P= 1.0 AIC= 345	1.1(1.3) P= 0.363 AIC= 345	2.32(2.61) P= 0.013 AIC= 353	2.50(2.8) P= 0.006 AIC= 356	2.14(2.34) P= 0.091 AIC = 347
Focal fibrosis with epithelial hyperplasia, grades 1-4 in males	0/86	5/81	19/85	1.72(2.7) P= 1.00 AIC= 132	1.6(2.7) P = 1.000 AIC = 132	1.79(2.8) undefined AIC= 134	1.79(2.8) P= 1.00 AIC= 132	1.79(2.75 P= 1.0 AIC= 132	1.7(2.4) P= 0.70 AIC= 131	2.98(3.5) P= 0.199 AIC= 134	3.17(3.69) P= 0.153 AIC= 135	2.68(3.1) P=0.552 AIC = 131
Focal fibrosis with epithelial hyperplasia, grades 1-4 in females	0/91	13/81	44/89	0.80(1.4) P= 1.00 AIC= 199	0.87(1.47) P = 1.000 AIC = 199	0.77 P= 0.99 AIC= 199	0.77(1.4) P=1.0 AIC=199	0.71(1.4) P= 1.00 AIC= 199	0.71(.88) P= 0.445 AIC= 198	1.76 P= 0.037 AIC= 205	1.89(2.2) P= 0.02 AIC= 207	1.7(1.9) P= 0.21 AIC = 200
Septal fibrosis, >18 mos, grades 1-4 in males	1/86	79/81	83/85	.003(.008) P= 0.35 AIC= 53	(failed)	0.07(.08) P= 0.000 AIC= 65	0.07(.08) P= 0.000 AIC= 65	0.07(.08) P= 0.000 AIC= 65	0.07(.08) P= 0.000 AIC= 65	0.29(.37) P= 0.000 AIC= 114	0.32(.44) P= 0.000 AIC= 86	0.42(0.47) P= 0.000 AIC = 100
Septal fibrosis, >18 mos, grades 1- 4 in females	2/91	75/81	87/89	0.009 (.05) P= NA AIC= 87	(failed)	0.08(.10) P= 0.003 AIC= 91	0.08(.10) P= 0.000 AIC= 91	0.08(.10) P= 0.003 AIC= 91	0.08(.10) P= 0.003 AIC= 91	0.32(.40) P= 0.000 AIC= 131	0.34(.45) P= 0.000 AIC= 109	0.46(.51) P= 0.000 AIC = 119

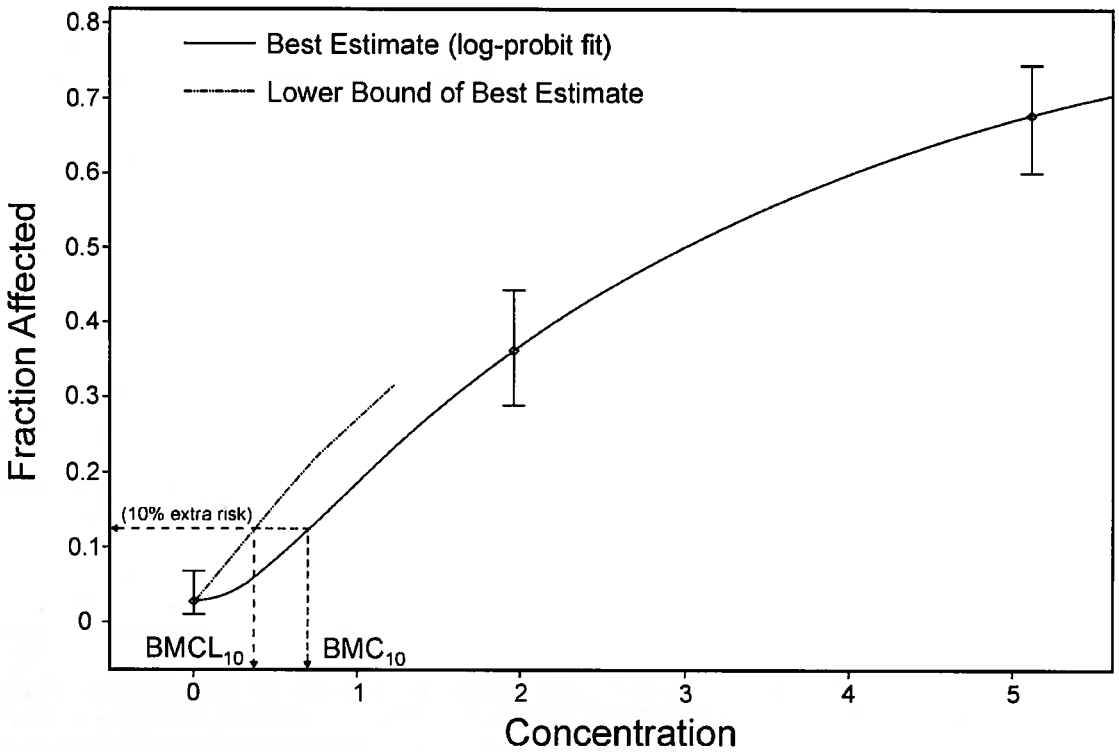

Figure B-1. Benchmark concentration analysis (log-probit) of chronic pulmonary inflammation in rats exposed to DPM from Nikula et al. (1995). $BMCL_{10}$, the lower confidence estimate of the concentration of DPM associated with a 10% incidence (extra risk); BMC_{10}, the corresponding estimate from the best (log-probit) fit. (◊) data with 95% error bounds.

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Appendix C

A Summary Review of Cancer Dose-response Analyses on Diesel Exhaust

C.1. INTRODUCTION

Several individuals and organizations have previously conducted dose-response assessments to estimate quantitatively the cancer risk from exposures to DE. Estimations were performed on the basis of either epidemiologic and/or experimental data. As concluded in Section 8.5, EPA finds that available epidemiologic data are too uncertain to confidently derive a unit risk estimate for DE-induced lung cancer, and that rat data are not suitable for estimating human risk. Nevertheless, a review of historical dose-response evaluations is provided here as background information. This information is not intended to constitute endorsement or a recommendation for use in quantitative risk assessment.

Early analyses to quantitatively assess the carcinogenicity of DE were hindered by a lack of positive epidemiologic studies and long-term animal studies. One means of overcoming these obstacles was the use of comparative potency methods based on combined epidemiologic and experimental data. By the late 1980s, the availability of dose-response data from animal bioassays and epidemiologic studies provided an opportunity for the derivation of both animal and human data-based estimates, although considerable uncertainties were generally acknowledged by the authors of these assessments.

C.2. COMPARATIVE POTENCY METHODS

In this method, the potency of diesel particulate matter (DPM) extract is compared with other combustion or pyrolysis products for which epidemiology-based unit risk estimates have been developed. Comparisons are made using short-term tests such as skin painting, mutations, and mammalian cell transformation. The ratio of the potency of DPM extract to each of these agents is then multiplied by their individual unit risk estimates to obtain the unit risk for DE. If epidemiology-based estimates from more than one pollutant are used, the derived potencies are generally averaged to obtain an overall mean. Major uncertainties of this method include the assumptions that (1) the cancer potency of DE can be determined on the basis of the relative effectiveness of the organic fraction alone; (2) the relative potency in short-term tests is an accurate predictor of lung cancer potency; and (3) DPM extracts are similar in chemical composition and proportion as combustion or pyrolysis products.

In the study by Albert et al. (1983), epidemiology-based unit cancer risk estimates for coke oven emissions, cigarette smoke condensate, and roofing tar were used. Samples of DPM were collected from three light-duty engines (a Nissan 220 C, an Oldsmobile 350, and a Volkswagen turbocharged Rabbit), all run on a highway fuel economy test cycle, and from a heavy-duty engine (Caterpillar 3304) run under steady-state, low-load conditions. The DPM extracts were tested in a variety of assays. Dose/concentration-dependent increases in response were obtained for the four assays listed below:

- Ames *Salmonella typhimurium* (TA98) reverse mutation,
- Gene mutation in L5178Y mouse lymphoma cells,
- Sencar mouse skin tumor initiation test, and
- Viral enhancement of chemical transformation in Syrian hamster embryo cells.

Only the first three assays were used to develop comparative potency estimates because of variability of responses in the enhancement of the viral transformation assay. The in vitro studies were carried out both in the presence and absence of metabolic activators. The potency, defined as the slope of the dose-response curve, was measured for each sample in each short-term assay.

The skin tumor initiation test was positive for all the engines tested except the Caterpillar engine. Only the Nissan engine, however, resulted in strong dose-response data. Because skin tumor initiation was considered to be the most biologically relevant test, it was used to derive potency estimates for the Nissan engine. An estimate for the Nissan engine was then derived by multiplying the epidemiology-based potency estimates for each of the three agents (coke oven emissions, roofing tar, and cigarette smoke condensate) by the ratios of their potencies in the skin
tumor initiation test to that of the Nissan diesel engine. According to this method, three 95% upper-bound estimates of lifetime cancer risk per microgram per cubic meter of extractable organic matter were derived for the Nissan diesel, based on potency comparisons with each of the three agents. These values are: coke oven emissions, 2.6×10^{-4}; roofing tar, 5.2×10^{-4}; and cigarette smoke condensate, 5.4×10^{-4}. The average of the three equals 4.4×10^{-4}.

The potency of the other diesel emission samples was not estimated directly because of the weak response in the skin tumor initiation test. Instead, their potency relative to the Nissan engine was estimated as the arithmetic mean of their potency relative to the Nissan in the Salmonella assay in strain TA98, the sister chromatid exchange assay in Chinese hamster ovary cells, and the mutation assay in mouse lymphoma cells. The estimated lifetime cancer risk per microgram per cubic meter of extractable organic matter for extracts from these engines are as follows: Volkswagen, 1.3×10^{-4}; Oldsmobile, 1.2×10^{-4}; and Caterpillar, 6.6×10^{-6}.

Harris (1983) developed comparative potency estimates for the same four engines used by Albert et al. (1983) but used only two epidemiology-based potency estimates: those for coke oven emissions and for roofing tar. He employed preliminary data from three of the same assays used by Albert et al. (1983): the Sencar mouse skin tumor initiation assay, enhancement of viral transformation in Syrian hamster embryo cells, and the L5178 mouse lymphoma test. The DE cancer potency estimates were then derived by multiplying the epidemiology-based cancer potency estimates for both coke oven emissions and roofing tar by the ratio of their potencies compared with DPM extract in each of the three bioassays. Harris (1983) derived an overall

mean relative risk value of 3.5×10^{-5} per $\mu g/m^3$ for the three light-duty engines with a 95% upper confidence limit of 2.5×10^{-4}. Individual mean values for each engine were not reported.

McClellan (1986), Cuddihy et al. (1981, 1984), and Cuddihy and McClellan (1983) estimated a risk of about 7.0×10^{-5} per $\mu g/m^3$ DPM using a comparative potency method similar to those reported in the preceding paragraph. The database was similar to that used by Albert et al. (1983) and Harris (1983).

C.3. EPIDEMIOLOGY-BASED ESTIMATION OF CANCER RISK

The first lung cancer risk estimates based on epidemiologic data were derived by Harris (1983). He assessed the risk of exposure to DE using data from the London Transport Worker Study reported by Waller (1981). Five groups of employees from the London Transport Authority (LTA) were used: bus garage engineers, bus drivers, bus conductors, engineers in central works, and motormen and guards. The first group was considered to have received the highest exposure; the next two, intermediate; and the last two groups, none. When cancer death rates for the high-exposure group were compared with those of London males, there was no increase in the observed-to-expected (O/E) ratios. The author, in fact, considered the results to be negative. However, because the low rate of lung cancer in all the LTA exposure groups may have been the result of a "healthy worker" effect, Harris (1983) compared the exposed groups with internal controls. He merged the three exposed groups and compared them with the two groups considered to be unexposed. An adjustment was made for the estimated greater exposure levels of garage engineers compared with bus drivers and conductors. Using this method, the relative risk of the exposed groups was greater than 1 but was statistically significant only for garage engineers exposed from 1950 to 1960. In that case, the O/E ratio was 29% greater than the presumed unexposed controls.

Harris (1983) identified a variety of uncertainties relative to potency assessment based on this study. These included:

- small unobserved differences in smoking incidences among groups, which could have a significant effect on lung cancer rates;
- uncertainty about the magnitude of exposure in the exposed groups;
- uncertainty regarding the extent of change in exposure conditions over time;
- random effects arising from the stochastic nature of the cancer incidence; and
- uncertainty in the mathematical specification of the model.

Taking the uncertainties into account, he derived a maximum likelihood excess relative risk estimate of 1.23×10^{-4}, with a 95% upper confidence limit of 5×10^{-4} per $\mu g/m^3$ DPM per year.

McClellan et al. (1989) reported risk estimates based on the Garshick et al. (1987) case-control study in which lung cancer in railroad workers was evaluated. Using a logistic regression, the expected relative risk of lung cancer death was estimated to rise 0.016 per year of exposure to DE. Adjustments were made to convert to continuous exposure (168 vs. 40 hours) for 70 years. Because exposure levels could not be defined exactly, two sets of calculations were made, assuming inhaled DPM concentrations of either 500 or 125 $\mu g/m^3$ DPM. The number of excess cancer deaths per year in the United States was estimated to be 3,800 (95% C.I. 400-7400 when an exposure of 125 $\mu g/m^3$ was used, and 950 (95% C.I. 100-1,900) when 500 $\mu g/m^3$ DPM was used.

The California EPA (Cal-EPA, 1998) derived unit risk estimates for lung cancer based upon the Garshick et al. (1987) case-control study and the Garshick et al. (1988) cohort study of U.S. railroad workers. A variety of exposure patterns were considered, characterized by two components: the average exposure concentration for the workers as measured by Woskie et al. (1988) and the extent of change in exposure from 1959 to 1980. The lowest lifetime risk estimate derived was 1.3×10^{-4} per $\mu g/m^3$ and the highest was 2.4×10^{-3} per $\mu g/m^3$. The geometric mean was 6×10^{-4} per $\mu g/m^3$.

Steenland et al. (1998) estimated lung cancer risk of truck drivers on the basis of a case-control study of decedents in the Teamsters Union (Steenland et al., 1990). Retrospective exposure estimates were made starting with a set of 1990 exposure measurements for different job categories and then retrospectively estimating from 1982 to about 1950 using various factors, including diesel vehicle miles traveled and engine emission rates per mile. The 1990 job category estimates came from an extensive industrial hygiene survey of elemental carbon (EC) exposures in the trucking industry by Zaebst et al. (1991). Lifetime (through age 75) excess risk of lung cancer death for male truck drivers was calculated with the aid of a cumulative exposure model. Assuming a most likely emissions scenario of 4.5 g/mile in 1970, and a 45-year exposure to 5 $\mu g/m^3$ of EC beginning at age 20 and ending at age 65, the estimated excess lung cancer risk was determined to be 1.6% (95% CI 0.4%-3.1%). Using the same data base, Stayner et al (1998) presented an estimate of excess lifetime risk of 4.5E-4 for a worker exposed to 1 $\mu g/m^3$ of DE for 45 years.

C.4. ANIMAL BIOASSAY-BASED CANCER POTENCY ESTIMATES

With the availability of chronic cancer bioassays, a considerable number of potency estimates were derived using lung tumor induction in rats. A high degree of uncertainty exists in the use of the rat data to predict human risk. Major uncertainties include: (1) differences in particle deposition patterns between rats and humans, (2) differences in sensitivity between rats and humans to the carcinogenic action of DE, and (3) extrapolation of rat lung tumor responses

at high concentrations to ambient concentrations without a clear understanding of the mode of action of DE. It is now widely recognized that the rat lung tumor response associated with any insoluble particles at high concentrations is mediated by a particle-overload mechanism (ILSI, 2000), suggesting that rat data for DE are not suitable for estimating human risk at low environmental concentrations.

The first risk estimate was reported by Albert and Chen (1986), based on the chronic rat bioassay conducted by Mauderly et al. (1987). Using a multistage model and assuming equivalent deposition efficiency in humans and rats, they derived a 95% upper confidence limit of 1.6×10^{-5} for lifetime risk of exposure to 1 $\mu g/m^3$. Pott and Heinrich (1987) also used a linear model and data reported by Brightwell et al. (1989), Heinrich et al. (1986), and Mauderly et al. (1987). They reported risk estimates ranging from 6×10^{-5} to 12×10^{-5} per $\mu g/m^3$. Smith and Stayner (1990), using time-to-tumor models based on the data of Mauderly et al. (1987), derived point (MLE) estimates ranging from 1.0×10^{-4} to 2.1×10^{-4} per $\mu g/m^3$ after converting from occupational to environmental exposure scenario.

Pepelko and Chen (1993) developed unit risk estimates based on the data of Brightwell et al. (1989), Ishinishi et al. (1986), and Mauderly et al. (1987) using a detailed dosimetry model to extrapolate dose to humans and a linearized multistage (LMS) model. Taking the geometric mean of individual estimates from the three bioassays, they derived unit risk estimates of 1.4×10^{-5} per $\mu g/m^3$ when dose was based on carbon particulate matter per unit lung surface area rather than whole DPM, and 1.2×10^{-4} per $\mu g/m^3$ when based on lung burden per unit body weight.

Hattis and Silver (1994) derived a maximum likelihood estimate for occupational exposure of 5.2×10^{-5} per $\mu g/m^3$ based on lung burden and bioassay data reported by Mauderly et al. (1987) and use of a five-stage Armitage-Doll low-dose extrapolation model. California EPA (CAL-EPA, 1998) derived a geometric mean estimate of 6×10^{-5} per $\mu g/m^3$ from five bioassays using an LMS model.

To demonstrate the possible influence of particle effects as well as particle-associated organics, an additional modeling approach was conducted by Chen and Oberdorster (1996). Employing a biologically based two-stage model and using malignant tumor data from Mauderly et al. (1987), the upper-bound risk estimate for exposure to 1 $\mu g/m^3$ was estimated to be 1.7×10^{-5}. This estimate is virtually identical to that using the LMS model, assuming nonthreshold effect of particles. If a threshold of particle effect is assumed, however, the estimated risk decreases about fivefold. The results also show that the mechanism of DE-induced lung tumor at high exposure concentrations may differ from that at low exposure concentrations, with the organics and particles playing primary roles of tumorigenesis, respectively, at low and high concentrations. Overall, the potency estimates on the basis of

animal bioassays are in the range of 10^{-6} to 10^{-4} per 1 $\mu g/m^3$ of DPM.

Valberg and Crouch (1999) conducted a meta-analysis of rat bioassays by pooling together data of low-dose groups from different bioassays. There are eight bioassays used in the meta-analysis; half of them had duration of 24 months, and the remaining studies had duration of 30 months or more. Animals with continuous lifetime exposure of less than 600 $\mu g/m^3$ of DE were included in the analysis. Continuous lifetime exposure is calculated by protracting actual DE exposure to 30 months (24 hours per day, 7 days per week). The researchers concluded that exposure of rats to DE at concentrations not associated with lung overload is consistent with no tumorigenic effect.

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Health Assessment Document For Diesel Engine Exhaust

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May 2002

Health Assessment Document for Diesel Engine Exhaust

National Center for Environmental Assessment
Office of Research and Development
U.S. Environmental Protection Agency
Washington, DC

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ABSTRACT

This assessment examined information regarding the possible health hazards associated with exposure to diesel engine exhaust (DE), which is a mixture of gases and particles. The assessment concludes that long-term (i.e., chronic) inhalation exposure is likely to pose a lung cancer hazard to humans, as well as damage the lung in other ways depending on exposure. Short-term (i.e., acute) exposures can cause irritation and inflammatory symptoms of a transient nature, these being highly variable across the population. The assessment also indicates that evidence for exacerbation of existing allergies and asthma symptoms is emerging. The assessment recognizes that DE emissions, as a mixture of many constituents, also contribute to ambient concentrations of several criteria air pollutants including nitrogen oxides and fine particles, as well as other air toxics. The assessment's health hazard conclusions are based on exposure to exhaust from diesel engines built prior to the mid-1990s. The health hazard conclusions, in general, are applicable to engines currently in use, which include many older engines. As new diesel engines with cleaner exhaust emissions replace existing engines, the applicability of the conclusions in this Health Assessment Document will need to be reevaluated.

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FOREWORD

The diesel engine has been a vital workhorse in the United States, powering many of its large trucks, buses, and farm, railroad, marine, and construction equipment. Expectations are that diesel engine use in these areas will increase due to the superior performance characteristics of the engine. Diesel engine exhaust (DE), however, contains harmful pollutants in a complex mixture of gases and particulates. Human exposure to this exhaust comes from both highway uses (on-road) as well as nonroad uses of the diesel engine.

EPA started evaluating and regulating the gaseous emissions from the heavy-duty highway use of diesel engines in the 1970s and particle emissions in the 1980s. The reduction of harmful exhaust emissions has taken a large step forward because of standards issued in 2000 which will bring about very large reductions in exhaust emissions for model year 2007 heavy-duty engines used in trucks, buses, and other on-road uses. A draft of this assessment, along with the peer review comments of the Clean Air Scientific Advisory Committee, was part of the scientific basis for EPA's regulation of heavy-duty highway engines completed in December 2000. The information provided by this assessment was useful in developing EPA's understanding of the public health implications of exposure to DE and the public health benefits of taking regulatory action to control exhaust emissions. EPA anticipates developing similarly stringent regulations for other diesel engine uses, including those used in nonroad applications.

Until these regulations take effect, EPA is partnering with state and local agencies to retrofit older, dirtier, engines to make them run cleaner and to develop model programs to reduce emissions from idling engines. In addition, EPA and local authorities are working to ensure early introduction of effective technologies for particulate matter control and the availability of low- sulfur fuel where possible in advance of the 2007 requirements. Today, at least one engine manufacturer is producing new engines with particulate traps that, when coupled with low-sulfur fuel, meet 2007 particulate emission levels. The Agency expects significant environmental and public health benefits as the environmental performance of diesel engines and diesel fuels improves.

The health assessment concludes that long-term (i.e., chronic) exposure to DE is likely to pose a lung cancer hazard as well as damage the lung in other ways depending on exposure. The health assessment's conclusions are based on exposure to exhaust from diesel engines built prior to the mid-1990s. Short-term (i.e., acute) exposures can cause transient irritation and inflammatory symptoms, although the nature and extent of these symptoms are highly variable across the population. The assessment also states that evidence is emerging that diesel exhaust

exacerbates existing allergies and asthma symptoms. The assessment recognizes that DE emissions, as a mixture of many constituents, also contribute to ambient concentrations of several criteria air pollutants including nitrogen oxides, sulfur oxides, and fine particles, as well as other hazardous air pollutants.

The particulate fraction of DE and its composition is a key element in EPA's present understanding of the health issues and formulation of the conclusions in the health assessment. The amount of exhaust particulate from on-road engines has been decreasing in recent years and is expected to decrease 90% from today's levels with the engines designed to meet the 2007 regulations. The composition of the exhaust particulates and the gases also will change. While EPA believes that the assessment's conclusions apply to the general use of diesel engines today, as cleaner diesel engines replace a substantial number of existing engines, the general applicability of the conclusions in this health assessment document will need to be reevaluated.

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PREFACE

This document is the U.S. Environmental Protection Agency's science-based *Health Assessment Document for Diesel Engine Exhaust*. The assessment was prepared by the National Center for Environmental Assessment which is the health risk assessment program in EPA's Office of Research and Development. The assessment broadly supports activities authorized in the 1990 Clean Air Act. This assessment was specifically prepared for EPA's Office of Transportation and Air Quality which requested information regarding the potential health hazards associated with diesel engine exhaust (DE) exposure. As DE emissions also contribute to urban air toxics and ambient particulate matter, other EPA air programs also have an interest in this assessment.

This document was preceded by five earlier drafts: a Workshop Review Draft (EPA/600/8-90/057A, July 1990), an External Review Draft (EPA/600/8-90/057B, December 1994), an SAB Review Draft (EPA/600/8-90/057C, February 1998), an SAB Review Draft (EPA/600/8-90/057D, November 1999), and an SAB Review Draft (EPA/600/8-90/057E, July 2000). There was an SAB Environmental Health Committee Review in 1990 of the July 1990 draft. The Science Advisory Board's Clean Air Scientific Advisory Committee (CASAC) reviewed the 1994 draft in public sessions in May 1995, the 1998 draft in May 1998, the 1999 draft in December 1999, and the July 2000 draft in October 2000. Public comment periods also were conducted concurrently with the CASAC reviews. In addition many reviewers, both within and outside the Agency, provided assistance at various review stages. This is the final version of the assessment which was prepared in response to CASAC advice and public comments received on the 2000 draft.

The scientific literature search for this assessment is generally current through January 2000, although a few later publications have been included.

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The authors wish to thank all those who sought to improve the quality of this report with their comments and are particularly grateful to the CASAC for its advice.

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1. EXECUTIVE SUMMARY

1.1. INTRODUCTION

This Health Assessment Document for Diesel Engine Exhaust (DE) represents EPA's first comprehensive review of the potential health effects from ambient exposure to exhaust from diesel engines. The assessment was developed to provide information about the potential for DE to pose environmental health hazards, information that would be useful in evaluating regulatory needs under provisions of the Clean Air Act. The assessment identifies and characterizes the potential human health hazards of DE (i.e, hazard assessment) and seeks to estimate the relationship between exposure and disease response for the key health effects (i.e., dose-response assessment). A full exposure assessment and risk characterization, the other two components of a complete risk assessment, are beyond the scope of this document.

The report has nine chapters and three appendices. Chapter 2 provides a characterization of diesel emissions, atmospheric transformation, and human exposures to provide a context for the hazard evaluation of DE. Chapters 3, 4, 5, and 7 provide a review of relevant information for the evaluation of potential health hazards of DE, including dosimetry (Chapter 3), mutagenicity (Chapter 4), noncancer effects (Chapter 5), and carcinogenic effects (Chapter 7). Chapters 6 and 8 contain dose-response analyses to provide insight about the significance of the key noncancer and cancer hazards. Chapter 9 summarizes and characterizes the overall nature of the health hazard potential in the environment and the overall confidence and/or uncertainties associated with the conclusions.

1.2. COMPOSITION OF DIESEL EXHAUST

DE is a complex mixture of hundreds of constituents in either a gas or particle form. Gaseous components of DE include carbon dioxide, oxygen, nitrogen, water vapor, carbon monoxide, nitrogen compounds, sulfur compounds, and numerous low-molecular-weight hydrocarbons. Among the gaseous hydrocarbon components of DE that are individually known to be of toxicologic relevance are the aldehydes (e.g., formaldehyde, acetaldehyde, acrolein), benzene, 1,3-butadiene, and polycyclic aromatic hydrocarbons (PAHs) and nitro-PAHs.

The particles present in DE (i.e., diesel particulate matter [DPM]) are composed of a center core of elemental carbon and adsorbed organic compounds, as well as small amounts of sulfate, nitrate, metals, and other trace elements. DPM consists of fine particles (fine particles have a diameter <2.5 μm), including a subgroup with a large number of ultrafine particles (ultrafine particles have a diameter <0.1 μm). Collectively, these particles have a large surface area which makes them an excellent medium for adsorbing organics. Also, their small size makes them highly respirable and able to reach the deep lung. A number of potentially

toxicologically relevant organic compounds are on the particles. The organics, in general, range from about 20% to 40 % of the particle weight, though higher and lower percentages are also reported. Many of the organic compounds present on the particle and in the gases are individually known to have mutagenic and carcinogenic properties. For example, PAHs, nitro-PAHs, and oxidized PAH derivatives are present on the diesel particles, with the PAHs and their derivatives comprising about 1% or less of the DPM mass.

DE emissions vary significantly in chemical composition and particle sizes between different engine types (heavy-duty, light-duty), engine operating conditions (idle, accelerate, decelerate), and fuel formulations (high/low sulfur fuel). Also, there are emission differences between on-road and nonroad engines simply because the nonroad engines to date are generally of older technology. The mass of particles emitted and the organic components on the particles from on-road diesel engines have been reduced over the years. Available data for on-road engines indicate that toxicologically relevant organic components of DE (e.g., PAHs, nitro-PAHs) emitted from older vehicle engines are still present in emissions from newer engines, though relative amounts have decreased. There is currently insufficient information to characterize the changes in the composition of DE from nonroad diesel engines over time.

1.3. DIESEL EXHAUST AS A COMPONENT OF AMBIENT PARTICULATE MATTER

DE is emitted from "on-road" diesel engines (vehicle engines) or "nonroad" diesel engines (e.g., locomotives, marine vessels, heavy-duty equipment, etc.). Nationwide, data in 1998 indicated that DE as measured by DPM made up about 6% of the total ambient $PM_{2.5}$ inventory (i.e., particles with aerodynamic diameter of 2.5 micrometers or less) and about 23% of the inventory, if natural and miscellaneous sources of $PM_{2.5}$ are excluded. Estimates of the DPM percentage of the total inventory in urban centers are higher. For example, estimates range from 10% to 36% in some urban areas in California, Colorado, and Arizona. Available data also indicate that over the years there have been significant reductions in DPM emissions from the exhaust of on-road diesel engines, whereas limited data suggest that exhaust emissions from nonroad engines have increased.

1.4. ATMOSPHERIC TRANSFORMATION OF DIESEL EXHAUST

After emission from the tailpipe, DE undergoes dilution and chemical and physical transformations in the atmosphere, as well as dispersion and transport in the atmosphere. The atmospheric lifetime for some compounds present in DE ranges from hours to days. DPM is directly emitted from diesel-powered engines (primary particulate matter) and can be formed from the gaseous compounds emitted by diesel engines (secondary particulate matter). Limited information is available about the physical and chemical transformation of DE in the

atmosphere. It is not clear what the overall toxicological consequences of DE's transformations are because some compounds in the DE mixture are altered to more toxic forms while others are made less toxic.

1.5. EXPOSURE TO DIESEL EXHAUST

DPM mass (expressed as μg DPM/m^3) has historically been used as a surrogate measure of exposure for whole DE. Although uncertainty exists as to whether DPM is the most appropriate parameter to correlate with human health effects, it is considered a reasonable choice until more definitive information about the mechanisms of toxicity or mode(s) of action of DE becomes available. In the ambient environment, human exposure to DE comes from both on-road and nonroad engine exhaust. A large percentage of the U.S. population also is exposed to ambient $PM_{2.5}$, of which DPM is typically a significant constituent. Although this document does not provide an exposure assessment, DE exposure information is included to provide a context for the health effects information. Exposure estimates for the early to mid-1990s suggest that national annual average DE exposure from on-road engines alone was in the range of about 0.5 to 0.8 μg DPM/m^3 of inhaled air in many rural and urban areas, respectively. Exposures could be higher if there is a nonroad DE source that adds to the exposure from on-road vehicles. For example, preliminary estimates show that, on a national average basis, accounting for nonroad DE emissions adds another twofold to the on-road exposure. For localized urban areas where people spend a large portion of their time outdoors, the exposures are higher and, for example, may range up to 4.0 μg DPM/m^3 of inhaled air.

1.6. HEALTH EFFECTS OF DIESEL EXHAUST

Available evidence indicates that there are human health hazards associated with exposure to DE. The hazards include acute exposure-related symptoms, chronic exposure-related noncancer respiratory effects, and lung cancer. The health hazard conclusions are based on exhaust emissions from diesel engines built prior to the mid-1990s. With current engine use including some new and many more older engines (engines typically stay in service for a long time), the health hazard conclusions, in general, are applicable to engines currently in use. As new and cleaner diesel engines, together with different diesel fuels, replace a substantial number of existing engines, the general applicability of the health hazard conclusions will need to be re-evaluated. With new engine and fuel technology expected to produce significantly cleaner engine exhaust by 2007 (e.g., in response to new federal heavy duty engine regulations), significant reductions in public health hazards are expected for those engine uses affected by the regulations.

1.6.1. Acute (Short-Term Exposure) Effects

Information is limited for characterizing the potential health effects associated with acute or short-term exposure. However, on the basis of available human and animal evidence, it is concluded that acute or short-term (e.g., episodic) exposure to DE can cause acute irritation (e.g., eye, throat, bronchial), neurophysiological symptoms (e.g., lightheadedness, nausea), and respiratory symptoms (cough, phlegm). There also is evidence for an immunologic effect–the exacerbation of allergenic responses to known allergens and asthma-like symptoms. The lack of adequate exposure-response information in the acute health effect studies precludes the development of recommendations about levels of exposure that would be presumed safe for these effects.

1.6.2. Chronic (Long-Term Exposure) Noncancer Respiratory Effects

Information from the available human studies is inadequate for a definitive evaluation of possible noncancer health effects from chronic exposure to DE. However, on the basis of extensive animal evidence, DE is judged to pose a chronic respiratory hazard to humans. Chronic-exposure, animal inhalation studies show a spectrum of dose-dependent inflammation and histopathological changes in the lung in several animal species including rats, mice, hamsters, and monkeys.

This assessment provides an estimate of inhalation exposure of DE (as measured by DPM) to which humans may be exposed throughout their lifetime without being likely to experience adverse noncancer respiratory effects. This exposure level, known as the reference concentration (RfC) for DE of 5 $\mu g/m^3$ of DPM was derived on the basis of dose-response data on inflammatory and histopathological changes in the lung from rat inhalation studies. In recognition of the presence of DPM in ambient $PM_{2.5}$, it also is appropriate to consider the wealth of $PM_{2.5}$ human health effects data. In this regard, the 1997 National Ambient Air Quality Standard for $PM_{2.5}$ of 15 $\mu g/m^3$ (annual average concentration) also would be expected to provide a measure of protection from DPM, reflecting DPM's current approximate proportion to $PM_{2.5}$.

1.6.3. Chronic (Long-Term Exposure) Carcinogenic Effects

This assessment concludes that DE is "likely to be carcinogenic to humans by inhalation" and that this hazard applies to environmental exposures. This conclusion is based on the totality of evidence from human, animal, and other supporting studies. There is considerable evidence demonstrating an association between DE exposure and increased lung cancer risk among workers in varied occupations where diesel engines historically have been used. The human evidence from occupational studies is considered strongly supportive of a finding that DE

exposure is causally associated with lung cancer, though the evidence is less than that needed to definitively conclude that DE is carcinogenic to humans. There is some uncertainty about the degree to which confounders are having an influence on the observed cancer risk in the occupational studies, and there is uncertainty evolving from the lack of actual DE exposure data for the workers. In addition to the human evidence, there is supporting evidence of DPM's carcinogenicity and associated DPM organic compound extracts in rats and mice by noninhalation routes of exposure. Other supporting evidence includes the demonstrated mutagenic and chromosomal effects of DE and its organic constituents, and the suggestive evidence for bioavailability of the DPM organics in humans and animals. Although high-exposure chronic rat inhalation studies show a significant lung cancer response, this is not thought predictive of a human hazard at lower environmental exposures. The rat response is considered to result from an overload of particles in the lung resulting from the high exposure, and such an overload is not expected to occur in humans at environmental exposures.

Although the available human evidence shows a lung cancer hazard to be present at occupational exposures that are generally higher than environmental levels, it is reasonable to presume that the hazard extends to environmental exposure levels. While there is an incomplete understanding of the mode of action for DE-induced lung cancer that may occur in humans, there is the potential for a nonthreshold mutagenic mode of action stemming from the organics in the DE mixture. A case for an environmental hazard also is shown by the simple observation that the estimated higher environmental exposure levels are close to, if not overlapping, the lower range of occupational exposures for which lung cancer increases are reported. These considerations taken together support the prudent public health choice of presuming a cancer hazard for DE at environmental levels of exposure. Overall, the evidence for a potential cancer hazard to humans resulting from chronic inhalation exposure to DE is persuasive, even though assumptions and uncertainties are involved. While the hazard evidence is persuasive, this does not lead to similar confidence in understanding the exposure/dose-response relationship.

Given a carcinogenicity hazard, EPA typically performs a dose-response assessment of the human or animal data to develop a cancer unit risk estimate that can be used with exposure information to characterize the potential cancer disease impact on an exposed population. The DE human exposure-response data are considered too uncertain to derive a confident quantitative estimate of cancer unit risk, and with the chronic rat inhalation studies not being predictive for environmental levels of exposure, EPA has not developed a quantitative estimate of cancer unit risk.

In the absence of a cancer unit risk, simple exploratory analyses were used to provide a perspective of the range of possible lung cancer risk from environmental exposure to DE. The analyses make use of reported lung cancer risk increases in occupational epidemiologic studies,

and the differences between occupational and environmental exposure. The purpose of having a risk perspective is to illustrate and have a sense of the possible significance of the lung cancer hazard from environmental exposure. The risk perspective cannot be viewed as a definitive quantitative characterization of cancer risk nor is it suitable for estimation of exposure-specific population risks.

1.7. SOURCES OF UNCERTAINTY

Even though the overall evidence for potential human health effects of DE is persuasive, many uncertainties exist because of the use of assumptions to bridge data and knowledge gaps about human exposures to DE and the general lack of understanding about underlying mechanisms by which DE causes observed toxicities in humans and animals. A notable uncertainty of this assessment is whether the health hazards identified from studies using emissions from older engines can be applied to present-day environmental emissions and related exposures, as some physical and chemical characteristics of the emissions from certain sources have changed over time. Available data are not sufficient to provide definitive answers to this question because changes in DE composition over time cannot be confidently quantified, and the relationship between the DE components and the mode(s) of action for DE toxicity is/are unclear. While recognizing the uncertainty, for this assessment a judgment is made that prior-year toxicologic and epidemiologic findings can be applied to more current exposures, both of which use DPM mass in air as the measure of DE exposure.

Other uncertainties include the assumptions that health effects observed at high doses may be applicable to low doses, and that toxicologic findings in laboratory animals generally are predictive of human responses. In the absence of a more complete understanding of how DE may cause adverse health effects in humans and laboratory animals, related assumptions (i.e., the presence of a biological threshold for chronic respiratory effects based on cumulative dosage and absence of a threshold for lung cancer stemming from subtle and irreversible effects) are considered reasonable and prudent.

Although parts of this assessment, particularly the noncancer RfC estimate, have been derived with a generic consideration of sensitive subgroups within the population, the actual spectrum of the population that may have a greater susceptibility to DE is unknown and cannot be better characterized until more information is available regarding the adverse effects of DPM in humans. Increased susceptibility, for example, could result from above-average increases in DE deposition and retention in the respiratory system or intrinsic differences in respiratory system tissue sensitivity. There is no DE-specific information that provides direct insight to the question of differential human susceptibility. Given the nature of DE's noncancer effects on the respiratory system it would be reasonable, for example, to consider possible vulnerable

subgroups to include infants/children, the elderly, or individuals with preexisting health conditions, particularly respiratory conditions.

In developing a perspective on the possible significance of the environmental cancer hazard of DE, this assessment uses information about the differences in the magnitude of DE exposures between the occupational and environmental settings. Although an appreciation for differences in exposure is needed only at an order-of-magnitude level for this assessment, one should recognize that individual exposure is a function of both the variable concentrations in the environment and the related breathing and particle retention patterns of the individual. Because of variations in these factors across the population, different subgroups could receive lower or higher exposure to DE than those groups mentioned in this assessment.

Lastly, this assessment considers only potential heath effects from exposures to DE alone. Effects of DE exposure could be additive to or synergistic with concurrent exposures to many other air pollutants. However, in the absence of more definitive data demonstrating interactive effects (e.g., potentiation of allergenicity effects, potentiation of DPM toxicity by ambient ozone and oxides of nitrogen) from combined exposures to DE and other pollutants, it is not possible to address this issue. Further research is needed to improve the knowledge and data on DE exposures and potential human health effects, and thereby reduce uncertainties of future assessments of the DE health effects data.

2. DIESEL EXHAUST EMISSIONS CHARACTERIZATION, ATMOSPHERIC TRANSFORMATION, AND EXPOSURES

2.1. INTRODUCTION

This chapter provides background information relating to the diesel engine, the pollutants it emits, the history of its use in highway vehicles and railroad locomotives, diesel exhaust composition and emissions trends, and air pollution regulatory standards for diesel engines in the United States. The chapter also provides specific information about the physical and chemical composition of diesel exhaust, descriptions of its atmospheric transformations, observations of measured and modeled ambient concentrations (considered alone and as a component of atmospheric particles in general), some estimates of population exposures as well as a comparison of DPM with ambient fine particulate matter ($PM_{2.5}$). In addition, this chapter gives background information that is used in conjunction with toxicology and epidemiology data to formulate conclusions about human health hazards that are discussed in later chapters of this document. The exposure information does not represent a formal or rigorous exposure assessment; it is intended only to provide a context for the health effects data and health hazard findings.

For the purposes of this document, carbonaceous matter, diesel exhaust, diesel particulate matter, elemental carbon, organic carbon, soluble organic fraction, and soot are defined below.

Carbonaceous matter: Carbon-containing compounds that are associated with particulate matter in diesel exhaust. In this document, the term carbonaceous matter includes all organic and elemental carbon-containing compounds that are found in the particle phase. In other documents, this term is sometimes used interchangeably to refer to the insoluble fraction of diesel particulate matter or the soot fraction.

Diesel engine exhaust (DE): Gaseous and particle-phase emissions resulting from the combustion of diesel fuel in an internal-combustion, compression-ignition engine. DE includes emissions from a diesel engine or diesel vehicle (inclusive of aftertreatment devices), but does not include emissions from brake and tire wear.

Diesel particulate matter (DPM): The particle-phase compounds emitted in DE. DPM can refer to both primary emissions and secondary particles that are formed by atmospheric processes. In this document, DPM refers to primary particles. Primary diesel particles are considered fresh after being emitted and aged after

undergoing oxidation, nitration, or other chemical and physical changes in the atmosphere. As used in this document, DPM refers to both fresh and aged DPM unless a distinction is made.

Elemental carbon (EC): Carbon that has undergone pyrolysis (i.e., has been stripped of hydrogen). In pure form, EC contains only carbon atoms, although EC as it exists in combustion particulate matter is likely to contain some hydrogen atoms.

Organic carbon (OC): Carbon- and hydrogen-containing molecules emitted in DE largely as the result of unburned diesel fuel and, to a lesser extent, from engine lubrication oil. OC compounds also can contain oxygen, nitrogen, and sulfur, as well as other elements in small quantities.

Soluble organic fraction (SOF): The organic portion of DPM that can be extracted from the particle matrix into solution. Extraction solutions and procedures vary and are described in Section 2.2.8.1.

Soot: Agglomerations of EC and OC particles. Soot also is often characterized as the insoluble portion of DPM, and is therefore considered to be mainly EC by some investigators.

This chapter begins with a history of dieselization for on-road vehicles and locomotives, followed by an introductory discussion of the formation of primary diesel emissions to assist the reader in understanding the complex factors that influence the formation of particulate matter (PM) and other DE emissions. The next section is a summary of EPA emission standards for on-road and locomotive diesel engines and a description of the national trends in emissions from on-road and nonroad diesel engine sources based on inventory modeling. The chapter continues with a discussion of diesel fuel use and the impact of fuel properties on emissions. The chronological assessment of emissions factors is presented in summaries of chassis and engine dynamometer testing and tunnel tests. This is followed by a description of engine technologies and their effect on emissions, and a description of the chemical and physical nature of emissions. The data describing the important atmospheric transformations of DE are summarized. The chapter concludes with a summary of the available literature regarding atmospheric concentrations of DPM and exposures to DE. EPA has assessed national and urban-area annual average exposure to DPM using the Hazardous Air Pollutant Exposure Model, and this assessment is presented in Section 2.4.3. A full exposure assessment would include the

distribution of ambient DE exposures in different geographic regions and among different demographic groups, the most highly exposed (90th percentile), exposures in microenvironments for short and long durations, the maximum exposure range (98th percentile), and the number of maximum-exposed individuals. However, such an assessment is not currently available. EPA is developing tools to provide a more complete exposure assessment.

2.2. PRIMARY DIESEL EXHAUST EMISSIONS

2.2.1. History of Dieselization

The diesel engine was patented in1892 by Rudolf Diesel, who conceived it as a prime mover that would provide much improved fuel efficiency compared with spark-ignition (SI) engines. To the present day, the diesel engine's excellent fuel economy remains one of its strongest selling points. In the United States, the diesel engine is used mainly in trucks, buses, agricultural and other nonroad equipment, locomotives, and ships.

The chief advantages of the diesel engine over the gasoline engine are its fuel economy and durability. Diesel engines, however, emit more PM per mile driven compared with gasoline engines of a similar weight. Over the past decade, modifications of engine components have substantially reduced particle emissions from both diesel and gasoline engines (Hammerle et al., 1994; Sawyer and Johnson, 1995).

The diesel engine compresses air to high pressure and temperature. Fuel, when injected into this compressed air, autoignites, releasing its chemical energy. The expanding combustion gases do work on the piston before being exhausted to the atmosphere. Power output is controlled by the amount of injected fuel rather than by throttling the air intake. Compared to its SI counterpart, the diesel engine's superior efficiency derives from a higher compression ratio and no part-load throttling. To ensure structural integrity for prolonged reliable operation at the higher peak pressures brought about by a higher compression ratio and autoignition, the structure of a diesel engine generally is more massive than its SI counterpart.

Diesel engines (also called compression-ignition) may be broadly identified as being either two- or four-stroke cycle, injected directly or indirectly, and naturally aspirated or supercharged. They also are classified according to service requirements such as light-duty (LD) or heavy-duty (HD) automotive/truck, small or large industrial, and rail or marine.

All diesel engines use hydraulic fuel injection in one form or another. The fuel system must meet four objectives if a diesel engine is to function properly over its entire operating range. It must: (1) meter the correct quantity of fuel, (2) distribute the fuel to the correct cylinder, (3) inject the fuel at the correct time, and (4) inject the fuel so that it is atomized and mixes well with the in-cylinder air. The first two objectives are functions of a well-designed injection pump, and the last two are mostly functions of the injection nozzle. Fuel injection

systems are moving toward the use of electronic components for more flexible control than is available with purely mechanical systems to obtain lower exhaust emissions without diminishing fuel efficiency.

Both the fuel and the lubricants that service diesel engines are highly finished petroleum-based products combined with chemical additives. Diesel fuel is a mixture of many different hydrocarbon molecules from about C_7 to about C_{35}, with a boiling range from roughly 350 °F to 650 °F. Many of the fuel and oil properties, such as specific energy content (which is higher than gasoline), ignition quality, and specific gravity, are related to hydrocarbon composition. Therefore, fuel and lubricant composition affect many aspects of engine performance, including fuel economy and exhaust emissions.

Complete and incomplete combustion of fuel in the diesel engine results in the formation of a complex mixture of gaseous (gas-phase hydrocarbons, CO, CO_2, NO, NO_2, SO_2) and particulate exhaust (carbonaceous matter, sulfate, and trace elements). Because of concerns over health effects associated with DE, EPA began regulating emissions from diesel engines in 1970 (for smoke) and then added regulations for gaseous emissions. EPA first regulated particulate emissions from HD diesels in 1988.

2.2.1.1. *Dieselization of the On-Road Fleet*

Because of their durability and fuel economy, the use of diesel engines, particularly in long-distance applications, has increased over the years. The Census of Transportation, Truck Inventory and Use Survey (TIUS) indicates that among Class 3-8 trucks, diesel engine use has increased more rapidly than gasoline engine use in the past 20 years. Truck classes are defined by gross vehicle weight as described in Table 2-1. Dieselization first occurred among Class 7 and 8 trucks. The TIUS indicates that 81.5% of diesel trucks on the road in 1963 were Class 7 or 8 trucks (Table 2-2). Class 7 sales became predominantly (>50%) diesel in the 1970s and Class 8 sales became predominantly diesel in the 1960s. Diesels did not make up a majority of class 5 and 6 sales until the 1990s (Figures 2-1 and 2-2). HD trucks have historically constituted the majority of diesel sales and mileage. However, an increasing number of LD diesel trucks have been sold domestically in recent years. In the 1990s, approximately one in three diesel trucks sold was a Class 1 or Class 2 vehicle. Diesel trucks have historically been driven more miles per truck than gasoline trucks. For example, the TIUS indicates that 59% of diesel trucks were driven more than 50,000 miles in 1963, compared with 3% of gasoline trucks.

Table 2-1. Vehicle classification and weights for on-road trucks

Class	Gross vehicle weight (lb)
1	<6,000
2	6,001–10,000
3	10,001–14,000
4	14,001–16,000
5	16,001–19,500
6	19,501–26,000
7	26,001–33,000
8A[a]	33,001–60,000
8B[a]	>60,000
Medium duty (MD)	10,001–19,500 (same as Classes 3–5)
Light-heavy duty (LHD)	19,501–26,000 (same as Class 6)
Heavy-heavy duty (HHD)	>26,001 (same as Class 7–8)

[a]Class 8A and Class 8B are often considered together.

Table 2-2. Total (gas and diesel) diesel trucks in the fleet in 1992

Truck class	1992 gas and diesel trucks	1992 diesel trucks	% Diesels
Class 1 and 2 (Light duty)	55,193,300	1,387,600	3
Class 3, 4, and 5 (Medium duty)	1,258,500	326,300	26
Class 6 (Light heavy-duty)	732,300	273,800	37
Class 7 and 8 (Heavy heavy-duty)	2,016,600	1,725,300	86

Source: Census of Transportation, 1995.

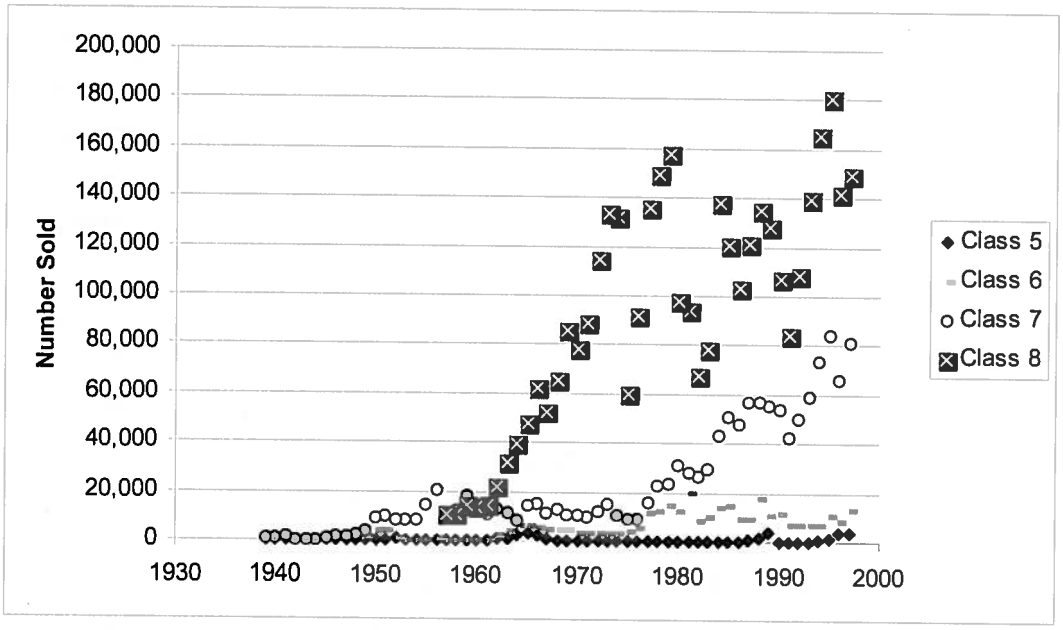


Figure 2-1. Diesel truck sales (domestic) for the years 1939-1997.
Source: AAMA, 1927-1974 and 1975-1998.

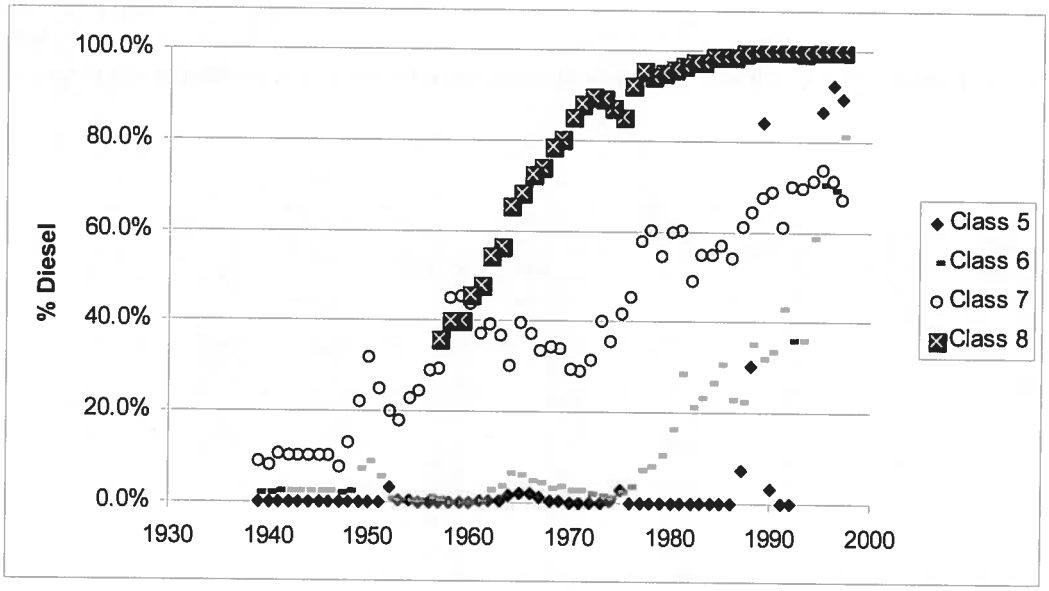
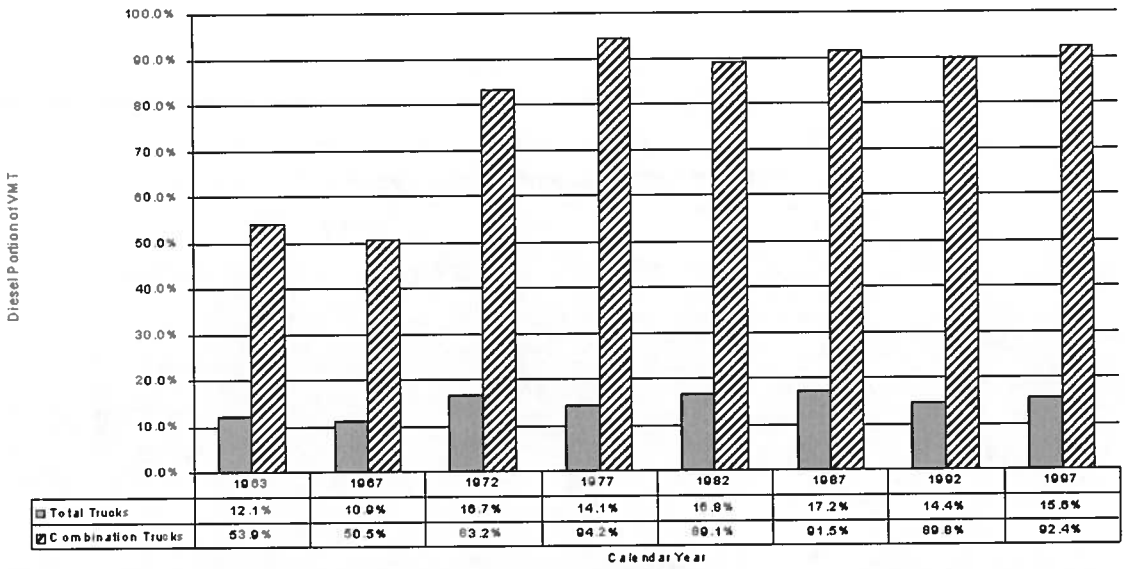


Figure 2-2. Diesel truck sales as a percentage of total truck sales for the years 1939-1997.
Source: AAMA, 1927-1974 and 1975-1998.

Among combination trucks, consisting of tractor-trailers and single-unit trucks with trailers, diesel vehicles have driven a majority of the miles since at least 1963, the first year in which TIUS was conducted (Figure 2-3).



	1963	1967	1972	1977	1982	1987	1992	1997
Total Trucks	12.1%	10.9%	16.7%	14.1%	16.8%	17.2%	14.4%	15.8%
Combination Trucks	53.9%	50.5%	83.2%	94.2%	89.1%	91.5%	89.8%	92.4%

Figure 2-3. Percentage of truck miles attributable to diesel trucks. VMT= vehicle miles traveled.
Source: U.S. Bureau of the Census, 1999b.

The longevity of diesel trucks is an important factor to understand past, current, and projected exposures to DE because older vehicles are subject to less stringent regulations and may remain in use for several decades after their manufacture. American Automobile Manufacturers Association publications (AAMA, 1927-1997) indicate that 53% of trucks from model years 1947-1956 were still on the road after 14 years. The proportion of trucks in use after 14 years was 63% for model years 1974-1983, suggesting that the lifespan of trucks built in later years is longer. According to the 1997 TIUS, vehicles older than 10 years made up 40% of Class 7 and 8 trucks and 16% of Class 7-8 vehicle miles traveled (VMT) (Figures 2-4 and 2-5). Almost all Class 7 and 8 trucks were diesel vehicles in the period 1982-1997 (93% in 1982 and 99% in 1997).

2.2.1.2. *Dieselization of Railroad Locomotive Engines*

Early in the 20th century the political and economic pressure on the railroads to replace steam locomotives was substantial. Railroads were losing business to other forms of transport. The diesel-electric locomotive provided 90% in-service time, compared with only 50% for steam locomotives, and had three times the thermal efficiency (Klein, 1991; Kirkland, 1983).

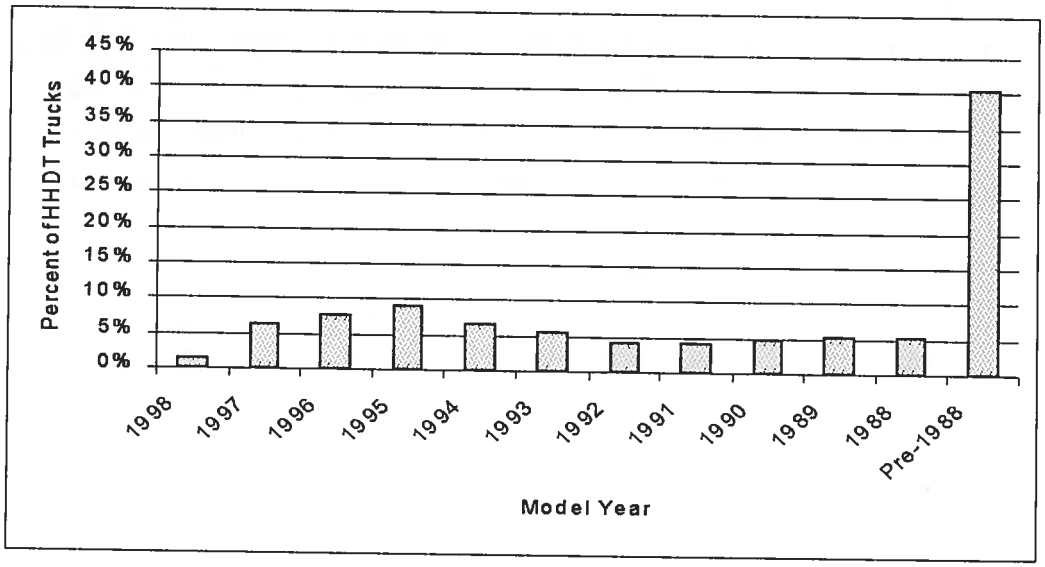


Figure 2-4. Model year distribution of in-use HD truck fleet in 1997.
Source: U.S. Bureau of the Census, 1999b.

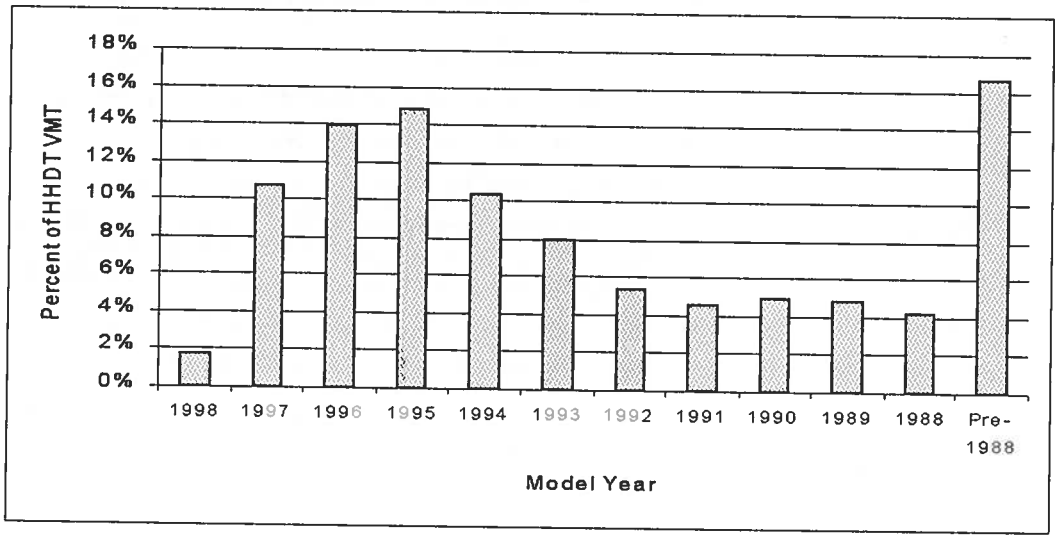


Figure 2-5. Model year distribution of vehicle miles traveled by the in-use HD truck fleet in 1997.
Source: U.S. Bureau of Census, 1999b.

Additionally, several cities had passed laws barring steam locomotives within the city limits because the large quantities of smoke obscured visibility, creating a safety hazard. The first prototype diesel locomotive was completed in 1917. By 1924 General Electric (GE) was producing a standard line of switching locomotives on a production basis. Electro-Motive Corporation was founded the same year to produce diesel locomotives in competition with GE. This company was purchased in 1929 by General Motors (GM) and became the Electro-Motive Division. After this acquisition, GM began to develop the two-stroke engine for this application. Up to this time, all locomotive diesel engines were four-stroke. Two-strokes offered a much higher power-to-weight ratio, and GM's strategy was to get a large increase in power by moving to the two-stroke cycle. The first true high-speed, two-stroke, diesel-electric locomotives were produced by GM in 1935. However, because of the economic climate of the Great Depression, few of these were sold until after the Second World War. At the end of the war, most locomotives were still steam-driven but were more than 15 years old, and the railroads were ready to replace the entire locomotive fleet. Few, if any, steam locomotives were sold after 1945 because the entire fleet was converted to diesel (Coifman, 1994).

The locomotive fleet has included significant percentages of both two- and four-stroke engines. The four-stroke diesel engines were naturally aspirated in the 1940s and 1950s. It is unlikely that any of the two-stroke engines used in locomotive applications were strictly naturally aspirated. Nearly all two-stroke diesel locomotive engines are uniflow scavenged, with a positive-displacement blower for scavenging assistance. In 1975, it was estimated that 75% of the locomotives in service were two-stroke, of which about one-half used one or more turbochargers in addition to the existing positive-displacement blower for additional intake boost pressure.

Almost all of the four-stroke locomotive engines were naturally aspirated in 1975. Electronic fuel injection for locomotive engines was first offered in the 1994 model year (U.S. EPA, 1998b). All locomotive engines manufactured in recent years are turbocharged, aftercooled or intercooled four-stroke engines. In part, this is because of the somewhat greater durability of four-strokes, although impending emissions regulations may have also been a factor in this shift. The typical lifespan of a locomotive has been estimated to be more than 40 years (U.S. EPA, 1998b). Many of the smaller railroads are still using engines built in the 1940s, although the engines may have been rebuilt several times since their original manufacture.

2.2.2. Diesel Combustion and Formation of Primary Emissions

A basic understanding of diesel combustion processes can assist in understanding the complex factors that influence the formation of DPM and other DE emissions. Unlike SI combustion, diesel combustion is a fairly nonhomogenous process. Fuel is sprayed at high

pressure into the compressed cylinder contents (primarily air with some residual combustion products) as the piston nears the top of the compression stroke. The turbulent mixing of fuel and air that takes place is enhanced by injection pressure, the orientation of the intake ports (inducement of intake-swirl tangential to the cylinder wall), piston motion, and piston bowl shape. In some cases, fuel and air mixing is induced via injection of the fuel into a turbulence-generating pre-chamber or swirl chamber located adjacent to the main chamber (primarily in older, higher speed engines and some LD diesels). Examples of typical direct injection and indirect injection combustion systems are compared in Figure 2-6. Diesel combustion can be considered to consist of the following phases (Heywood, 1988; Watson and Janota, 1982):

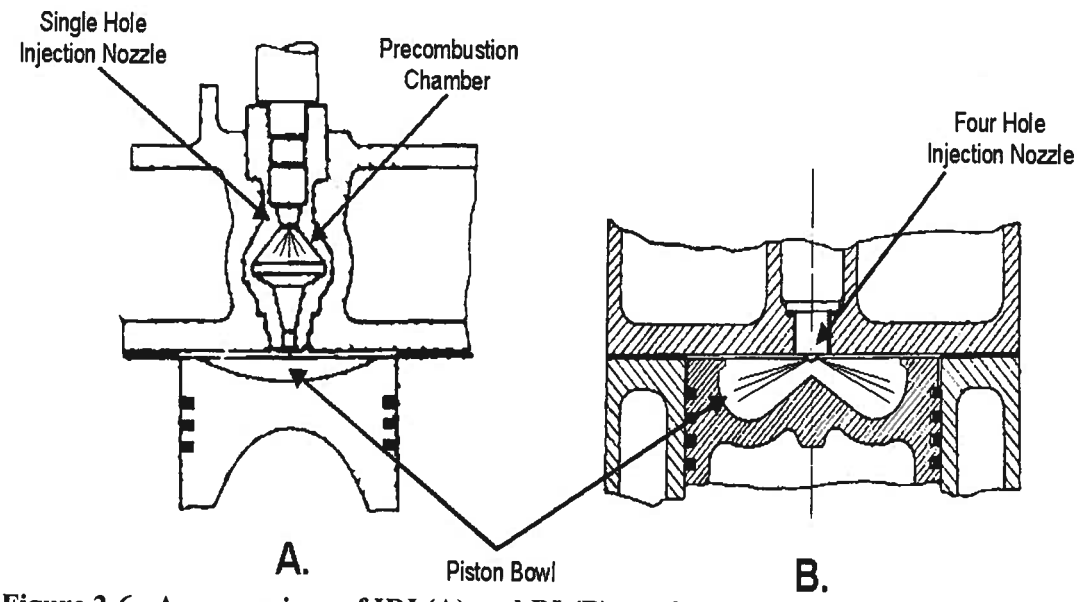


Figure 2-6. A comparison of IDI (A) and DI (B) combustion systems of high-speed HD diesel truck engines. DI engines almost completely replaced IDI engines for these applications by the early 1980s. (IDI = indirect injection, DI=direct injection)

- An ignition delay period, which starts after the initial injection of fuel and continues until the initiation of combustion. The delay period is governed by the rate of fuel and air mixing, diffusion, turbulence, heat transfer, chemical kinetics, fuel vaporization, and fuel composition. Fuel cetane rating is an indication of ignition delay.
- Rapid, premixed burning of the fuel and air mixture from the ignition delay period.
- Diffusion-controlled burning, where the fuel burns as it is injected and diffuses into the cylinder.
- A very small amount of rate-controlled burning during the expansion stroke, after the end of injection.

Engine speed and load are controlled by the quantity of fuel injected. Thus, the overall fuel-to-air ratio varies greatly as engine speed and load vary. On a macro scale, the cylinder contents are always fuel-lean. Depending on the time available for combustion and the proximity of oxygen, the fuel droplets are either completely or partially oxidized. At temperatures above 1,300 K, much of the unburned fuel that is not oxidized is pyrolized (stripped of hydrogen) to form EC (Dec and Espey, 1995). In addition to EC, other carbonaceous matter is present, largely from unburned fuel. The agglomeration of elemental and OC forms particles that are frequently referred to as "soot" particles. In this document, the terms "EC" and "OC" are used to refer to the carbon-containing components of DPM, and collectively, they are referred to as the carbonaceous fraction of a diesel particle.

Carbonaceous particle formation occurs primarily during the diffusion-burn phase of combustion, and is highest during high load and other conditions consistent with high fuel-air ratios. Most of the carbonaceous matter formed (80% to 98%) is oxidized during combustion, most likely by hydroxyl radicals (Kittelson et al., 1986; Foster and Tree, 1994).

DPM is defined by the measurement procedures summarized in the Code of Federal Regulations, Title 40 CFR, Part 86, Subpart N (CFR 40:86.N). These procedures define DPM emissions as the mass of material collected on a filter at a temperature of 52 °C or less after dilution of the exhaust with air. DPM is formed by a number of physical processes acting in concert as the exhaust is cooled and diluted. These are nucleation, coagulation, condensation, and adsorption. The core DE particles are formed by nucleation and coagulation from primary spherical particles consisting of solid carbonaceous (EC) material and ash (trace metals and other elements). To these, through coagulation, adsorption, and condensation, are added organic and sulfur compounds (sulfate) combined with other condensed material (Figure 2-7). Because of

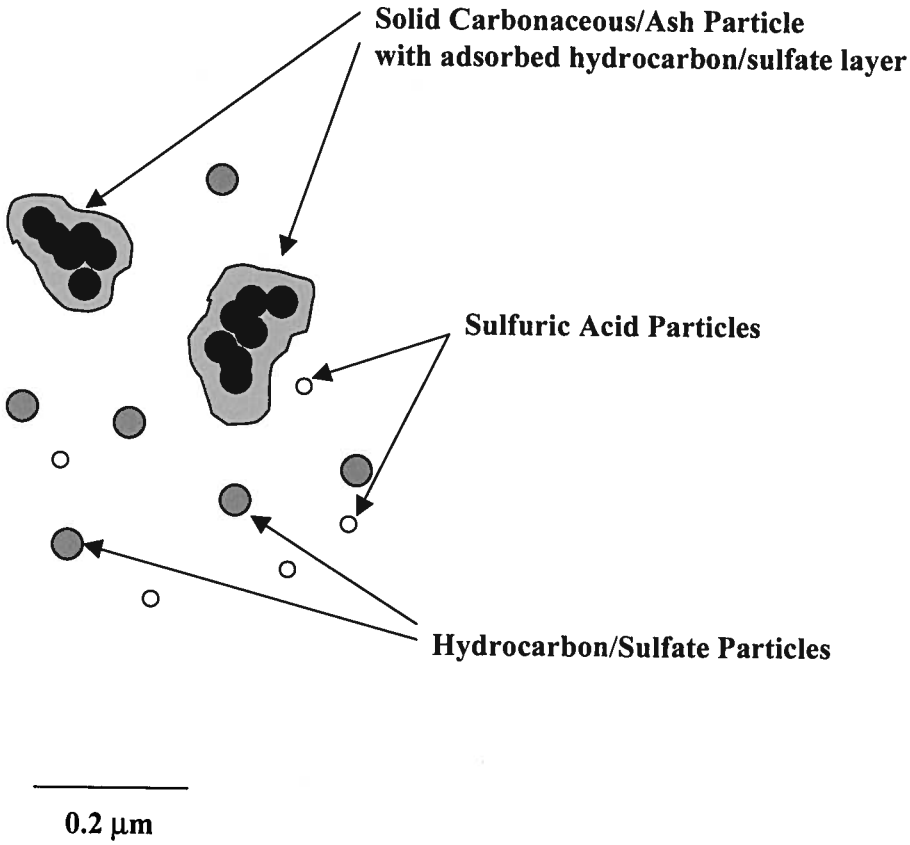


Figure 2-7. Schematic diagram of diesel engine exhaust particles.

Source: Modified from Kittelson, 1998.

their size, <0.5 mm, these particles have a very large surface area per gram of mass, which makes them able to adsorb large quantities of ash, organic compounds, and sulfate. The specific surface area of the EC core has been measured to be approximately 30–50 m^2/g (Frey and Corn, 1967). Pierson and Brachaczek (1976) report that after the extraction of adsorbed organic material, the surface area of the diesel particle core is approximately 90 m^2/g.

The organic material associated with diesel particles originates from unburned fuel, engine lubrication oil, and small quantities of partial combustion and pyrolysis products. This is frequently quantified as the SOF, which is discussed in much more detail in Section 2.2.7. The formation of sulfate in DE depends primarily on fuel sulfur content. During combustion, sulfur compounds present in the fuel are oxidized to sulfur dioxide (SO_2). Approximately 1% to 4% of fuel sulfur is oxidized to form sulfuric acid (H_2SO_4) (Wall et al., 1987; Khatri et al., 1978; Baranescu, 1988; Barry et al., 1985). Upon cooling, sulfuric acid and water condense into an aerosol that is nonvolatile under ambient conditions. The mass of sulfuric acid DPM is more than doubled by the mass of water associated with the sulfuric acid under typical DPM measurement conditions (50% relative humidity, 20–25 °C) (Wall et al., 1987).

Emissions from combustion engines produce oxide of nitrogen (NO_x) primarily (at least initially) as of NO. High combustion temperatures cause reactions between oxygen and nitrogen to form NO and some NO_2. Most NO_2 formed during combustion is rapidly decomposed. NO can also decompose to N_2 and O_2, but the rate of decomposition is very slow (Heywood, 1988; Watson and Janota, 1982). Thus, almost all of the NO_x emitted is NO.

Some organic compounds from unburned fuel and from lubricating oil consumed by the engine can be trapped in crevices or cool spots within the cylinder and thus are not sufficiently available to conditions that would lead to their oxidation or pyrolysis. These compounds are emitted from the engine and either contribute to gas-phase organic emissions or to DPM emissions, depending on their volatility. Within the exhaust system, temperatures are sufficiently high that these compounds are entirely present within the gas phase (Johnson and Kittelson, 1996). Upon cooling and mixing with ambient air in the exhaust plume, some of the less volatile organic compounds can adsorb to the surfaces of the EC agglomerate particles. Lacking sufficient EC adsorption sites, the organic compounds may condense on sulfuric acid nuclei to form a heterogeneously nucleated organic aerosol (Abdul-Khalek et al., 1999).

Although not unique to DE, the high content of EC associated with typical DPM emissions has long been used by some investigators to distinguish diesel engine sources of this particle from other combustion aerosols. Diesel particles from newer HD engines are typically composed of ~75% EC (EC can range from 33% to 90%), ~20% OC (OC can range from 7% to 49%), and small amounts of sulfate, nitrate, trace elements, water, and unidentified components (Figure 2-8). Metallic compounds from engine component wear, and from compounds in the fuel and lubricant, contribute to DPM mass. Ash from oil combustion also contributes trace amounts.

Ambient $PM_{2.5}$ measured in the eastern United States is dominated by sulfate (34%), whereas ambient $PM_{2.5}$ in the western United States is dominated by OC (39%) (Table 2-3) (U.S. EPA, 1999a). Many sources contribute to ambient $PM_{2.5}$, and these sources and their relative contribution to ambient $PM_{2.5}$ can be identified on the basis of the chemical species present. The OC fraction of DPM is increasingly being used to assist investigators in identifying the contribution of diesel engine emissions to ambient $PM_{2.5}$. In particular, hopane and sterane compounds (aromatic compounds, $>C_{30}$) have been used in addition to other polycyclic aromatic hydrocarbons (PAHs) and long-chain alkanes to distinguish DPM from other mobile source PM and from ambient PM (Schauer et al., 1996; Fujita et al., 1998). Although PAH compounds make up 1% or less of DPM mass, diesel emissions have been observed to have elevated concentrations of methylated naphthalenes and methylated phenanthrene isomers compared to other combustion aerosols (Benner et al., 1989; Lowenthal et al., 1994; Rogge et al., 1993). Enrichment of benzo[*a*]anthracene and benzo[*a*]pyrene (B[*a*]P) in DPM has also been

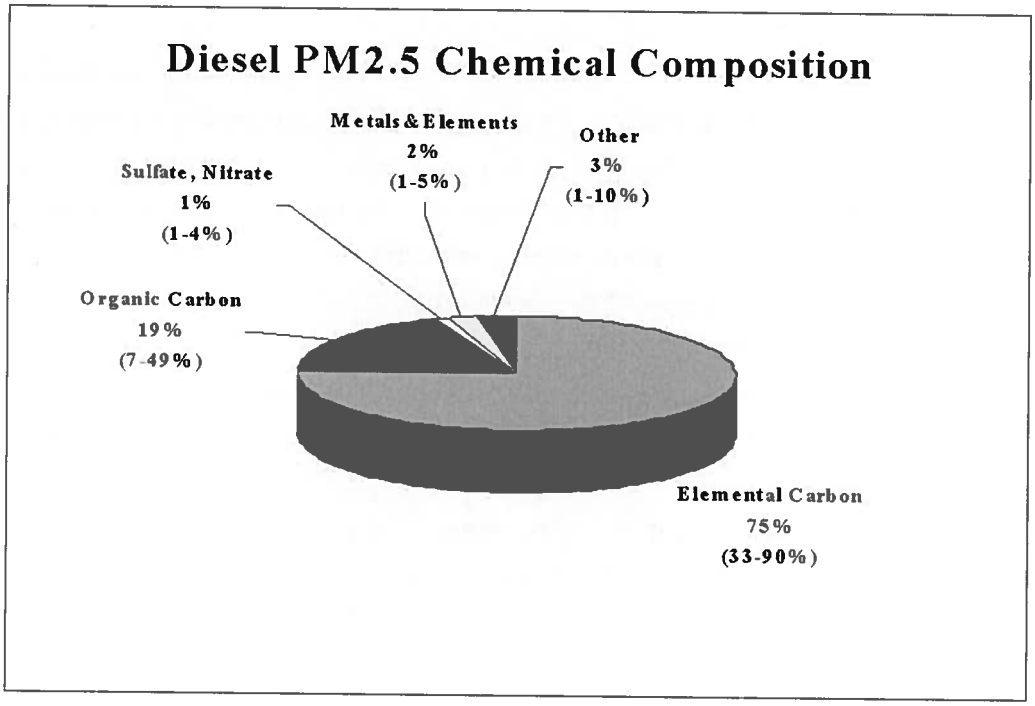


Figure 2-8. Typical chemical composition for diesel particulate matter ($PM_{2.5}$) from new (post-1990) HD diesel vehicle exhaust.

Table 2-3. Typical chemical composition of fine particulate matter

	Eastern U.S.	Western U.S.	Diesel $PM_{2.5}$
Elemental carbon	4%	15%	75%
OC	21%	39%	19%
Sulfate, nitrate, ammonium	48%	35%	1%
Minerals	4%	15%	2%
Unknown	23%	–	3%

Source: U.S. EPA, 1999a.

observed under some conditions and has been used to assess the relative contribution of DE to ambient PM.

Although specific OC species are being used to help distinguish DPM aerosols from other combustion aerosols, up to 90% of the organic fraction associated with DPM is currently classified as unresolvable complex material. Ultrafine DPM (5–50 nm) accounts for the majority (50% to 90%) of the number of particles but only 1% to 20% of the mass of DPM. A study conducted by Gertler (1999) in the Tuscarora Mountain tunnel demonstrated an increase in 20 nm diameter particles as the fraction of diesel vehicles in the tunnel increased from 13% to 78%. The contribution of nuclei-mode particles from a freeway on an ambient aerosol size distribution was reported by Whitby and Sverdrup (1980).

In summary, four main characteristics of DPM are (1) the high proportion of EC, (2) the large surface area associated with the carbonaceous particles in the 0.2 μm size range, (3) enrichment of certain polycyclic organic compounds, and (4) 50%–90% of the number of DPM particles in diesel engine exhaust are in the nuclei-mode size range, with a mode of 20 nm.

2.2.3. Diesel Emission Standards and Emission Trends Inventory

EPA set a smoke standard for on-road HD diesel engines beginning with the 1970 model year and added a carbon monoxide (CO) standard and a combined hydrocarbon (HC) and NO_x standard for the 1974 model year (Table 2-4). Beginning in the 1979 model year, EPA added a HC standard while retaining the combined HC and NO_x standard. All of the testing for HC, CO, and NO_x was completed using a steady-state test procedure. Beginning in the 1985 model year,EPA added a NO_x standard (10.7 g/bhp-hr), dropped the combined HC and NO_x standard, and converted from steady-state to transient testing for HC, CO, and NO_x emissions. EPA introduced a particulate standard for 1988 model year diesel engines using the transient test (0.6 g/bhp-hr). Transient testing involves running an engine on a dynamometer over a range of load and speed set points.

Since the 1985 model year, only the NO_x and particulate standards have been tightened for on-road diesel engines. For truck and bus engines, the particulate standard was reduced to 0.25 g/bhp-hr in 1991, and it was reduced again in 1994 for truck engines to 0.1 g/bhp-hr. For urban bus engines, the particulate standard was reduced in 1994 to 0.07 g/bhp-hr and again in 1996 to 0.05 g/bhp-hr. The NO_x standard was reduced to 4.0 g/bhp-hr in 1998 for all on-road diesel engines (bus and truck engines). The standards for nonmethane hydrocarbon (NMHC) and NO_x combined were further lowered in a 1997 rulemaking, to take effect in 2004. EPA has recently finalized a regulation that will further reduce NO_x, NMHC, and PM emissions from diesel engines starting in 2007.

Table 2-4. U.S. emission standards: HD highway diesel engines

Model year	Pollutant (g/bhp-hr)					Smoke[a]
	HC	CO	NO_x	HC + NO_x	Particulate (PM) t=truck, b=bus, ub=urban bus	
1970	—	—	—	—	—	A:40%; L:20%
1974	—	40	—	16[b]	—	A:20%; L:15%; P:50%
1979	1.5	25	—	10[b]	—	A:20%; L:15%; P:50%
1985[c]	1.3	15.5	10.7	—	—	A:20%; L:15%; P:50%
1988	1.3	15.5	10.7	—	0.60	A:20%; L:15%; P:50%
1990	1.3	15.5	6.0	—	0.60	A:20%; L:15%; P:50%
1991	1.3	15.5	5.0	—	0.25	A:20%; L:15%; P:50%
1993	1.3	15.5	5.0	—	0.25 t, 0.10 b	A:20%; L:15%; P:50%
1994	1.3	15.5	5.0	—	0.10 t, 0.07 ub	A:20%; L:15%; P:50%
1996	1.3	15.5	5.0	—	0.10 t, 0.05 ub	A:20%; L:15%; P:50%
1998	1.3	15.5	4.0	—	0.10 t, 0.05 ub	A:20%; L:15%; P:50%
2004	1.3	15.5	—	2.4 NMHC[d]	0.10 t, 0.05 ub	A:20%; L:15%; P:50%
2007		15.5	0.2	0.14 NMHC	0.01	A:20%; L:15%; P:50%

[a]Emissions measured in percent opacity during different operating modes: A=acceleration; L=lug; P=peaks during either mode.

[b]Total HC.

[c]In 1985, test cycle changed from steady-state to transient operation for HC, CO, and NO_x measurement and in 1988 for PM.

[d]Or 2.5 plus a limit of 0.5 nonmethane hydrocarbon (NMHC).

In December 1997, EPA adopted emission standards for NO_x, HC, CO, PM, and smoke for newly manufactured and remanufactured railroad locomotives and locomotive engines. The rulemaking, which took effect in the year 2000, applies to locomotives originally manufactured in 1973 or after, and any time they are manufactured or remanufactured (locomotives originally manufactured before 1973 are not regulated). Three sets of emission standards have been adopted (Tier 0, 1, and 2); they apply to locomotives and locomotive engines originally manufactured from 1973 through 2001 (Tier 0), from 2002 through 2004 (Tier 1), and in 2005 and later (Tier 2) (Table 2-5; see EPA web page at http://www.epa.gov/omswww/ or http://www.dieselnet.com/standards/ for current information on mobile source emission standards). The emissions are measured over two steady-state test cycles that represent two

Table 2-5. U.S. emission standards: locomotives (g/bhp-hr)

	Year[a]	CO	HC	NO_x	PM
Line-haul	1973-2001 (Tier 0)	5.0	1.0	9.5	0.6
Switch	1973-2001 (Tier 0)	8.0	2.1	14.0	0.72
Line-haul	2002-2004 (Tier 1)	2.2	0.55	7.4	0.45
Switch	2002-2004 (Tier 1)	2.5	1.2	11.0	0.54
Line-haul	2005 + (Tier 2)	1.5	0.3	5.5	0.20
Switch	2005 + (Tier 2)	2.4	0.6	8.1	0.24

[a]Date of engine manufacture.

different types of service, including line-haul (long-distance transport) and switch (involved in all transfer and switching operations in switchyards) locomotives.

Emission standards for nonroad equipment are not as stringent as current standards for on-road equipment and are being phased in within the next decade. Currently, Federal PM standards exist for nonroad equipment of several horsepower ratings. For equipment between 175 and 750 horsepower, the PM standard was set at 0.4 g/bhp-hr in 1996 and will decrease to 0.15 g/bhp-hr between 2001 and 2003 depending on the power rating (Table 2-6). This equipment includes construction, agricultural, and industrial such as bulldozers, graders, cranes, and tractors. The current PM standard for this equipment is only slightly lower than the 0.6 g/bhp-hr PM standard in place for on-road HD diesel engines in the late 1980s.

The EPA emission trends report (U.S. EPA, 2000a) provides emission inventories for criteria pollutants (PM_{10}, $PM_{2.5}$, SO_2, NO_x, volatile organic compounds [VOC], CO, Pb, and NH_3) from point, area, and mobile sources, which indicate how emissions have changed from 1970 to 1998. The emission trends are based on the EPA mobile source inventory models MOBILE, PART5, and the draft NONROAD model. PART5 derives particulate emission rates for HD diesel vehicles using data generated for new engine certification purposes. PART5 is currently being modified to account for deterioration, in-use emissions, poor maintenance, and tampering effects, all of which would increase emission factors. PM, SO_2, NO_x, and VOC emissions trends from the report are discussed below. Ambient urban/suburban PM samples rarely reflect the large fraction of natural and miscellaneous sources suggested by the national inventory, owing to removal of a large portion of these emissions close to their sources as well as dispersion from these sources to urban/suburban sites. The removal of natural and miscellaneous PM_{10} (largely fugitive dust) near their source is a result of the lack of inherent thermal buoyancy, low release height, and interaction with their surroundings (impaction and filtration by vegetation).

Table 2-6. U.S. emission standards for nonroad diesel equipment (g/bhp-hr)

Power rating	Model year	Pollutant (g/bhp-hr)					Smoke %[a]
		HC	CO	NO_x	NMHC + NO_x	PM	
11 < hp	2000	—	6.0	—	7.8 (ABT)	0.74 (ABT)	
	2005+	—	6.0	—	5.6 (ABT)	0.60 (ABT)	
11≤ hp < 25	2000	—	4.9	—	7.0 (ABT)	0.60 (ABT)	
	2005+	—	4.9	—	5.6 (ABT)	0.60 (ABT)	
25≤ hp < 50	2000	—	4.1	—	7.0 (ABT)	0.60 (ABT)	
	2005+	—	4.1	—	5.6 (ABT)	0.44 (ABT)	
50≤ hp <100	1998+	—	—	6.9 (ABT)	—	—	20/15/50
	2004	—	3.7		5.6 (ABT)	0.30 (ABT)	
	2008+	—	3.7		3.5 (ABT)	—	
100≤ hp <175	1997+	—	—	6.9 (ABT)	—	—	20/15/50
	2003	—	3.7	—	4.9 (ABT)	0.22 (ABT)	
	2007+	—	3.7	—	3.0 (ABT)	—	
175≤ hp < 750	1996+	1.0	8.5	6.9 (ABT)	—	0.4	20/15/50
175≤ hp < 300	2003	—	2.6	—	4.9 (ABT)	0.15 (ABT)	
	2006+	—	2.6	—	3.0 (ABT)	—	
300≤ hp < 600	2001	—	2.6	—	4.8 (ABT)	0.15 (ABT)	
	2006+	—	2.6	—	3.0 (ABT)	—	
600≤ hp < 750	2002	—	2.6	—	4.8 (ABT)	0.15 (ABT)	
	2006+	—	2.6	—	3.0 (ABT)	—	
≥750 hp	2000+	1.0	8.5	6.9 (ABT)	—	0.4	20/15/50
	2006+	—	2.6	—	4.8 (ABT)	0.15 (ABT)	

[a]Emissions measured in percent opacity during different operating modes: acceleration/lug/peaks during either mode.
ABT=average banking and trading.

Note: The standards for engines less than 50 hp also apply to diesel marine engines.

For the summaries presented here, natural and miscellaneous sources are excluded from the national PM and NO_x inventories.

From 1970 to 1998, PM_{10} emissions decreased from slightly over 12,200,000 tons to just over 2,800,000 tons (Figure 2-9). PM_{10} emissions from on-road and nonroad diesel engines increased from 320,000 tons to more than 521,000 tons during this same period, so that in 1970 diesel engine emissions were 3% of the PM_{10} inventory whereas in 1998, diesel engine emissions were 18% of the PM_{10} inventory. Diesel engines also contribute to secondary PM formation from NO_x and SO_2 emissions that are converted to nitrate and sulfate. VOCs from diesel engines also contribute to secondary organic particle formation. The contribution of secondary PM is not included in the national trends inventories cited here.

Mobile sources of PM include both gasoline- and diesel-powered on-road vehicles and a variety of nonroad equipment. Nonroad diesel engine sources include construction equipment, agricultural equipment, marine vessels, locomotives, and other sources. The EPA emission trends report (U.S. EPA, 2000a) indicates that, excluding natural and miscellaneous sources, mobile sources were responsible for 25% of PM_{10} emissions in 1998. Diesel engines (on-road and nonroad combined) were estimated to contribute 72% of mobile-source PM_{10} emissions.

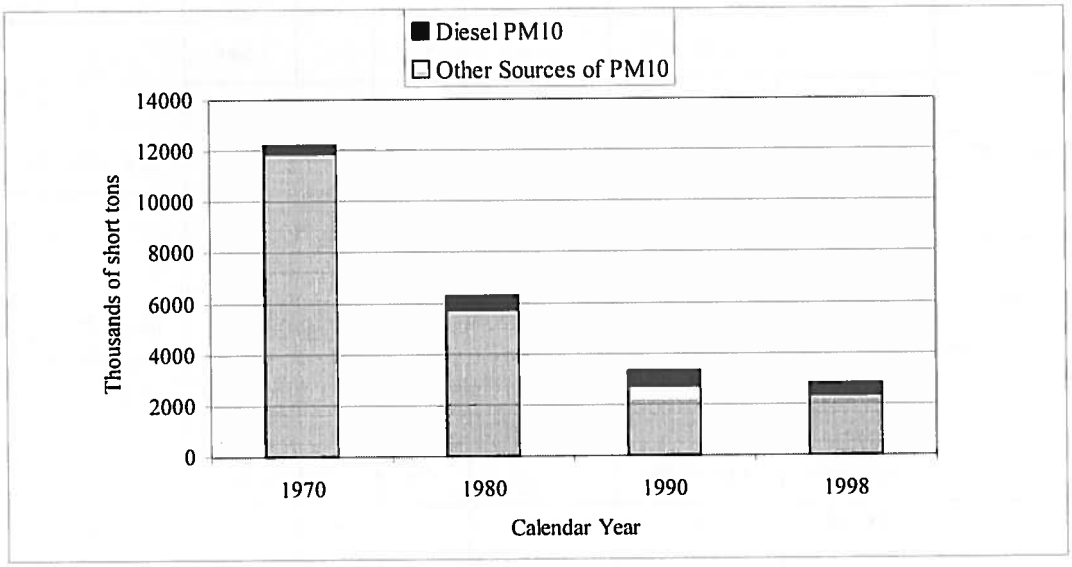


Figure 2-9. Trends in PM_{10} emissions from on-road and nonroad engines combined and other anthropogenic sources of PM_{10} from 1970 to 1998 (excludes miscellaneous and natural sources).

Source: U.S. EPA, 2000a, National Air Pollutant Emission Trends, 1900-1998.

Because of the high concentration of fine particles in engine emissions, diesel engines (on-road and nonroad combined) were estimated to contribute 77% of mobile-source $PM_{2.5}$ emissions and 23% of total $PM_{2.5}$ in 1998 (excluding natural and miscellaneous emissions). If natural and miscellaneous $PM_{2.5}$ sources are included in the inventory, diesel $PM_{2.5}$ contributes 6% to the national inventory.

Gram per mile particulate emissions from diesel vehicles are much greater than those from gasoline-fueled vehicles, accounting for the large contribution of diesel engine emissions to the national inventory in spite of the smaller number of diesel engines in use. Particulate emissions (PM_{10}) from gasoline-fueled engines decreased dramatically in 1975 with the widespread introduction of unleaded gasoline. Particulate emissions from diesel highway vehicles have decreased recently because of EPA emission standards for new model year HD diesel trucks that were first implemented in 1988 and became increasingly stringent in 1991, 1994, and 2000, as presented in Table 2-4. A decrease in on-road HD DPM emissions since the mid-1980s is confirmed by in-use vehicle testing, as described in Section 2.2.5. Because of the implementation of existing regulations, DPM emissions from on-road sources are expected to decrease 37% from 1998 to 2007; however, nonroad DPM emissions are expected to increase 15% in the same period (Figure 2-10).

The EPA emission trends report (U.S. EPA, 2000a) indicates that annual on-road vehicle PM_{10} emissions decreased from 397,200 tons to 257,080 tons from 1980 to 1998.[1] Passenger car particulate emissions decreased 53% (from 119,000 to 56,000 tons) in this timeframe, while on-road diesel vehicle PM_{10} emissions decreased 27% (from 208,000 to 152,000 tons) (Figure 2-10). Nonroad diesel engine PM_{10} emissions increased 17% (from 314,000 tons in 1980 to 69,000 tons in 1998). Emissions data for $PM_{2.5}$ are available only for the period from 1990 to 1998. Between 1990 and 1998, $PM_{2.5}$ emissions from mobile sources decreased by 14%, largely as the result of decreased on-road emissions.

From 1970 to 1998, NO_x emissions increased from 20,598,000 tons to 24,126,000 tons (Figure 2-11). NO_x emissions from on-road and nonroad diesel engines increased from 1,748,000 tons to 4,753,000 tons during this same period, so that in 1970 diesel engine emissions were 8% of the NO_x inventory while in 1998, diesel engine emissions were 20% of the NO_x

[1]Exhaust emissions constitute the majority of PM emissions from mobile sources, with tire and brake wear contributing the remainder. To compare trends estimates from past years with future projections (which are provided for exhaust emissions only), the fraction of brake and tire wear would need to be omitted from these estimates as reported in the emission trends report (U.S. EPA, 2000a). On average in the late 1990s 39% and 64% of gasoline vehicle particulate emissions originated from exhaust and 95% and 98% of on-road diesel emissions originated from exhaust for PM_{10} and $PM_{2.5}$, respectively.

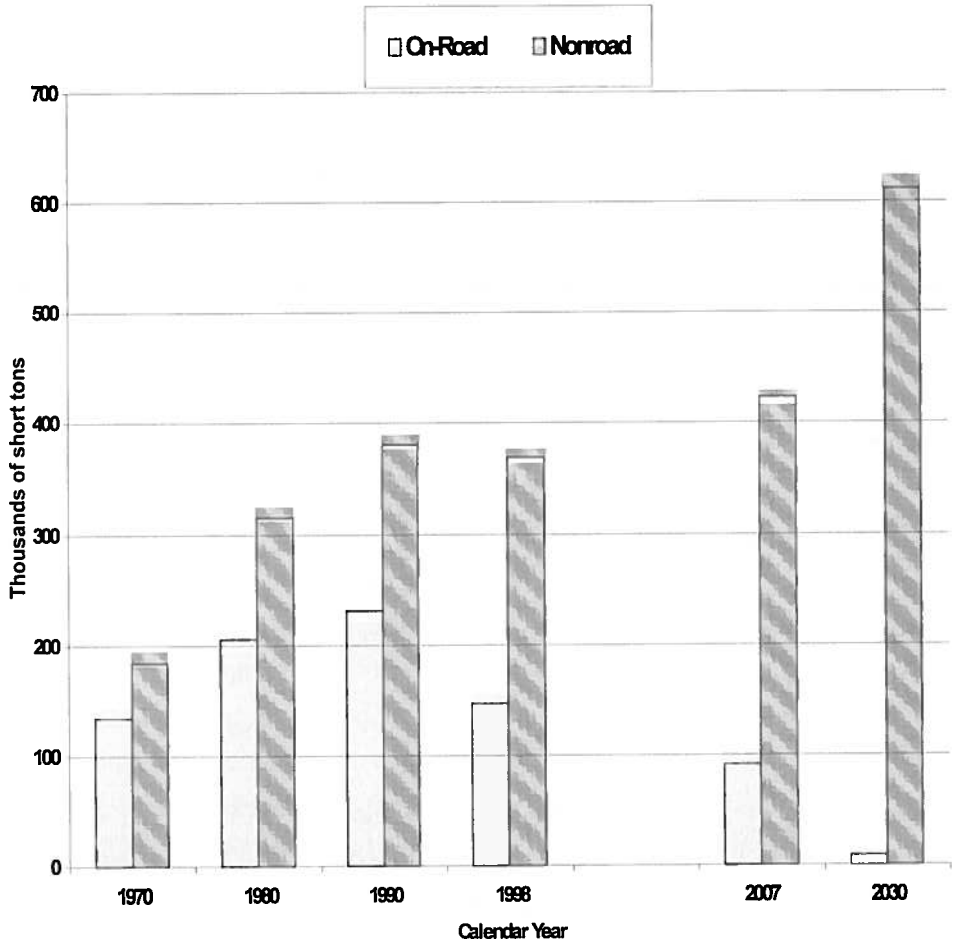


Figure 2-10. Trends in PM_{10} emissions from on-road and nonroad diesel engines from 1970 to 1998 and projections of emissions to 2007 and 2030*.

Source: U.S. EPA, 2000a, National Air Pollutant Emission Trends, 1900-1998.
*Projection to 2030 includes implementation of the recently finalized regulation "Control of Air Pollution from New Motor Vehicles: Heavy-Duty Engine and Vehicle Standards and Highway Diesel Fuel Sulfur Control Requirements" U.S. EPA, 2000b.

inventory. As mentioned above, some of this NO_x will be converted to particulate nitrate in the atmosphere, and this contribution to ambient PM is not quantified in national inventories.

In 1998, 53% of total emitted NO_x came from mobile sources, with diesels responsible for 57% of the mobile-source contribution. Overall, NO_x emissions from mobile sources have remained relatively constant over time, increasing an estimated 7% from 1980 to 1998. Whereas

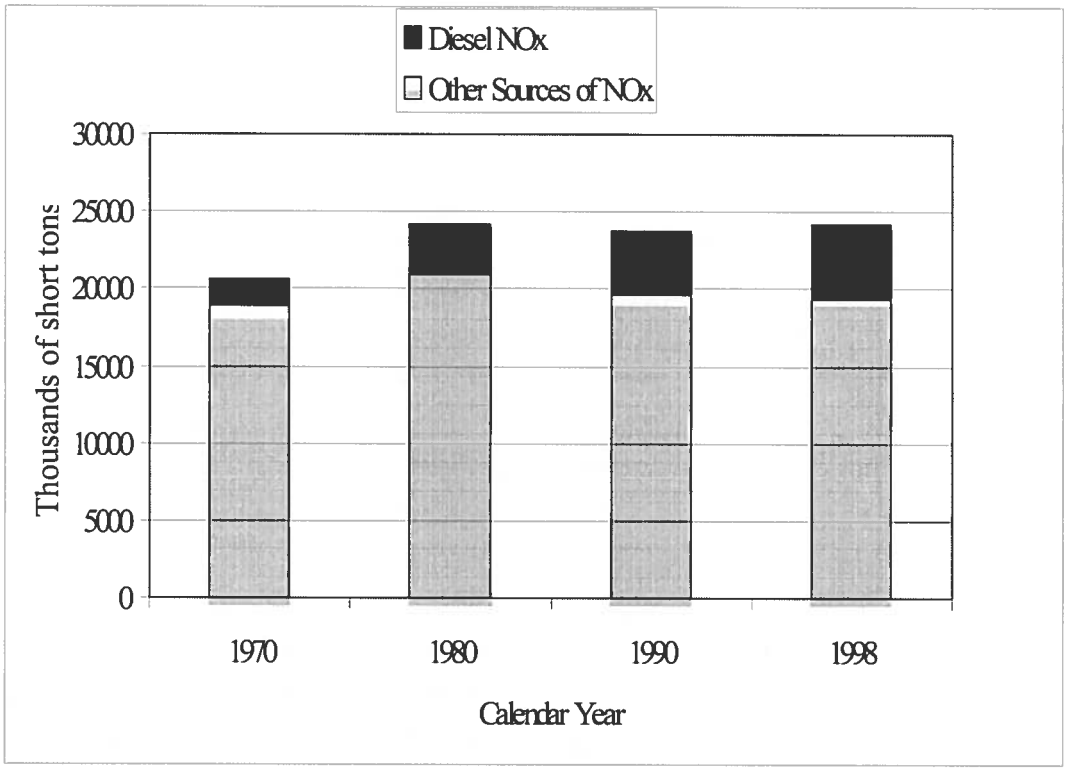


Figure 2-11. Trends in NO_x emissions from on-road and nonroad diesel engines combined and other anthropogenic sources of NO_x from 1970 to 1998 (excludes miscellaneous and natural sources).

Source: U.S. EPA, 2000a, National Air Pollutant Emission Trends, 1900-1998.

NO_x from LD gasoline vehicles decreased from 1980 to 1998, resulting in an overall decrease in on-road NO_x emissions of 9%, NO_x from diesel trucks and buses increased 7% (from 2,463,390 tons in 1980 to 2,630,120 tons in 1998), owing to the illegal use of electronic control devices that bypassed the trucks' emission control systems, as discussed in Section 2.2.5. NO_x emissions from nonroad diesel engines (including commercial marine and locomotives) have increased 46% (from 3,251,600 tons in 1980 to 4,752,800 tons in 1998) (Figure 2-12).

About 7% of SO_2 came from mobile sources in 1998, with diesels responsible for 74% of that total. EPA regulations for on-road diesel fuel sulfur content (which started in 1993) have significantly reduced SO_2 emissions from highway diesels. SO_2 emissions from highway diesel

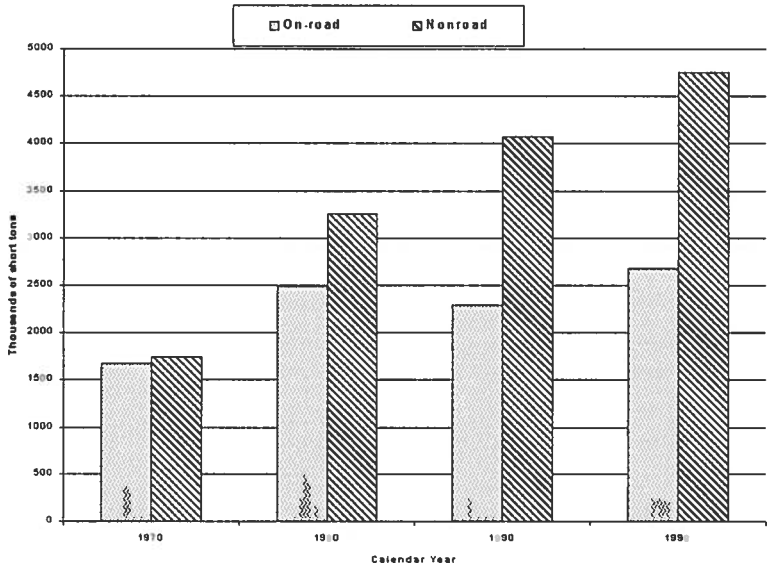


Figure 2-12. Trends in NO_x emissions from on-road and nonroad diesel engines from 1970 to 1998.

Source: U.S. EPA, 2000a, National Air Pollutant Emission Trends, 1900-1998.

engines have decreased 72% (from 303,000 tons in 1980 to 85,000 tons in 1998) (Figure 2-13). Similar trends are not apparent for nonroad diesels, although in 1998 nonroad diesel engines, excluding commercial marine vessels, emitted 785,000 tons of SO_2, accounting for 56% of mobile-source SO_2 emissions in 1998.

Diesel engines are not a large source of VOC emissions compared with gasoline engines. VOC emissions from diesel engines in 1998 were estimated at 2% of the total emissions from all sources. VOC emissions from diesel mobile sources decreased 9% (from 779,000 tons in 1980 to 721,000 tons in 1998) (Figure 2-14).

Diesel engines are also not a large source of CO emissions compared with gasoline engines. In 1998, mobile sources emitted 79% of all CO, and diesel engines accounted for 4% of the mobile-source CO. CO emissions from on-road diesel vehicles increased 34% between 1980 and 1998, during which time nonroad diesel emissions of CO increased 45% (Figure 2-15).

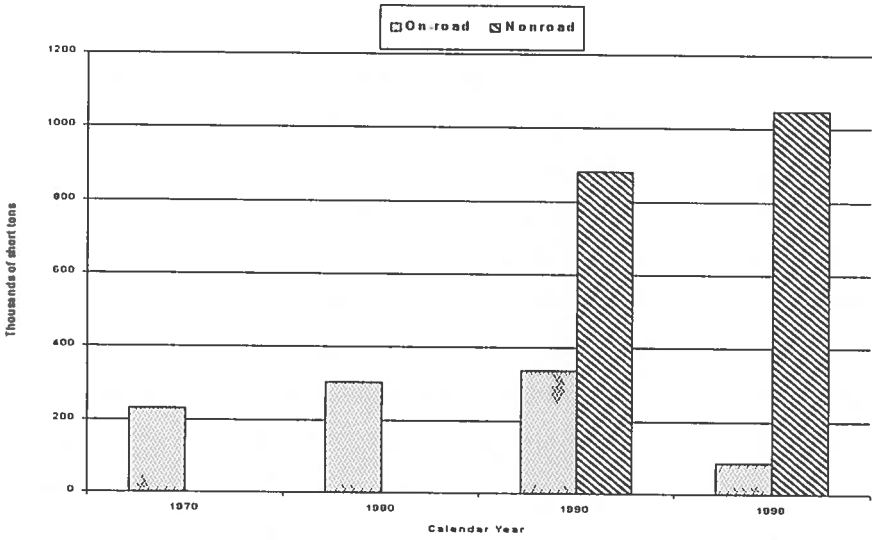


Figure 2-13. Trends in SO_2 emissions from on-road diesel engines from 1970 to 1998 and nonroad diesel engines from 1990 to 1998.

Source: U.S. EPA, 2000a, National air pollutant emission trends, 1900-1998.

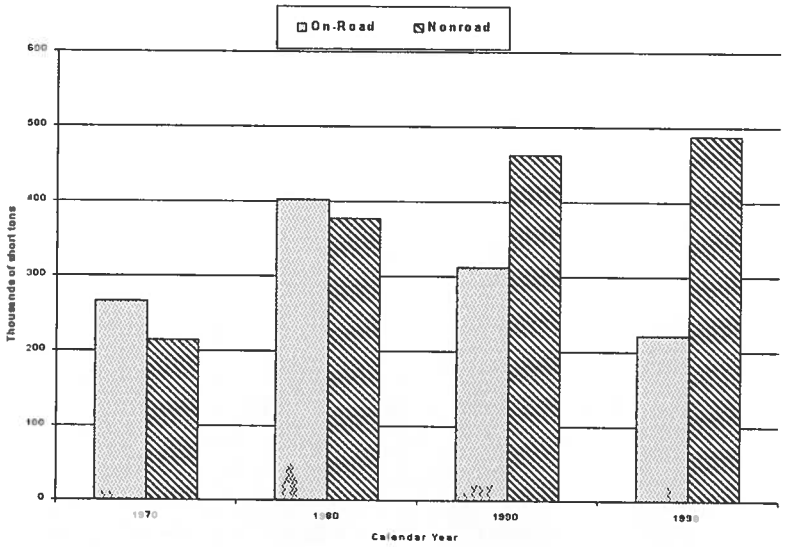


Figure 2-14. Trends in VOC emissions from on-road and nonroad diesel engines from 1970 to 1998.

Source: U.S. EPA, 2000a, National air pollutant emission trends, 1900-1998.

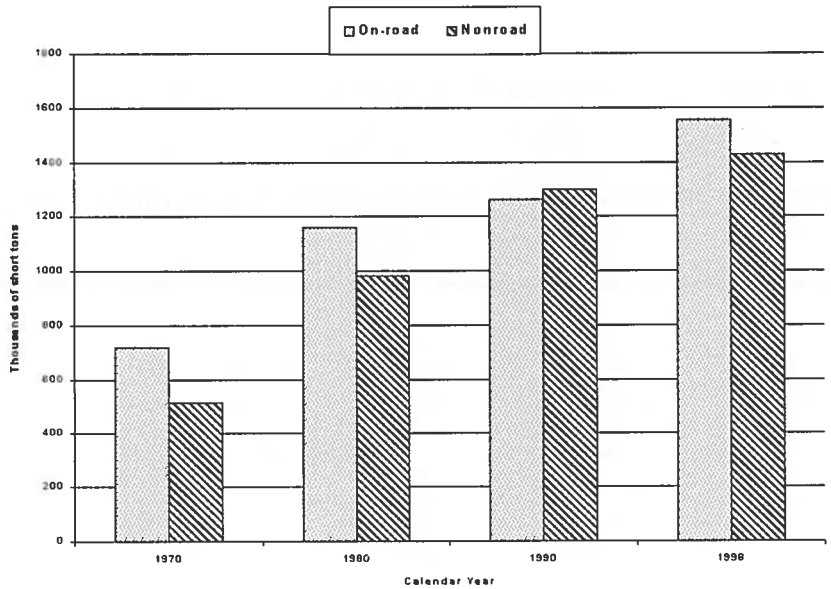


Figure 2-15. Trends in CO emissions from on-road and nonroad diesel engines from 1970 to 1998.

Source: U.S. EPA, 2000a, National Air Pollutant Emission Trends, 1900-1998.

2.2.4. Historical Trends in Diesel Fuel Use and Impact of Fuel Properties on Emissions

Use of diesel fuel increased steadily in the second half of the 20th century. According to statistics from the Federal Highway Administration (1995, 1997), in 1949 diesel fuel was approximately 1% of the total motor fuel used, and in 1995 it was about 18%. Over the same time, diesel fuel consumption in the United States increased from about 400 million gallons to 26 billion gallons per year, an increase by a factor of more than 60 (Figures 2-16 and 2-17).

The chemistry and properties of diesel fuel have a direct effect on emissions of regulated pollutants from diesel engines. Researchers have studied the NOx and DPM effect of sulfur content, total aromatic content, polyaromatic content, fuel density, oxygenate content, cetane number, and T90 on emissions of regulated pollutants. T90 is the 90% distillation point temperature. An increase in T90 has been observed to cause an increase in DPM emissions (Cunningham et al., 1990; Sienicki et al., 1990). Cetane number is a measure of the ignition quality, or ignition delay time, of a diesel fuel. The percent of cetane (less commonly referred to as hexadecane, $C_{16}H_{34}$) by volume in a blend with alpha-methylnaphthalene ($C_{10}H_7CH_3$) defines the cetane number that provides the same ignition delay time as the fuel in use.

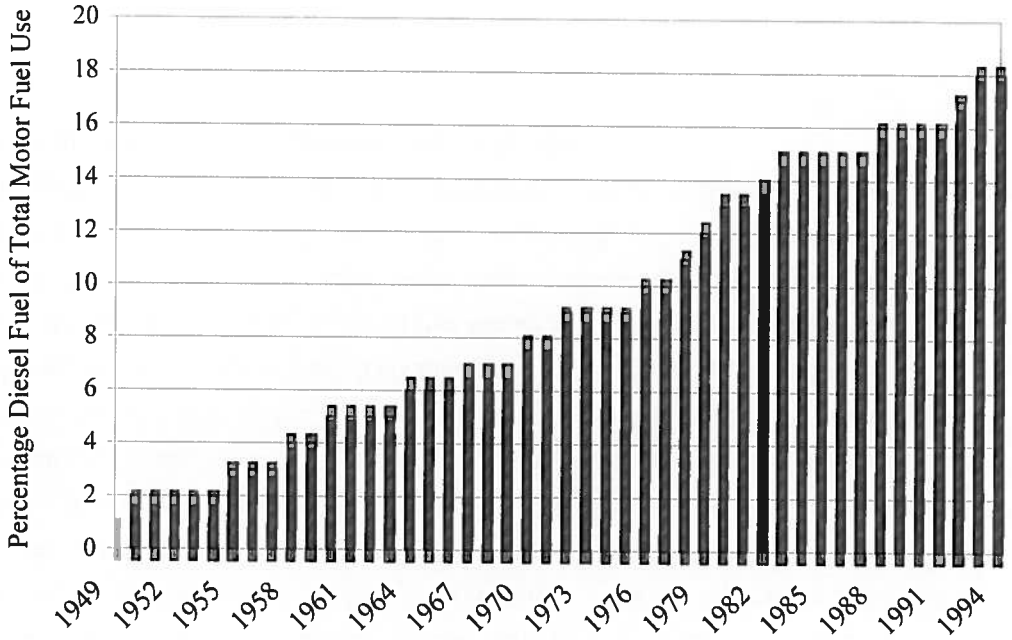


Figure 2-16. Percentage of total motor fuel use that is on-road diesel fuel since 1949.

Source: Federal Highway Administration, 1995.

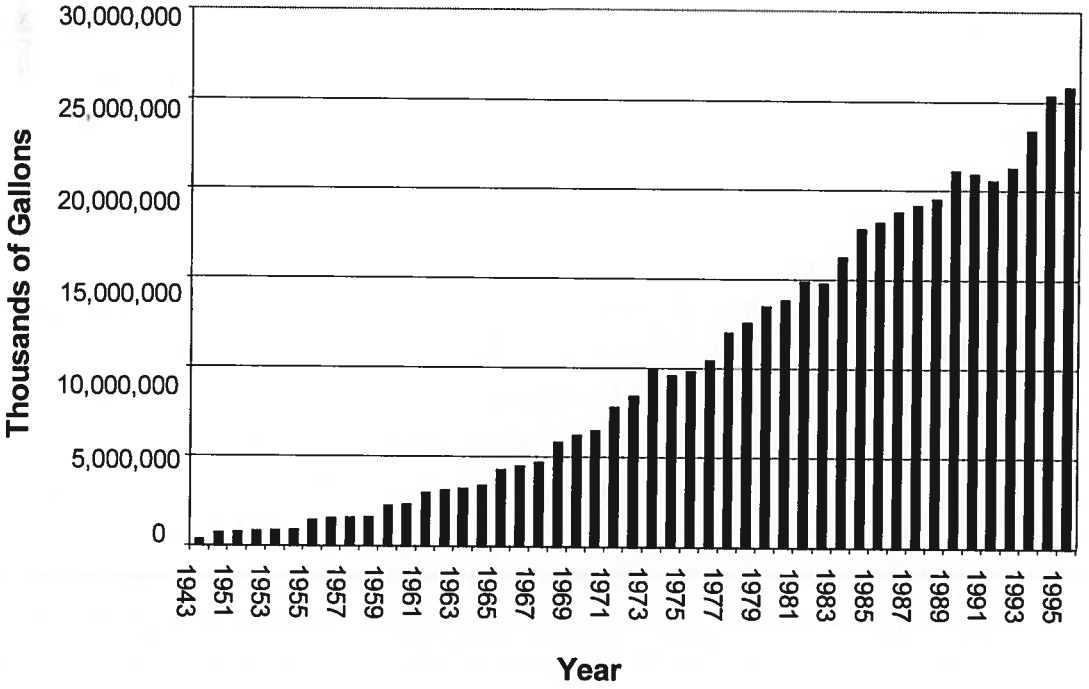


Figure 2-17. On-highway diesel fuel consumption since 1943, values in thousands of gallons.

Source: Federal Highway Administration, 1995.

Before 1993, diesel fuel sulfur levels were not federally regulated in the United States, although the State of California had such regulations. Industry practices that were in place (e.g., the ASTMD 975 specification for No. 2 oils) limited sulfur to 0.5%. During the years 1960 to 1986, fuel sulfur content showed no chronological increasing or decreasing trends and ranged from 0.23 to 0.28 wt% (NIPER, 1986). A maximum allowable on-road diesel fuel sulfur content in the United States was established at 0.05 mass % in 1993, in advance of the 1994 0.10 g/bhp-hr PM standard for HD on-highway trucks. Nationally, on-road fuels averaged 0.032% sulfur in 1994 while nonroad fuels averaged 10-fold the sulfur level of on-road fuel, or 0.32% (Dickson and Sturm, 1994). The reduction in diesel fuel sulfur reduced total DPM mass emissions through reduction of sulfate PM (primarily present as sulfuric acid).

Considerably higher sulfuric acid PM emissions are possible with DE aftertreatment systems containing precious metals (oxidation catalysts, lean NO_x catalysts, catalyzed DPM traps). At temperatures over 350 °C to 500 °C (depending on device), SO_2 in the exhaust can be oxidized to sulfuric acid (McClure et al., 1992; McDonald et al., 1995; Wall, 1998). Sulfur content remains at unregulated levels for off-highway diesel fuels and fuels used in railroad locomotives.

The chemical makeup of diesel fuel has changed over time, in part because of new regulations and in part because of technological developments in refinery processes. EPA currently regulates on-road diesel fuel and requires the cetane index (a surrogate for actual measurements of cetane number) to be greater than or equal to 40, or the maximum aromatic content to be 35% or less (CFR 40:80.29). EPA recently finalized a regulation that will limit the sulfur content of on-road diesel fuel to 15 ppm starting in 2006 (U.S. EPA, 2000b). California has placed additional restrictions on the aromatic content of diesel fuel (California Code of Regulations, Title 13, Sections 2281-2282) and requires a minimum cetane number of 50 and an aromatics cap of 10% by volume, with some exceptions for small refiners and alternative formulations as long as equivalent emissions are demonstrated. Diesel fuel from larger refiners is limited to 10% aromatic content, and for three small refiners (a small fraction of diesel sales) to 20% aromatic content. The refiners can also certify a fuel with higher aromatic content as being emissions-equivalent to the 10% (or 20%) aromatic content fuels by performing a 7-day engine dynamometer emissions test. This method is chosen by most, if not all, California refiners, and so a typical California diesel fuel has an aromatic content above 20%. Emissions equivalence has been obtained through use of cetane enhancers, oxygenates, and other proprietary additives. Nonroad diesel fuel is not regulated, and consequently, cetane index, aromatic content, and sulfur content vary widely with nominal values for cetane number around 43, 31% aromatics, and sulfur approximately 3,000 ppm.

The average cetane number of U.S. diesel fuel declined steadily from 50.0 to 45.1, or about 0.2% per year, from 1960 to 1986 (NIPER, 1986). The decline in cetane number was likely accompanied by an increase in aromatic content and density (Lee et al., 1998). A number of EPA-sponsored studies refer to fuels with nominally 22% aromatics content as "national average fuel" during the 1970s (Hare, 1977; Springer, 1979), whereas by the 1980s a so-called national average fuel contained 30% aromatics (Martin, 1981a,b). Shelton (1979, 1977) has reported a trend of increasing T90 from 1960 through the late 1970s, which is consistent with increasing density, aromatic content, and polyaromatic content. Unfortunately, aromatic content was not commonly measured before the 1980s.

Studies measuring the emissions impact of changes in cetane number and aromatic content for roughly 1990 model year engine technology find that increasing the aromatic content from 20% to 30%, with an accompanying decrease in the cetane number from 50 to 44, results in a 2% to 5% increase in NO_x and a 5% to 10% increase in total DPM (McCarthy et al., 1992; Ullman et al., 1990; Sienicki et al., 1990; Graboski and McCormick, 1996). These ranges may be reasonable upper bounds for the effect of changes in fuel quality on NO_x and DPM emissions during the years 1960–1990.

In the northern United States during wintertime, on-road No. 2 diesel may contain some percentage of No. 1 diesel to improve cold-flow properties. Discussions with refiners indicate that a typical wintertime No. 1 diesel blending level is 15 volume %; however, this number must be taken as a rough estimate. Blending of No. 1 may lower the aromatic content, resulting in improved emissions performance. Nationally, on-highway No. 1 fuels averaged 17% aromatic content in 1994 (Dickson and Sturm, 1994). Thus, there may also be some small but perceptible seasonal changes in emissions from diesel engines.

Railroad-grade diesel fuel is currently unregulated. Typically, railroad-grade diesel fuel is a blend of approximately 10% on-road fuel and 90% nonroad diesel fuel. There are no recent data on the composition of railroad-grade diesel fuel. Somewhat dated diesel fuel oil surveys (Shelton, 1979) reported that railroad-grade diesels had lower cetane number, higher density, and higher T90. Also, the cetane index for these fuels can be as much as 9 cetane units higher than the cetane number, an indication of a high aromatic content in railroad-grade diesels.

Fuel chemistry is also important for emission of particle-associated PAHs. In studies performed over more than a decade, Williams and Andrews of the University of Leeds have shown that the solvent-extractable PAHs from diesel particulate originate almost entirely in the fuel (Williams et al., 1987; Andrews et al., 1998; Hsiao-Hsuan et al., 2000). The PAH molecules are relatively refractory, so a significant fraction survive the combustion process and condense onto the DPM. These studies have been confirmed by other research groups (Crebelli et al., 1995; Tancell et al., 1995). There is a consensus among these researchers that

pyrosynthesis of PAHs occurs only at the highest temperature operating conditions in a diesel engine. Under these conditions, most of the DPM and other pyrolysis products are ultimately burned before exiting the cylinder. These results indicate that emissions of PAHs are more a function of the PAH content of the fuel than of engine technology. For a given refinery and crude oil, diesel fuel PAH correlates with total aromatic content and T90. Representative data on aromatic content for diesel fuels in the United States do not appear to be available before the mid-1980s. However, the decreasing trend in cetane number, increasing trend in T90, and the increasing use of light cycle oil from catalytic cracking beginning in the late 1950s suggest that diesel PAH content has increased over the past 40 years. Because PAHs have been implicated as one potential contributing component to the observed toxicity of DE, changes in PAH content of diesel fuel over time, as well as differences between diesel fuels used in different applications (on-road, nonroad, locomotive), may influence the hazard observed in exposed populations from different occupations. However, such a relationship would be difficult to differentiate in an epidemiologic study because there are several other properties of DE that may be contributing to the observed toxicity. Historical trends in PAH-measured emissions are discussed in Section 2.2.8.2.

2.2.5. Chronological Assessment of Emission Factors

2.2.5.1. *On-Road Vehicles*

Numerous studies have been conducted on emissions from in-use on-road HD diesel vehicles. HD vehicles are defined as having a rated gross vehicle weight (GVWR) of greater than 8,500 lb, and most over-the-road trucks have a GVWR of 80,000 lb. Emissions of regulated pollutants from these studies have been reviewed (Yanowitz et al., 2000); the review findings, which encompass vehicles from model years 1976 to 1998, are summarized below. In addition, a large amount of engine dynamometer data on HD diesel engines have been published since the mid-1970s. These data are used below to confirm and expand upon the findings from in-use vehicle testing.

Figure 2-18 shows chassis dynamometer data for more than 200 different vehicles (approximately one-half of which are transit buses), reported in 20 different published studies, as well as a large amount of additional data collected by West Virginia University (Yanowitz et al., 1999; Warner-Selph and Dietzmann, 1984; Dietzmann et al., 1980; Graboski et al., 1998a,b; McCormick et al., 1999; Clark et al., 1995, 1997; Bata et al., 1992; Brown and Rideout, 1996, Brown et al., 1997; Dunlap et al., 1993; Ferguson et al., 1992; Gautam et al., 1992; Katragadda

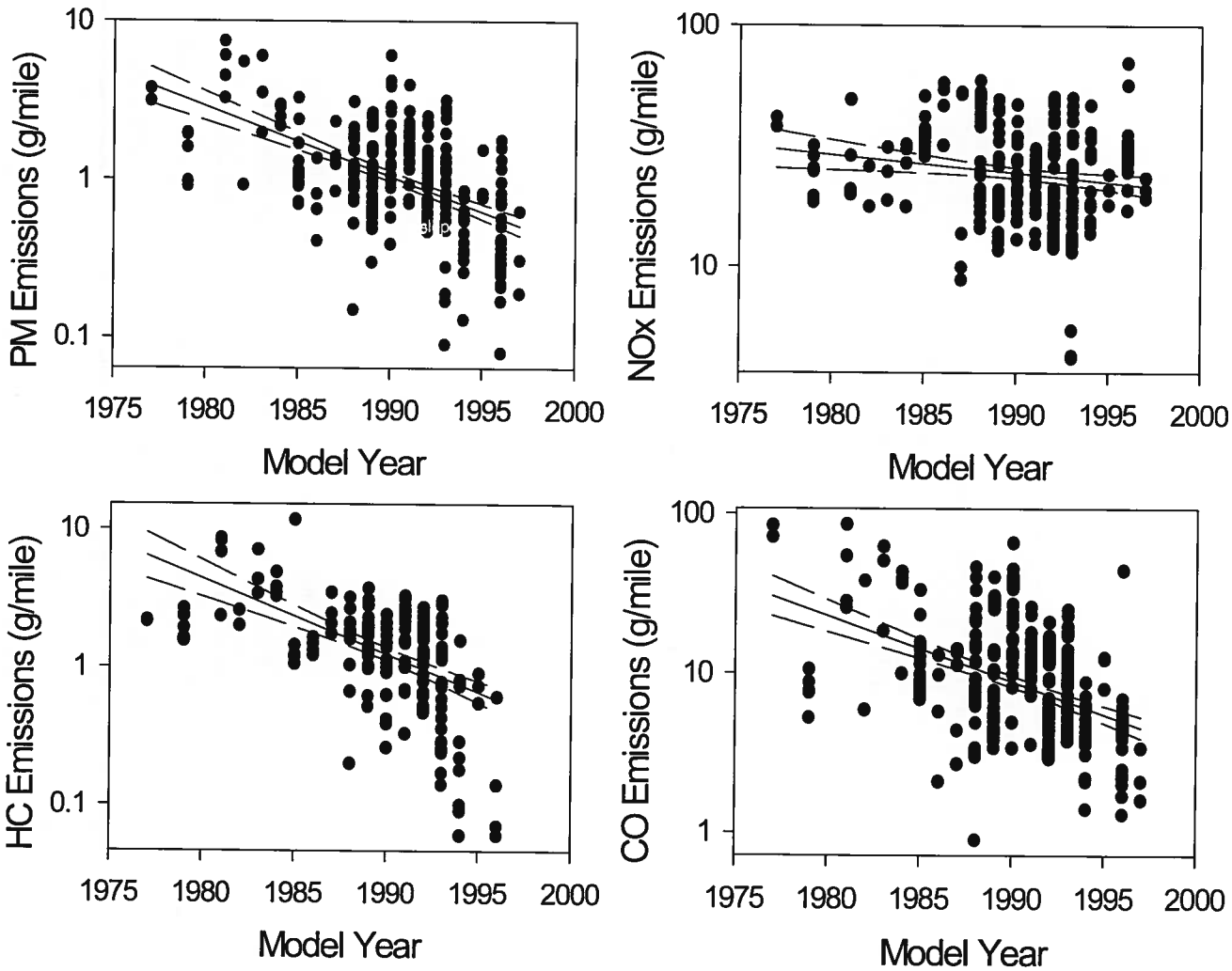


Figure 2-18. Model year trends in PM, NO_x, HC, and CO emissions from HD diesel vehicles (g/mile).

Source: Yanowitz et al., 2000.

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et al., 1993; Rideout et al., 1994; Wang et al., 1993, 1994; Williams et al., 1989; Whitfield and Harris, 1998; West Virginia University data available on the World Wide Web at www.afdc.nrel.gov). The results from vehicles tested more than once using the same test cycle, and without any additional mileage accumulated between tests, are averaged and reported as one data point. Buses were tested using the Central Business District (CBD) cycle, while most trucks were tested using the Urban Dynamometer Driving Schedule (UDDS), also known as the Schedule 1d cycle. Some of the trucks were tested using the West Virginia 5-peak cycle, which generates considerably lower g/mi emissions than the CBD or UDDS (Yanowitz et al., 1999). Emissions results from vehicles tested under different test cycles or at different points in the engine's life cycle have been reported as separate data points. Note that all NO_x mass emissions data are reported as equivalent NO_2. Table 2-7 compares the make-up of the fleet of trucks that was tested with the in-use truck fleet according to the 1997 Vehicle Inventory and Use Survey (U.S. Bureau of the Census, 1999a). The tested fleet is mostly vehicles in the 33,000-60,000 lb range. Analysis of the tested fleet also shows that the model year distribution is skewed toward newer vehicles. The 1997 Vehicle Inventory and Use Survey indicates a flat distribution with roughly the same number of in-use vehicles for each of the model years in the decade preceding 1997. The 1992 Truck Inventory and Use Survey (U.S. Bureau of the Census, 1995) shows the same trend, as shown in Figure 2-1. Analysis of odometer mileage for the tested fleet shows that 45% of the vehicles had less than 50,000 miles at the time of testing. Only 10% of the vehicles had more than 250,000 miles. Although the mileage distribution of the in-use fleet is unknown, it seems unlikely to be as heavily weighted to low-mileage vehicles. Because of the relatively low mileage of most of the vehicles tested, deterioration of emissions may not be reflected in the

Table 2-7. Comparison of in-use truck fleet with truck fleet tested on chassis dynamometer, percent of total vehicles

Class	In-use trucks, 1995 census	Tested trucks
3	17.7	1
4 & 5	13.3	0
6 & 7	25.0	17
8A	20.9	52
8B	23.1	30

results. Yanowitz and co-workers (2000) report that average emissions of regulated pollutants for vehicles of the different classes listed in Table 2-7 are approximately the same. This is clearly a reflection of the small number of vehicles in the lighter weight classes for this dataset, but it also indicates no real difference in emissions for vehicles in Classes 6–8. The data are mainly for vehicles of 19,500 lb and greater GVWR (Classes 6 and 7 and heavier), and predominantly for vehicles of 33,000 lb and greater GVWR (Class 8 trucks and buses).

Figure 2-18 shows emissions trends in g/mi. Least-squares linear regressions and 95% confidence intervals are plotted on each graph and yield the following equations for predicting emissions trends (applicable to the years 1976–98):

$$\text{Log } NO_x \text{ (g/mile)} = (\text{Model year} * -0.008) + 16.519 \quad R^2 = 0.024 \tag{2-1}$$

$$\text{Log PM (g/mile)} = (\text{Model year} * -0.044) + 88.183 \quad R^2 = 0.28 \tag{2-2}$$

$$\text{Log HC (g/mile)} = (\text{Model year} * -0.055) + 109.39 \quad R^2 = 0.27 \tag{2-3}$$

$$\text{Log CO (g/mile)} = (\text{Model Year} * -0.041) + 82.876 \quad R^2 = 0.22 \tag{2-4}$$

As shown in Figure 2-18, changes in NO_x emissions have been relatively small, with an emission rate averaging about 26 g/mi. The data reported in Figure 2-18 are real-world, in-use emissions measurements and therefore more accurately reflect emission factors than engine test data during this period. There are two potential causes for the relative constancy of NO_x emissions as described by Figure 2-18. The first is emissions deterioration due to engine wear. Weaver and Klausmeier (1988) have shown that diesel engine deterioration results in lower NO_x emissions and higher DPM emissions, and this finding has recently been confirmed by McCormick and co-workers (2000). Wear of mechanical devices that limit smoke, fuel pumps, and fuel injectors alters the effective injection timing to decrease NO_x. Because deterioration is more a function of maintenance than vehicle age or mileage, deterioration introduces a wide range in NO_x emission factors measured in the chassis dynamometer studies. The lack of a decreasing trend in NO_x emissions can also be attributed to the use of illegal emissions control devices that bypassed the trucks' emission control systems under some driving conditions such as steady-state cruise. EPA has reached a settlement with the diesel engine manufacturers to discontinue use of these devices. The illegal devices produced low NO_x emissions on the transient test (HD FTP) but operated in a high-NO_x/high-fuel-economy mode in use under highway cruise conditions.

Figure 2-19 shows engine certification data for NO_x emissions reported in the many studies that have employed the transient test over the past 25 years. The engine testing data are also listed in Table 2-8. The data compiled in Figure 2-19 show a significant decline in NO_x

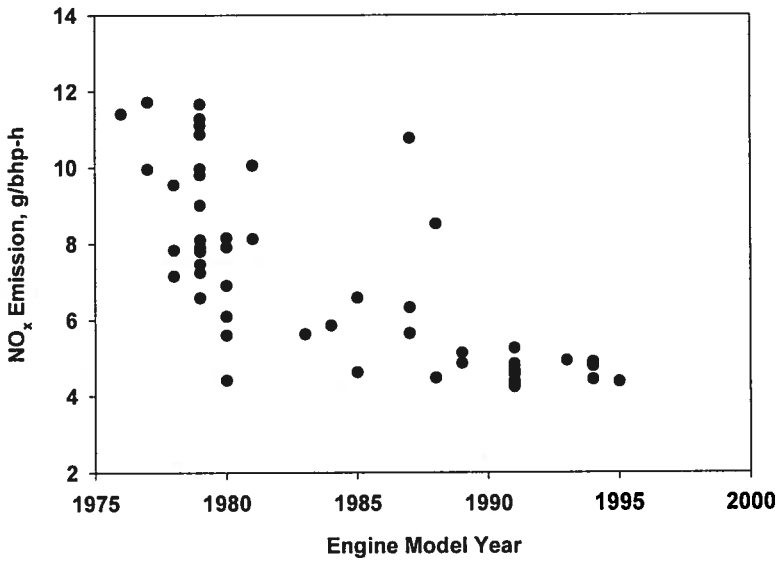

Figure 2-19. Diesel engine certification data for NO_x emissions as a function of model year.

Source: Data are from the transient test results provided in Table 2-8.

emissions, and all engines would appear to meet the regulatory standards for their year of manufacture because of the illegal emissions devices. From 1980 to 1997, the EPA emissions trends report (U.S. EPA, 1998a) predicted a decline in NO_x emissions from HD diesel vehicles because these data are based on engine test data. The emissions trend includes the growth in vehicle miles traveled over time as well as changes in emission factors. The more recent trends inventory (U.S. EPA, 2000a, discussed earlier) includes emission from the illegal emissions devices and accordingly demonstrates a slight increase in NO_x emissions from on-road HD diesel vehicles from 1990 to 1998.

DPM, CO, and THC emissions, although widely variable within any model year, have shown a pronounced declining trend (Figure 2-18). DPM emissions from chassis dynamometer tests decreased from an average of 3-4 g/mi in 1977 to an average of about 0.5 g/mi in 1997, suggesting a decrease in DPM emissions of a factor of about 6. Note that these data are for vehicles or engines tested on in-use or industry-average fuel at the time they were tested. Indications are that the observed decline in DPM is caused primarily by changes in engine

Table 2-8. Diesel engine emissions data from engine dynamometer tests

Reference	Engine[a]	Year	Test[b]	NO_x g/bhp-hr	PM g/bhp-hr	CO g/bhp-hr	THC g/bhp-hr	SOF g/bhp-hr	SOF Meth[c]	Total aldehyde, mg/bhp-hr	B[*a*]P (PAH) ug/bhp-hr[d]	1-NP (NPAH) ug/bhp-hr[e]
Hare, 1977	Cat 3208 (NA)	1976	SS	7.98	0.871	4.04	1.11	0.103	c-hexane		0.76	
	DDC 6V71 (blower)	1976	SS	10.24	1.92	6.55	0.71	0.937	c-hexane		0.24	
Springer, 1979	Mack ETAY(B)673A (DI, TC,AC)	1977	SS	6.613	0.61	1.588	0.476	0.098	Benz/cyc	65	2.23	
	Cat 3208 (EGR, NA)	1977	SS	3.747	2.21	6.200	1.163		Benz/cyc	161	1.72	
	Cat 3406 (DI, TC, AC)	1977	SS	9.79	0.35	2.34	0.35	0.063	Benz/cyc	73	0.15	
	Cat 3406 (DI, TC, AC, EGR)	1977	SS	5.49	0.93	4.81	0.17	0.181		80	0.08	
	Cat 3406 (IDI, TC, AC)	1977	SS	5.14	0.28	1.26	0.12	0.031	Benz/cyc	80	0.11	
	DB OM-352A (DI, TC, AC)	1977	SS	8.93	0.56			0.190	Benz/cyc	280	0.87	
	DB OM-352A (DI, NA)	1977	SS	7.46	0.99			0.287	Benz/cyc	280	1.07	
Perez, 1980	Cat (DI, NA)	1978	SS	8.12	0.77	5.92	0.77	0.19	DCM		1.08	
	Cat (DI, EGR)	1978	SS	5.16	1.21	5.37	0.57	0.079	DCM		4.34	
	Cat (DI, TC, AC)	1978	SS	7.66	0.33	2.20	0.27	0.037	DCM		0.34	
Martin, 1981a	Cat 3208	1978	T	7.83	1.06							
	Cummins NTC350	1976	T	11.41	0.81							
	DDC 6V92T (2S)	1978	T	9.55	0.72							
	Cummins NTCC350	1979	T	6.58	0.52							
	DDC 8V71N (2S)	1978	T	7.15	0.92							
	DDC 6V92TA (2S)	1979	T	7.80	0.65							
	IH DTI466B	1979	T	7.46	0.48							
	Mack ETAY(B)673A	1979	T	9.01	0.77							
	Mack ETSX676-01	1980	T	6.90	0.85							
	Cummins VTB-903	1979	T	8.10	0.53							
	Cat 3406	1979	T	11.28	0.69							
	Cat 3406PCTA	1979	T	7.24	0.49							
	Cummins BigCam NTC350	1979	T	9.97	0.54							
	IH DT466	1979	T	7.91	0.71							
	DDC 6V92TA (2S)	1979	T	11.66	0.73							
	DDC 8V71TA (2S)	1979	T	9.81	0.51							
	Cummins NTC290	1979	T	11.10	0.78							
	Cummins NH-250	1979	T	10.87	0.97							
Martin, 1981b	Cummins VTB-903	1980	T	5.59	0.67	2.0	2.23	0.228	DCM			
	DDC 8V71TA (2S)	1980	T	7.91	0.44	2.28	0.73	0.176	DCM			
	IH DTI466B	1980	T	4.41	0.62	2.35	0.87	0.186	DCM			
Ullman et al., 1984	DDAD 6V-71 (2S)	1980	T	6.09	0.56	3.86	1.42	0.298	DCM	23	--	
Martin, 1984	Cummins NTC300	1981	T	8.13	0.45	2.70	1.36	--				
Barry et al., 1985	Cat 3406B	1985	T	6.58	0.48	2.1	0.5	0.061	DCM	70	1	
	DDC 8V-92 TA (2S)	1980	T	8.15	0.45	2.61	0.53	--				

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Table 2-8. Diesel engine emissions data from engine dynamometer tests (continued)

Reference	Engine[a]	Year	Test[b]	NO_x g/bhp-hr	PM g/bhp-hr	CO g/bhp-hr	THC g/bhp-hr	SOF g/bhp-hr	SOF Meth[c]	Total aldehyde, mg/bhp-hr	B[*a*]P (PAH) ug/bhp-hr[d]	1-NP (NPAH) ug/bhp-hr[e]
			SS	6.64	0.36	1.83	0.38	0.0255				
Enga et al., 1985	DDC 8V-71 TAC (2S)	1984	T	5.85	1.26	2.99	1.48	--		--	--	
Baines, 1986	Cummins NTCC-400	1985	T	4.62	0.55	3.21	0.53					
Wachter, 1990	Iveco 8460	1991	T		0.22			0.0957	?			
McCarthy et al., 1992	Navistar DTA466 ES210	1993	T	4.93	0.082	1.3	0.28	0.0237	SFE			
Perez and Williams, 1989	Engine 1	1982	T		0.93			0.179	DCM		26	0.83
	Engine 2	1982	T		0.86			0.145	DCM		5.8	--
	Engine 3	1982	T		0.59			0.185	DCM		4.9	0.89
	Engine 4	1982	T		0.96			0.325	DCM		26	1.2
	Engine 5	1982	T		1.06			0.076	DCM		5.3	--
	Engine 6	1982	T		0.88			0.344	DCM			
Needham et al., 1989	Average of 16 engines	1988	T		0.37			0.12	DCM			
	Average of 3 engines	1991	T		0.24			0.10	DCM			
Kreso et al., 1998	Cummins L10-300	1988	SS	5.15	0.103		0.26	0.030	DCM			
	Cummins L10-310	1991	SS	4.70	0.035		0.067	0.022	DCM			
	Cummins M11-330E	1995	SS	3.82	0.037		0.16	0.016	DCM			
Bagley et al., 1998	Cat 3304 (IDI, NA) non-road	1983	SS		0.56			0.319	Benz/cyc		1.5(133)	2.2
Graboski, 1998b (and references therein)	DDC 6V-71N-77 (MUI, 2S)	1977	T	9.96	0.83	3.59	2.01	0.729	DCM			
	DDC 6V-92TA-91 (DDECII)	1991	T	4.23	0.197	1.51	0.72	0.0788	?			
	DDC-6V-92TA-87 (2S)	1987	T	10.77	0.59	0.71	--	--				
	DDC-6V92TA-83 (MUI, 2S)	1983	T	5.62	0.265	1.19	0.435	0.133	DCM			
	DDC 6V-92TA -88 (DDECII, 2S)	1988	T	8.52	0.2	1.6	0.6	0.116	Tol/EtOH			
	DDC 6V-92TA-91 (DDECII, 2S)	1991	T	4.4	0.276	1.65	0.42	0.07	Tol/EtOH			
	DDC 6V-71N-77 (MUI, 2S)	1977	T	11.72	0.282	3.18	0.86	0.212	DCM			
	DDC 6V-92TA-81/89 (MUI, 2S)	1981	T	10.06	0.268	2.16	0.42	0.144	DCM	--	--	
	DDC 6V-92TA-91 (DDECII, 2S)	1991	T	4.84	0.227	1.51	0.44	--		--	--	
	DDC 6V-92TA-89 (DDECII, 2S)	1989	T	4.855	0.338	2.499	0.526	--		--	--	
	DDC Series 60-91 DDECII	1991	T	4.635	0.300	4.458	0.164	--				
	Cummins L-10-87 (MUI)	1987	T	5.64	0.309	2.33	0.89	--				
	DDC Series 60-91 (DDECII)	1991	T	4.68	0.220	2.26	0.08	0.066	DCM			
	Cummins N-14-87 (MUI)	1987	T	6.32	0.369	2.20	0.58	0.100	?			
	DDC Series 60-89 (DDECII)	1989	T	5.128	0.252	4.008	0.154	--				--
	DDC Series 60-91 (DDECII)	1991	T	4.303	0.182	2.004	0.392	0.061	Tol/EtOH	--	--	
	Cummins B5.9	1995	T	4.37	0.106	1.47	0.30	0.05	DCM		0.24((18.5)	
Spreen et al., 1995	Navistar DTA466	1994	T	4.779	0.090	0.989	0.181	0.035	DCM	26		
Norbeck et al., 1998b	Cummins L10	1991	T	4.77	0.224	2.26	0.53	--		80	20(1725)	1.95(4.92)
	DDC Series 60	1994	T	4.89	0.112	1.402	0.065	0.043	DCM	17		
Sienicki et al., 1990	Navistar DTA466	1991	T	5.25	0.22	--	0.23	0.05	DCM			

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Table 2-8. Diesel engine emissions data from engine dynamometer tests (continued)

Reference	Engine[a]	Year	Test[b]	NO_x g/bhp-hr	PM g/bhp-hr	CO g/bhp-hr	THC g/bhp-hr	SOF g/bhp-hr	SOF Meth[c]	Total aldehyde, mg/bhp-hr	B[*a*]P (PAH) ug/bhp-hr[d]	1-NP (NPAH) ug/bhp-hr[e]
Ullman et al., 1990	DDC Series 60	1991	T	4.552	0.188	2.102	0.508	--				
Kado et al., 1998	Cat 3406E	1997	T						DCM		0.07(30)	0.34
Ullman, 1988	Cummins NTCC400	1988	T	4.47	0.42	2.22	0.53					
Mitchell et al., 1994	DDC Series 60	1994	T	4.43	0.111	2.17	0.22	0.021	DCM	34	(141)	0.04(0.12)
	Navistar DTA466	1994	T	4.86	0.099	1.10	0.34	0.046	DCM	56	0.11(242)	0.3(0.6)
Tanaka et al., 1998	Unknown	1994	SS	4.934	0.143	0.807	0.352	0.036	DCM		.076	
Rantanen et al., 1993	Scania	1990	SS	9.30	0.157			0.031	DCM			
	Valmet	1990	SS	8.67	0.157							
	Volvo	1990	SS	9.87	0.262							
	Volvo	1995	SS	4.56	0.135							

[a]NA=naturally aspirated. TC=turbocharged (engines not designated as NA or TC are turbocharged). AC=aftercooled. DI=direct injection. IDI=indirect injection. EGR=exhaust gas recirculation. 2S=two-stroke (engines not designated as 2S are four-stroke). MUI=mechanical unit injector (not electronically controlled). DDEC=Detroit Diesel Corporation's engine control module (electronic control).
[b]SS=various single or multimode steady-state tests. T=heavy-duty FTP (transient test).
[c]SOF extraction method. SFE=Supercritical fluid extraction. All others by Soxhlet extraction using the indicated solvents (? for unreported). DCM=dichloromethane. Tol/EtOH=toluene/ethanol mixture. Benz/cyc=benzene/cyclohexane mixture. C-hexane=cyclohexane.
[d]Number in parentheses is the total PAH emission obtained by summing emissions of all PAHs reported.
[e]Number in parentheses is the total NPAH emission obtained by summing emissions of all NPAHs reported.

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technology that often result from emission standards, as well as by the lowering of on-road diesel fuel sulfur content in 1993.

As the discussion above indicates, there is a reasonable amount of data upon which to base emission factor estimates for late 1970s and later HD vehicles. However, very little transient test data are available on engines earlier than the mid-1970s. The limited data available from six pre-1976 vehicles tested using the transient cycle suggests that PM emission rates ranged from 1.6 g/mi to 9.0 g/mi, which is a substantially greater range than in post-1976 engines (Fritz et al., 2001).

Although a substantial decreasing trend in DPM emissions from in-use chassis dynomometer testing and engine testing (Figure 2-20) is evident, these data reflect a wide range in emission factors within any given model year. For example, emission factors for model year 1996 range from less than 0.1 g/mi to more than 1 g/mi (Yanowitz et al., 2000; Graboski et al., 1998b). The high variability in DPM emissions measured in the chassis dynamometer tests is observed because of several factors, including differences in measurement methods and test conditions at the various testing facilities, deterioration, and engine-to-engine variation. Although there can be excellent agreement between chassis dynamometer testing facilities (Graboski et al., 1998a), there is no standard HD chassis dynamometer Federal test procedure, and no detailed procedures for such testing are described in any authoritative source such as the Code of Federal Regulations, which does contain such procedures for engine dynamometer

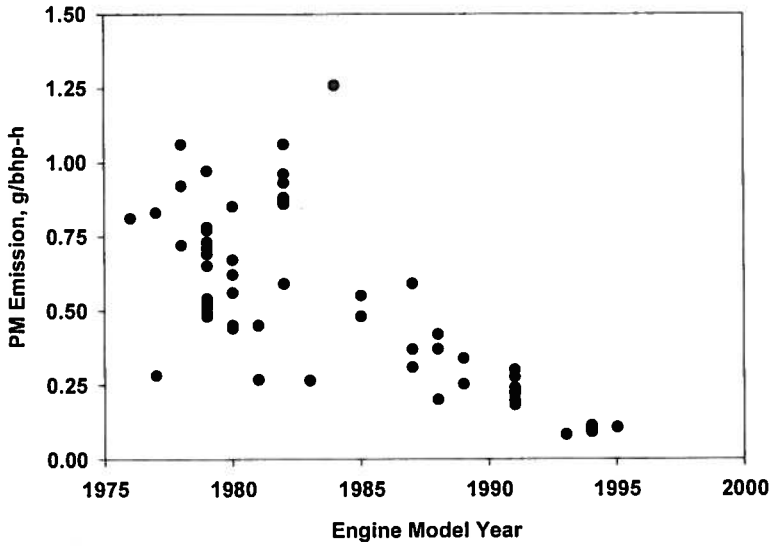


Figure 2-20. Diesel engine certification data for PM emissions as a function of model year.

Source: Data are from the transient test results provided in Table 2-8.

testing used for EPA emission regulations. Therefore, each facility has developed its own approach to HD testing. Clark et al. (1999) report that the test cycle can have a substantial effect on DPM emissions, with higher DPM emissions reported from test cycles that incorporate full-power accelerations. Test cycles incorporating full-power accelerations reflect urban HD vehicle driving for several types of vehicles (garbage trucks, buses) operating in urban areas. Clark et al. (1999) also report that aggressive acceleration produces higher DPM emission rates than does conservative acceleration, and Clark and co-workers suggest that real in-use driving is more likely to mimic aggressive acceleration. Although figures are currently unquantified, it is generally believed that the majority of DPM is generated under transient conditions such as heavy acceleration.

Weaver and Klausmeier (1988) have examined potential causes and frequency of DPM emissions deterioration for in-use HD diesel vehicles. Potential causes include manufacturing defects and malfunctions such as retarded timing, fuel injector malfunction, smoke-limiting mechanism problems, clogged air filter, wrong or worn turbocharger, clogged intercooler, engine mechanical failure, excess oil consumption, and electronics that have been tampered with or have failed. The recent report by McCormick and co-workers (2000) indicates that many of these malfunctions can have very large effects on DPM emissions, resulting in DPM increases of typically 50% to 100%. Although Yanowitz and co-workers (1999) found that DPM emissions were positively correlated with odometer mileage for a fleet of 21 vehicles, it is more likely that the vehicle state of maintenance will be more important than mileage for determining the degree of emissions deterioration. In fact, in a similar analysis performed on the chassis dynamometer results included in the review of Yanowitz et al. (2000), DPM emissions could not be correlated with odometer mileage. Differences in testing methods between various facilities as well as varying states of maintenance for vehicles of the same mileage and model year probably account for this lack of correlation.

It is difficult, given current information, to quantitatively assess the contribution of high-emitting or smoking diesel vehicles to ambient DPM. Emission models used to prepare diesel particulate emission inventories do not account for deterioration. The relative contribution of high-emitting diesel vehicles to the total mass and overall chemical composition of diesel particulates is being quantified. Some studies report numerous smoking diesel trucks. A study of the smoke opacity-based inspection and maintenance program in California found failure rates of 20% and higher, suggesting that high-emitting vehicles are not uncommon (CARB/EEAI, 1997). In the Northeast, smoke opacity testing conducted on 781 HD trucks found that 15% of the vehicles failed the smoke standard (40% opacity for 1991 and newer HD diesel vehicles and 50% opacity for pre-1991 HD diesel vehicles) (Cooper, 1999). Although the correlation between smoke and particulate emissions tends to be qualitative or semiquantitative (discussed

below), there is a good correlation between opacity and EC concentrations, and it is expected that high-emitting diesel vehicles may be an important part of the DPM emission inventory.

Others have attempted to determine if the effects of deterioration could be detected for in-use vehicles. In a study of 21 vehicles (Yanowitz et al., 1999), a linear multivariate regression analysis found that DPM emissions were positively correlated with odometer mileage (several other correlation factors were also identified, including model year). A similar analysis performed on the chassis dynamometer results included in the review of Yanowitz et al. (2000) found that DPM emissions could not be correlated with odometer mileage, probably because of differences in testing methods between the various facilities.

Other approaches for measuring emissions from in-use on-road diesel vehicles include tunnel tests and remote sensing, the latter of which measures gaseous, but not DPM, emissions. The literature reports of those studies are summarized in Tables 2-9 and 2-10. Several tunnel test studies have reported DPM emission factors (Pierson and Brachaczek, 1976; Japar et al., 1984; Pierson et al., 1983; Kirchstetter et al., 1999; Gertler et al., 1996, 1999).

The method for determining emission rates for vehicles traveling through a tunnel is explained in detail by Pierson et al. (1996). Briefly, the emissions of a species are determined by measuring the concentration of a pollutant entering and leaving a tunnel along with knowledge of the cross-section of the tunnel and measurements of the wind flux at the inlet and outlet of the tunnel. The emission rate is calculated by dividing the mass of the pollutant by the number of vehicles that passed through the tunnel and the length of the tunnel. The diesel and gasoline vehicle contributions to the total emission of the pollutant are separated by a simple regression analysis where the intercepts (100% HD and 100% LD) are the diesel and gasoline emission rates, respectively.

Emission factors from tunnel studies provide a snapshot of real-world emissions under driving conditions experienced in the tunnel and reflect emission factors representative of the mix of in-use vehicles and the atmospheric dilution and short-term transformation processes of DE. Emission factors derived from tunnel studies are often used as one source of information to study the impact of improved technology and fleet turnover on emissions because they allow random sampling of large numbers of vehicles, including a range of ages and maintenance conditions. However, tunnel studies are limited in that they represent driving conditions on a single roadway passing through a tunnel and represent mostly steady-state driving conditions, whereas most DPM is generated during transient modes of operation; also, tunnel studies do not include cold-start operations. Both of these factors need to be assessed to understand emission rates for DPM to which people are exposed (U.S. EPA, 1992, 1995). DPM emission factors from in-use fleets derived from tunnel studies in the 1970s and 1980s compared with the 1990s

Table 2-9. HD diesel emissions results from tunnel tests (adapted from Yanowitz et al., 1999)

Test	Tunnel location, year of study	Fuel efficiency (mi/gal)	NO_x[a] (g/mi)	NMHC (g/mi)	CO (g/mi)	DPM (g/mi)	CO_2 (g/mi)	NO_x[a] (g/gal)	NMHC (g/gal)	CO (g/gal)	DPM (g/gal)
Pierson and	Allegheny, 1974	5.42[b]				.90-1.80					4.9-9.8
Brachaczeck, 1983	Allegheny, 1975					1.75 ± 0.19					9.49±1.03
	Allegheny, 1976					1.5 ± 0.10					8.1 ± 0.54
	Allegheny, 1976					1.4 ± 0.07					7.6 ± 0.4
	Tuscarora, 1976					1.3 ± 0.19					7.0 ± 1.0
	Tuscarora, 1976					1.39 ± 26					7.5 ± 1.40
	Allegheny, 1977					1.3 ± 0.08					7.0 ± 0.43
	Allegheny, 1979					1.2 ± 0.03					6.5 ± 0.16
	Allegheny, 1979					1.4 ± 0.04					7.6 ± 0.19
Rogak et al., 1998	Cassiar Tunnel, 1995, Vancouver	8.03[b]	19.50 ± 4.22	-0.16 ± 0.88	6.79 ± 11.78		1,280 ± 40	157 ± 34	-1 ± 7	55 ± 95	
Miguel et al., 1998	Caldecott Tunnel, 1996, San Francisco	5.42[c]	23.82 ± 4.17			1.67 ± 0.24[d]		129 ± 23			9.0 ± 1.3[d]
Weingartner et al., 1997b	Gubrist Tunnel, 1993, Zurich	5.60[c]				0.62 ± 0.02[f]					3.5 ± 0.1[f]
Pierson et al., 1996	Fort McHenry Tunnel, downhill, 1992, Baltimore	11.46[b]	9.66 ± 0.32	0.92 ± 0.21	6.8 ± 1.5		897 ± 48	111 ± 4	11 ± 2	78 ± 17	
Pierson et al., 1996	Fort McHenry Tunnel, uphill, 1992, Baltimore	5.42[b]	22.50 ± 1.00	2.55 ± 1.05	14.3 ± 5.5		1,897 ± 168	122 ± 5	14 ± 6	78 ± 30	
Pierson et al., 1996	Tuscarora Tunnel 1992, Pennsylvania	6.44[b]	19.46 ± 0.85	0.68 ± 0.20	6.03 ± 1.61		1,596 ± 78	125 ± 5	4 ± 1	39 ± 10	
Kirchstetter et al., 1999	Caldecott Tunnel, 1997, San Francisco	5.42[c]	23.82 ± 2.98			1.43 ± 0.12[g]		129 ± 16			7.7 ± 0.6[g]
Gertler,1999	Tuscarora Tunnel, 1999, Pennsylvania					0.29					

[a]NO_x reported as NO_2.
[b]Calculated from observed CO_2 emissions assuming fuel density 7.1 lb/gal and C is 87% of diesel fuel by weight.
[c]Since CO_2 emissions not available, fuel efficiency assumed to be the same as in slightly uphill tunnel (Fort McHenry).
[d]Reported as black carbon, assumed that 50% of total PM emissions are BC.
[e]Slope of tunnel unknown, so used average fuel efficiency for the United States.
[f]PM_3.
[g]$PM_{2.5}$.
[h]Uncertainty reported as ±1.0 standard deviation, except where literature report did not specify standard deviation; in those cases uncertainty listed as reported.

Table 2-10. Remote sensing results for HD vehicles

	Reference	Year study conducted	Emissions (g/gal)
NO_x	Jimenez et al., 1998	1997	150 [a,b,c]
	Cohen et al., 1997	1997	108 [a,b,c]
	Countess et al., 1999	1998	187 [a,b,c]
CO	Bishop et al., 1996	1992	59 [b]
	Cohen et al., 1997	1997	54 [b]
	Countess et al., 1999	1998	85 [b]
THC	Bishop et al., 1996	1992	0.002 HC/CO_2 mole ratio [d]
	Cohen et al., 1997	1997	0.00073 HC/CO_2 mole ratio [d]

[a]Remote sensing measures NO. The reported value was corrected to a NO_x (as NO_2) value by assuming 90% (mole fraction) of NO_x is NO.
[b]Emissions in g/gal calculated by assuming that fuel density is 7.1 lb/gal and C is 87% by weight of fuel.
[c]No humidity correction factor is included.
[d]In order to calculate emissions in g/gal, an average molecular weight is needed.

Source: Yanowitz et al., 1999.

suggest approximately a fivefold decrease in DPM mass emission factors over that time, with the most recent data from 1999 reporting an emission factor of 0.29 g/mi for the on-highway HD diesel fleet (Figure 2-21).

Emission factors vary substantially for the various tunnels, with NO_x emissions ranging from 9.7 to 23.8 g/mi in the 1990s, CO emissions ranging from 6 to 14 g/mi, and THC emissions ranging from 0.16 to 2.55 g/mi.

Remote sensing reports emission factors in terms of pollutant emissions per unit of fuel, not on a per-mile basis. Agreement between remote sensing and tunnel studies for NO_x emissions is reasonably good for the fleet as a whole, suggesting an average level for the fleet of about 130 g/gal, comparable to the average emissions factor measured in chassis dynamometer studies (remote sensing can measure emissions from an individual vehicle, whereas tunnel studies measure emissions from the fleet as a whole). Generally, chassis dynamometer tests and engine dynamometer test results are corrected for ambient humidity, in accordance with the Federal Test Procedure (CFR 40, Subpart N). Tunnel tests and remote sensing tests have typically not included corrections for humidity. Appropriate humidity corrections for NO_x and DPM can be greater than 20% and 10%, respectively (or a total difference of more than 45% and 20%, respectively, between low- and high-humidity areas), under normally occurring climatic conditions. Additionally, the remote sensing literature has not addressed how to determine the

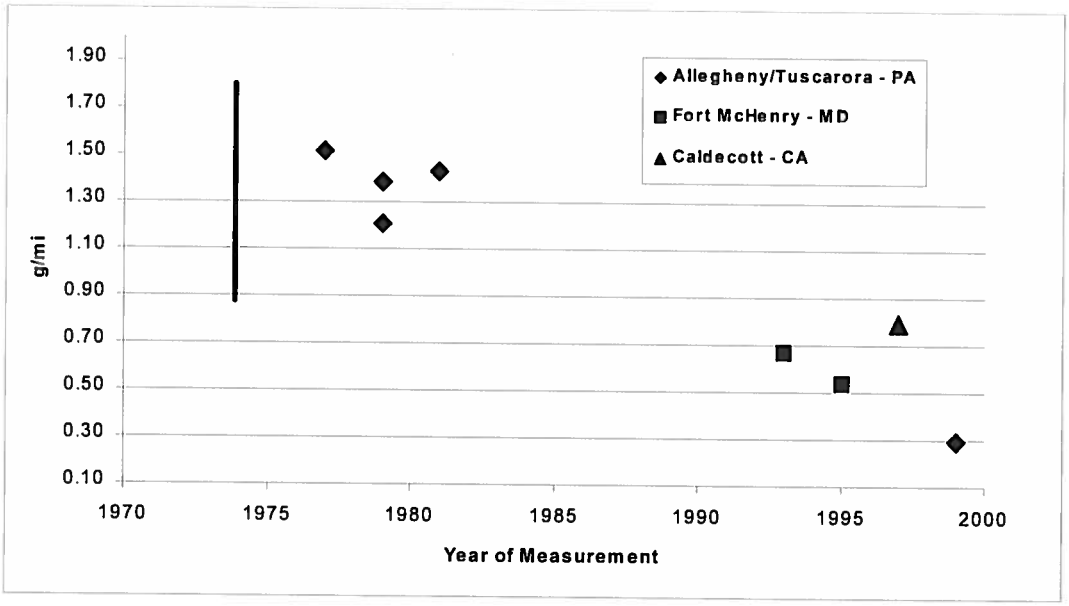


Figure 2-21. Emission factors from HD diesel vehicles from tunnel studies.

Source: Data from Pierson and Brachaczek, 1976; Japar et al., 1984; Pierson et al., 1996; Kirchstetter et al., 1999; Gertler et al., 1995, 1996; Gertler, 1999.

correct value for the NO/NO_x ratio, and there is reason to believe that this value may differ systematically from site to site, although almost all of the NO_x is NO as it leaves the vehicle.

In addition to the humidity correction discussed above, several factors must be taken into account when comparing DPM measurements from tunnel tests to chassis dynamometer measurements (Yanowitz et al., 2000): (1) Chassis testing measures only tailpipe emissions; tunnel tests can include emissions from other sources (tire wear, etc.), and (2) tunnel tests typically measure emissions under steady-speed freeway conditions, whereas most chassis dynamometer tests are measured on cycles that are more representative of stop-and-go urban driving conditions. This latter limitation also applies to remote sensing readings, which measure instantaneous emissions versus emissions over a representative driving cycle.

Because THC emissions for diesel vehicles are very low in total mass in comparison with gasoline vehicles, tunnel test results for THC have a high degree of uncertainty. A regression analysis to determine the contribution of the limited number of HD vehicles to THC emissions is unstable; small errors in the total measurements can change estimates substantially. Similarly,

CO emissions are comparable to automobile emissions on a per-vehicle-mile basis, but because there are generally many more automobiles than HD diesels in tunnel tests, CO measurements from diesels may also have a high degree of uncertainty.

2.2.5.2. *Locomotives*

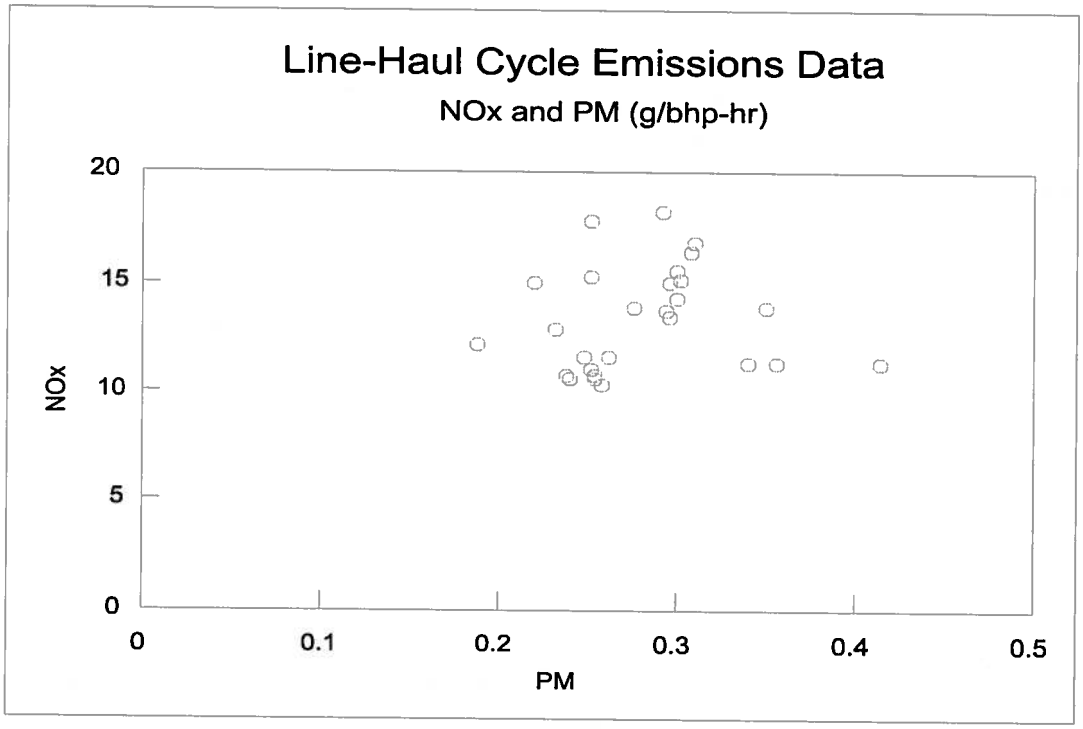
Locomotive engines generally range from 1,000 horsepower up to 6,000 horsepower. Similar to the much smaller truck diesel engines, the primary pollutants of concern are NO_x, DPM, CO, and HC. Unlike truck engines, most locomotive engines are not mechanically coupled to the drive wheels. Because of this decoupling, locomotive engines operate in specific steady-state modes rather than the continuous transient operation normal for trucks. Because the locomotive engines operate only at certain speeds and torques, the measurement of emissions is considerably more straightforward for locomotive engines than for truck engines. Emissions measurements made during the relatively brief transition periods from one throttle position to another indicate that transient effects are very short and thus could be neglected for the purposes of overall emissions estimates.

Emissions measurements are made at the various possible operating modes with the engine in the locomotive, and then weighting factors for typical time of operation at each throttle position are applied to estimate total emissions under one or more reasonable operating scenarios. In the studies included in this analysis, two scenarios were considered: line-haul (movement between cities or other widely separated points) and switching (the process of assembling and disassembling trains in a switchyard).

The Southwest Research Institute made emissions measurements for three different engines in locomotives in 1972 (Hare and Springer, 1972) and five more engines in locomotives using both low- and high-sulfur fuel in 1995 (Fritz, 1995). Two engine manufacturers (the Electro-Motive Division of GM, and GE Transportation Systems) tested eight different engine models and reported the results to EPA (U.S. EPA, 1998b). All available data on locomotives are summarized in the regulatory impact assessment and shown in Figure 2-22.

2.2.6. Engine Technology Description and Chronology

NO_x emissions, DPM emissions, and brake-specific fuel consumption (BSFC) are among the parameters that are typically considered during the development of a diesel engine. Many engine variables that decrease NO_x can also increase DPM and BSFC. One manifestation of the interplay among NO_x, DPM, and BSFC is that an increase in combustion temperatures will tend to increase NO formation. Higher temperatures will also often improve thermal efficiency, can improve BSFC, and can increase the rate of DPM oxidation, thus lowering DPM emissions. One example of this is the tradeoff of DPM emissions and BSFC versus NO_x emissions with fuel



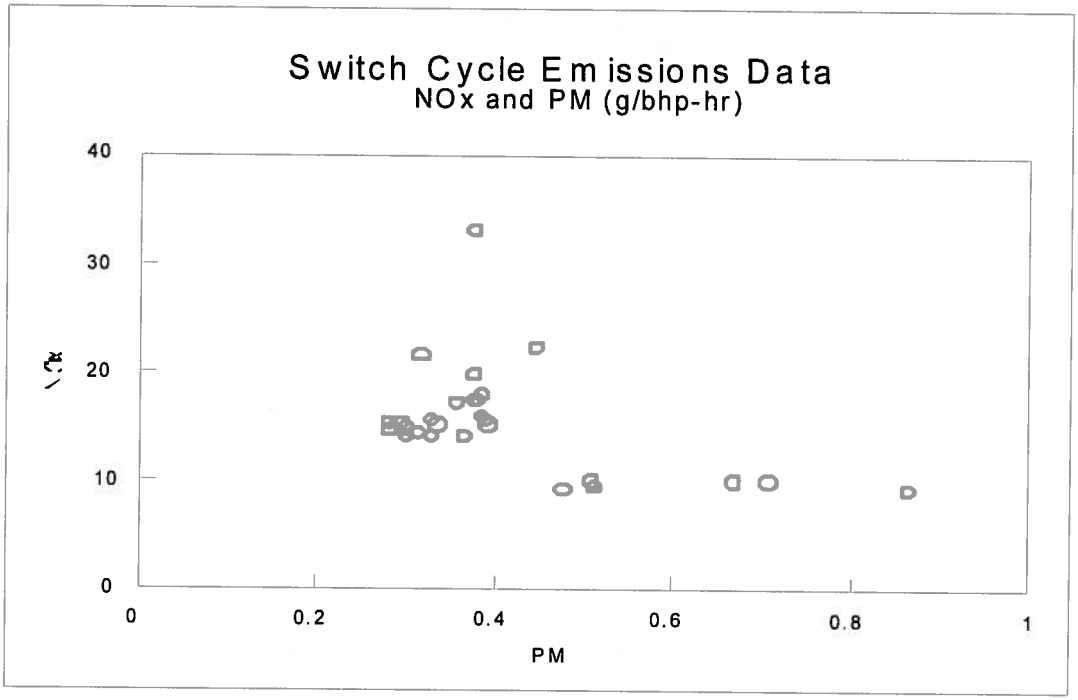


Figure 2-22. Line-haul and switch emissions data.

Source: U.S. EPA, 1998a.

injection timing. Many recent advances in reducing the emissions of diesel engines without aftertreatment are combinations of technologies that provide incremental improvements in the tradeoffs among these emissions and fuel consumption. The sum total, however, can be considerable reductions in regulated emissions within acceptable levels of fuel consumption.

The majority of current HD diesel truck engines certified for use in the United States utilize:

- A four-stroke cycle
- Direct-injection, high-pressure (1,200 bar to >2,000 bar) fuel injection systems with electronic control of injection timing and, in some cases, injection rate
- Centrally located multihole injection nozzles
- Three or four valves per cylinder
- Turbochargers
- In many cases, air-to-air aftercooling
- In some cases, the use of an oxidation catalyst.

These features have phased into use with HD truck engines because they offer a relatively good combination of fuel consumption, torque-rise, emissions, durability, and the ability to better "tune" the engines for specific types of applications. Fuel consumption, torque-rise, and drivability have been maintained or improved while emissions regulations have become more stringent. Many Class 8a and 8b diesel truck engines are now capable of 700,000 to 1,000,000 miles of driving before their first rebuild and can be rebuilt several times because of their heavy construction and the use of removable cylinder liners. These engines are expected to last longer and therefore have a useful life longer than the regulatory estimate of full useful life for HD engines (~1,000,000 miles) previously used by EPA (for 1980 engines that were driven less than 300,000 miles between rebuilds and were rebuilt up to three times). Current four-stroke locomotive engines use engine technology similar to on-highway diesel engines, except that electronic controls have only recently been introduced.

It is difficult to separate the components of current high-speed diesel engines for discussion of their individual effects on emissions. Most of the components interact in numerous ways that affect emissions, performance, and fuel consumption.

2.2.6.1. *Indirect and Direct Injection High-Speed Diesel Engines*

Prior to the 1930s, diesel engine design was limited to relatively low-speed applications because sufficiently high-pressure fuel injection equipment was not available. With the advent of high-speed and higher pressure pump-line-nozzle systems, introduced by Robert Bosch in the

1930s, it became possible to inject the fuel directly into the cylinder for the first time, although indirect injection (IDI) diesel engines continued in use for many years. As diesels were introduced into the heavy truck fleet in the 1930s through the 1950s, both IDI and direct injection (DI) naturally aspirated variants were evident. A very low-cost rotary injection pump technology was introduced by Roosa-Master in the 1950s, reducing the cost of DI systems and allowing their introduction on smaller displacement, higher speed truck engines. After this time, only a small fraction of truck engines used an IDI system.

DI diesel engines have now all but replaced IDI diesel engines for HD on-highway applications.[2] IDI engines typically required much more complicated cylinder head designs but generally were capable of using less sophisticated, lower pressure injection systems with less expensive single-hole injection nozzles. IDI combustion systems are also more tolerant of lower grades of diesel fuel. Fuel injection systems are likely the single most expensive component of many diesel engines. Caterpillar continued producing both turbocharged and naturally aspirated IDI diesel engines for some on-highway applications into the 1980s. Caterpillar and Deutz still produce engines of this type, primarily for use in underground mining applications. IDI combustion systems are still used in many small-displacement (<0.5 L/cylinder), very high-speed (>3,000 rpm rated speed) diesel engines for small nonroad equipment (small imported tractors, skid-steer loaders), auxiliary engines, and small generator sets, and they were prevalent in diesel automotive engines in the 1980s; IDI designs continue to be used in automotive diesel engines.

IDI engines have practically no premixed burn combustion and thus are often quieter and have somewhat lower NO_x emissions than DI engines. Electronic controls, high-pressure injection (e.g., GM 6.5), and four-valve/cylinder designs (e.g., the six-cylinder Daimler LD engine) can be equally applied to IDI diesel engines as in DI, but they negate advantages in cost over DI engines. DI diesel engines of the same power output consume 15% to 20% less fuel than IDI engines (Heywood, 1988). Considering the sensitivity of the HD truck market to fuel costs, this factor alone accounts for the demise of IDI diesel engines in these types of applications. Throttling and convective heat transfer through the chamber-connecting orifice, and heat rejection from the increased surface area of IDI combustion systems, decrease their efficiency and can cause cold-start difficulties when compared to DI designs. Most IDI diesel engine designs require considerably higher than optimum compression ratios (from an efficiency standpoint) to aid in cold-starting (19:1 to 21:1 for IDI engines vs. ~15:1 to 17:1 for DI engines).

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[2]The GM Powertrain/AM General 6.5L electronically controlled, turbocharged IDI-swirl chamber engine, certified as a light HD diesel truck engine, is the last remaining HD on-highway IDI engine sold in the United States.

Because of the early introduction of DI technology into truck fleets, it is likely that by the end of the 1960s, only a small fraction of the HD diesel engines sold for on-highway use were IDI engines. It is unlikely that the shift from IDI to DI engine designs through the 1950s and 1960s occurred rapidly and likely that this shift had little significant impact on emissions. Springer (1979) reports a comparison of nearly identical Caterpillar 3406 engines (turbocharged and aftercooled) in DI and IDI configurations tested on an engine dynamometer under steady-state conditions, which limits the usefulness of these data. There was no significant difference in emissions of DPM, SOF, aldehydes, or DPM-associated B[*a*]P (Table 2-8). Note that IDI designs continue to be used in automotive diesel engines.

2.2.6.2. *Injection Rate*

Decreasing the duration of diffusion combustion and promoting EC oxidation during the expansion stroke can reduce formation of EC agglomerates (Stone, 1995) and reduce the particulate carbon fraction at high load (Needham et al., 1989). Both of these effects are enhanced by increasing the fuel injection rate. The primary means of accomplishing this is by increasing fuel injection pressure. In 1977 Robert Bosch introduced a new type of high-pressure pump capable of producing injection pressures of 1,700 bar at the nozzle (Voss and Vanderpoel, 1977). This increased fuel injection pressure by roughly a factor of 10. Unit injection, which combines each fuel injection nozzle with individual cam-driven fuel pumps, can achieve very high injection pressures (>2,000 bar). The first combination of unit injectors with electronically controlled solenoids for timing control was offered in the United States by Detroit Diesel Corporation in the 1988 model year (Hames et al., 1985). Replacement of the injection cam with hydraulic pressure, allowing a degree of injection rate control, was made possible with the hydraulic-electronic unit injection jointly developed by Caterpillar and Navistar, introduced on the Navistar T444E engine (and variants) in 1993.

It is widely known that high fuel injection pressures have been used to obtain compliance with the PM standards that went into effect in 1988 (Zelenka et al., 1990). Thus, it is likely that a transition to this technology began in the 1980s, with the vast majority of new engine sales employing this technology by 1991, when the 0.25 g/bhp-hr Federal PM standard went into effect.

The use of electronic control of injection rate is rapidly increasing on medium HD diesel engines. Engines are currently under development, perhaps for 2002–2004 introduction, that use common-rail fuel injection systems with even more flexible control over injection pressure and timing than previous systems.

Increased injection rate and pressure can significantly reduce EC emissions, but it can also increase combustion temperatures and cause an increase in NO_x emissions (Springer, 1979;

Watson and Janota, 1982; Stone, 1995). Low NO_x, low DPM, and relatively good BSFC and brake mean engine pressure (BMEP) are possible when combined with turbocharging, aftercooling, and injection timing retard.

2.2.6.3. *Turbocharging, Charge-Air Cooling, and Electronic Controls*

Use of exhaust-driven turbochargers to increase intake manifold pressure has been applied to both IDI and DI diesel engines for more than 40 years. Turbocharging can decrease fuel consumption compared with a naturally aspirated engine of the same power output. Turbocharging utilizes otherwise wasted exhaust heat and pressure to generate intake boost. The boosted intake pressure effectively increases air displacement and increases the amount of fuel that can be injected to achieve a given fuel-air ratio. Turbocharging increases the power density of an engine. Boosting intake pressure via turbocharging and reducing fuel-to-air ratio at a constant power can significantly increase both intake temperatures and NO_x emissions. Increased boost pressure can significantly reduce ignition delay, which reduces VOC and DPM SOF emissions (Stone, 1995) and increases the flexibility in selection of injection timing. Injection timing on turbocharged engines can be retarded further for NO_x emission control with less of an effect on DPM emissions and fuel consumption. This allows a rough parity in NO_x emissions between turbocharged (non-aftercooled) and naturally aspirated diesel engines (Watson and Janota, 1982).

Turbocharging permits the use of higher initial injection rates (higher injection pressure),

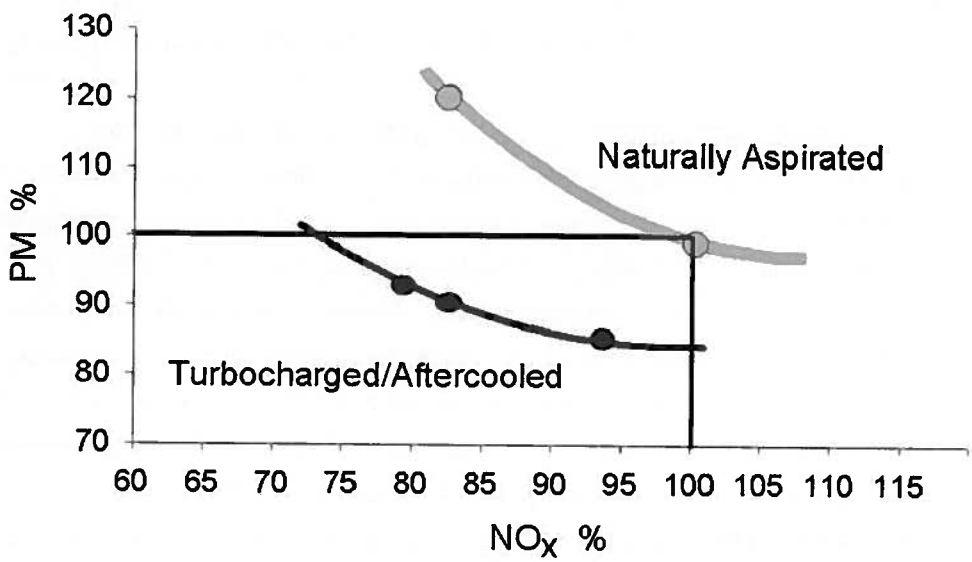

Figure 2-23. Effect of turbocharging and aftercooling on NO_x and PM.

Source: Mori, 1997.

which can reduce particulate emissions. Although this may offer advantages for steady-state operation, hard accelerations can temporarily cause overly fuel-rich conditions because the turbocharger speed lags behind a rapid change in engine speed (turbo-lag). This can cause significant increases in DPM emissions during accelerations. Before the advent of electronic controls, the effect of acceleration on DPM emissions could be limited by mechanically delaying demand for maximum fuel rate with a "smoke-puff eliminator." Because this device also limited engine response, there was considerable incentive for the end-users to remove or otherwise render the device inactive. Charge-air cooling, for example, using an air-to-air aftercooler (air-cooled heat exchanger) between the turbocharger compressor and the intake manifold, can greatly reduce intake air and peak combustion temperatures. When combined with injection timing retard, charge-air cooling allows a significant reduction in NO_x emissions with acceptable BSFC and DPM emissions when compared to either non-aftercooled or naturally aspirated diesel engines (Hardenberg and Fraenkle, 1978; Pischinger and Cartellieri, 1972; Stone, 1995). The use of charge-air cooling effectively shifts the NO_x-DPM tradeoff curve, as shown in Figure 2-23.

Electronic control of fuel injection timing allowed engine manufacturers to carefully tailor the start and length of the fuel injection events much more precisely than through mechanical means. Because of this, newer on-highway turbocharged truck engines have virtually no visible smoke on acceleration (although emissions of DPM are substantial during this driving mode). Electronic controls also allowed fuel injection retard under desirable conditions for NO_x reduction, while still allowing timing optimization for reduced VOC emissions on start-up, acceptable cold-weather performance, and acceptable performance and durability at high altitudes. Previous mechanical unit injected engines (e.g., the 1980s Cummins L10, the Non-Electronic Control Detroit Diesel 6V92) were capable of reasonably high injection pressures, but they had fixed injection timing that only varied based on the hydraulic parameters of the fuel system. Many other engines with mechanical in-line or rotary injection pumps had only coarse injection timing control or fixed injection timing.

Precise electronic control of injection timing over differing operating conditions also allowed HD engine manufacturers to retard injection timing to obtain low NO_x emissions during highly transient urban operation, similar to that found during emissions certification. HD engine manufacturers also advanced injection timing during less transient operation (such as freeway driving) for fuel consumption improvements (~3% to 5%) at the expense of greatly increased NO_x emissions (approximately three to four times regulated levels). This particular situation resulted in the recent consent decree settlements between the Federal Government and most HD engine manufacturers to ensure effective NO_x control in all driving conditions, including on-

highway high-speed steady-state driving.

Turbocharged engines entered the market very slowly beginning in the 1960s. Data for DPM emissions from naturally aspirated engines of model years 1976 to 1983 are compared with DPM emissions from turbocharged engines in Figure 2-24. There is no consistent difference in DPM emissions between turbocharged and naturally aspirated engines. Although not plotted, the data also show no difference in emissions of NO_x, DPM SOF, or DPM-associated B[*a*]P and 1-nitropyrene (1-NP).

Charge-air cooling was introduced during the 1960s and was initially performed in a heat exchanger using engine coolant. Cooling of the charge air using ambient air as the coolant was introduced into heavy trucks by Mack in 1977 with production of the ETAY(B)673A engine (Heywood, 1988). Use of ambient air allowed cooling of the charge air to much lower temperatures. Most HD diesel engines sold today employ some form of charge air cooling, with air-to-air aftercooling being the most common. Johnson and co-workers (1994) have presented a comparison of similar engines that differ in that the charge air is cooled by engine coolant (1988 engine) and by ambient air, with a higher boost pressure for the second (1991 engine). The 1991 engine also used higher pressure fuel injectors. The 1991 engine exhibited both lower DPM emissions (50% lower than the 1988 engine) and lower NO_x emissions. Higher injection pressure is likely to have enabled the reduced DPM emissions, whereas the lower charge-air

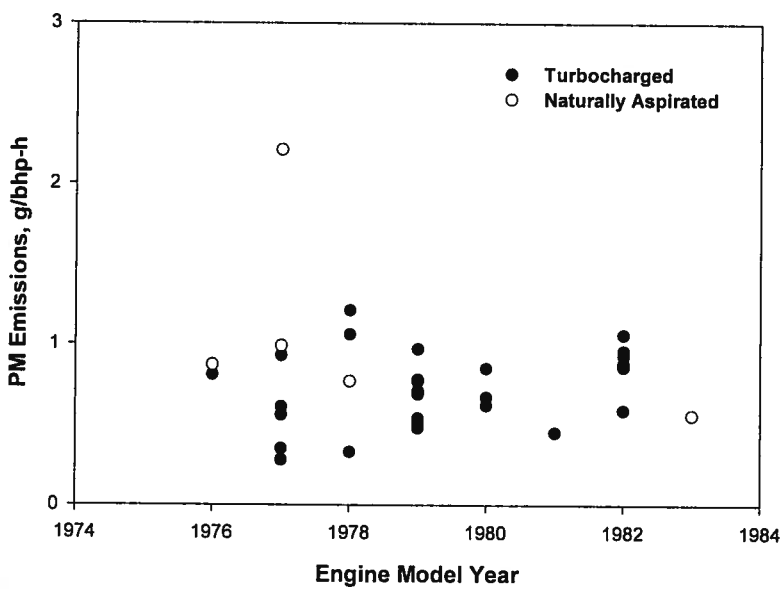

Figure 2-24. Comparison of diesel engine dynamometer PM emissions for four-stroke, naturally aspirated, and turbocharged engines.

Source: Data are from Table 2-8.

temperature and the ability to electronically retard the injection timing under some conditions likely enabled the lower NO_x emissions.

It is apparent on the basis of both the literature and certification data that turbochargers with aftercoolers can be used in HD engines in conjunction with other changes to produce a decrease in emissions. On the advent of a NO_x standard in 1985, NO_x was probably reduced on the order of 10% to 30% in turbocharged aftercooled engines with retarded injection timing. This decrease is not evident in the in-use chassis testing data because of deterioration and the use of illegal emissions devices as described above. Overall, it is expected that engines in the 1950s to mid-1970s timeframe would have similar DPM emission rates, whereas post-1970 engines would have somewhat lower DPM emission rates.

2.2.6.4. *Two-Stroke and Four-Stroke High-Speed Diesel Engines*

A detailed discussion of the two- and four-stroke engine cycles can be found in the literature (Heywood, 1988; Taylor, 1990; Stone, 1995). Nearly all high-speed two-stroke diesel engines utilize uniflow scavenging assisted by a positive-displacement blower (Figure 2-25). Uniflow-scavenged two-stroke diesels use poppet exhaust valves similar to those found in four-stroke engines. The intake air enters the cylinder through a pressurized port in the cylinder wall. A crankshaft-driven, positive-displacement blower (usually a roots-type) pressurizes the intake port to ensure proper scavenging. A turbocharger may be added to the system to provide additional boost upstream of the blower at higher speeds and to reduce the size and parasitic losses associated with the positive-displacement blower.

Two-stroke diesel engines can achieve efficiency comparable to four-stroke counterparts and have higher BMEP (torque per unit displacement) (Heywood, 1988). It is useful to note that two-stroke cycle fires each cylinder once every revolution, whereas the four-stroke cycle fires every other revolution. Thus, for a given engine size and weight, two-strokes can produce more power. However, two-stroke diesel engines are less durable than their four-stroke counterparts. Lubricating oil is transferred from the piston rings to the intake port, which causes relatively high oil consumption relative to four-stroke designs. Durability and low oil consumption are desirable for on-highway truck applications. This may be why four-stroke engines have been favored for these applications since the beginning of dieselization in the trucking industry, with the notable exception of urban bus applications. Although it is no longer in production, the Detroit Diesel 6V92 series of two-stroke diesel engines is still the most popular for urban bus applications, where the high power density allows the engine to be more easily packaged within limited spaces. The primary reason that two-stroke engines like the 6V92 are no longer offered for urban bus applications is excessive DPM emissions. The lubricating oil control with two-strokes tends to be lower than for four-stroke engines, and therefore, emissions have higher VOC

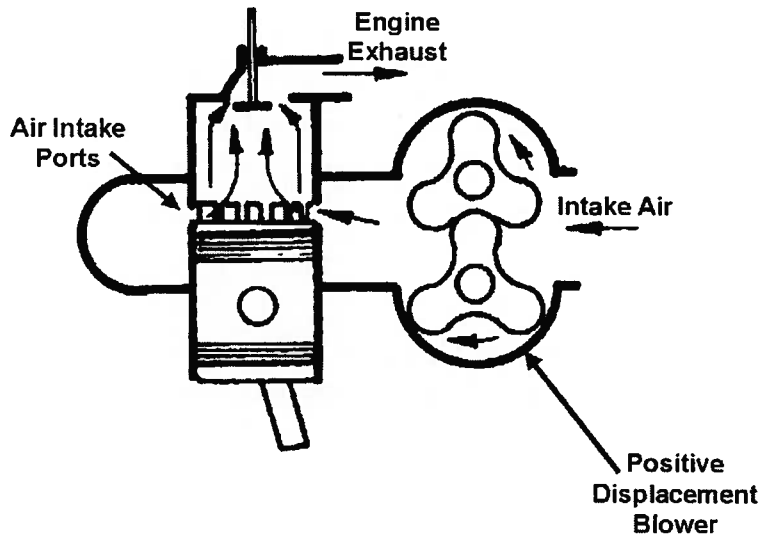

Figure 2-25. An example of uniflow scavenging of a two-stroke diesel engine with a positive displacement blower. Scavenging is the process of simultaneously emptying the cylinder of exhaust and refilling with fresh air.

Source: Adapted from Taylor, 1990.

and organic DPM emissions relative to four-stroke designs. This was particularly problematic for urban bus applications because urban bus engines must meet tighter Federal and California PM emissions standards. The current urban bus PM standard (0.05 g/bhp-hr) is one-half of the current on-highway HD diesel engine PM standard, although EPA is in the process of proposing more strict standards for HD diesel truck engines along with further reductions in diesel fuel sulfur levels. No two-stroke diesel engine designs have been certified to meet the most recent urban bus PM emissions standards, and Detroit Diesel Corporation has not certified a two-stroke diesel engine for on-highway truck use since 1995.

A comprehensive review of emissions from hundreds of vehicles (1976–98 model years) that had been tested on chassis dynamometers found that DPM emissions vary substantially within a given model year and that within that variation there are no discernible differences in DPM emissions between two- and four-stroke vehicles (Figure 2-26) (Yanowitz et al., 2000). DPM emission factors reported for engine tests also indicate that two- and four-stroke engines have comparable emission factors, as these engines all had to meet the same regulatory standard (Figure 2-27). In contrast to DPM emissions, evidence suggests that mid-1970s two-stroke engines exhibited very high SOF levels compared with four-stroke engines, with later model years showing similar SOF emissions for two- and four-stroke engines (Figure 2-28). For aldehydes, benzo[a]pyrene, and 1-nitropyrene, data are available for only one two-stroke engine,

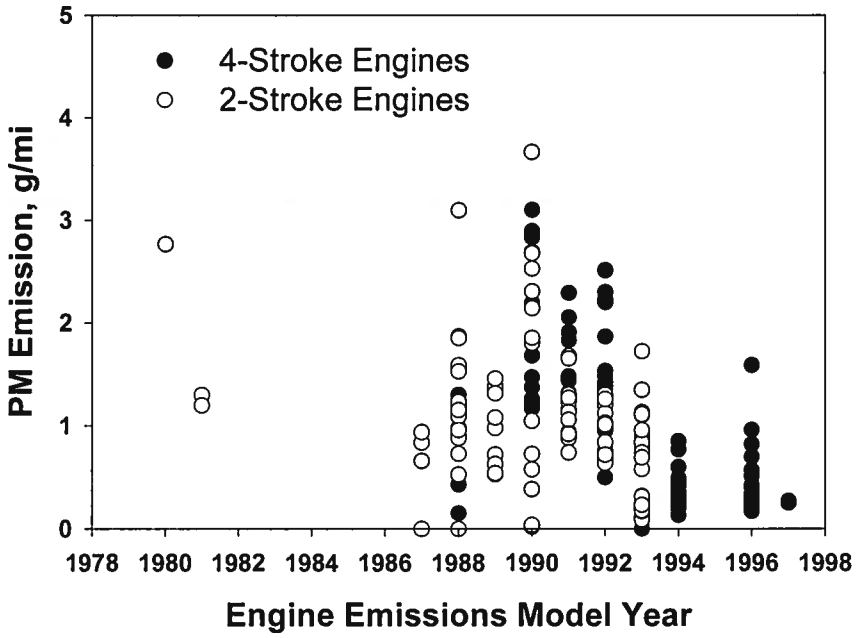

Figure 2-26. Comparison of two- and four-stroke vehicle diesel PM emissions from chassis dynamometer studies.

Source: Yanowitz et al., 2000.

but they indicate no significant difference in emissions from comparable model year four-stroke engines. Overall, regulated emissions changes attributable to changing proportions of two- and four-stroke engines in the in-use fleet do not appear to have influenced DPM emission levels, but the transition to four-stroke engines in the 1970s would have decreased the fraction of SOF associated with the DPM. It appears that the proportion of two-stroke engines in the in-use fleet was relatively constant until the late 1980s, when it began to decline.

2.2.7. Air Toxic Emissions

HD diesel vehicle exhaust contains several substances that are known, likely, or possible human or animal carcinogens, or that have serious noncancer health effects. These substances include, but are not limited to, benzene, formaldehyde, acetaldehyde, 1,3-butadiene, acrolein, dioxin, PAH, and nitro-PAH (the complete list of chemically characterized compounds present in DE is provided in Section 2.3.1). Very few historical data are available to examine changes in emission rates over time. In this section, trends in aldehyde emissions over time and a summary

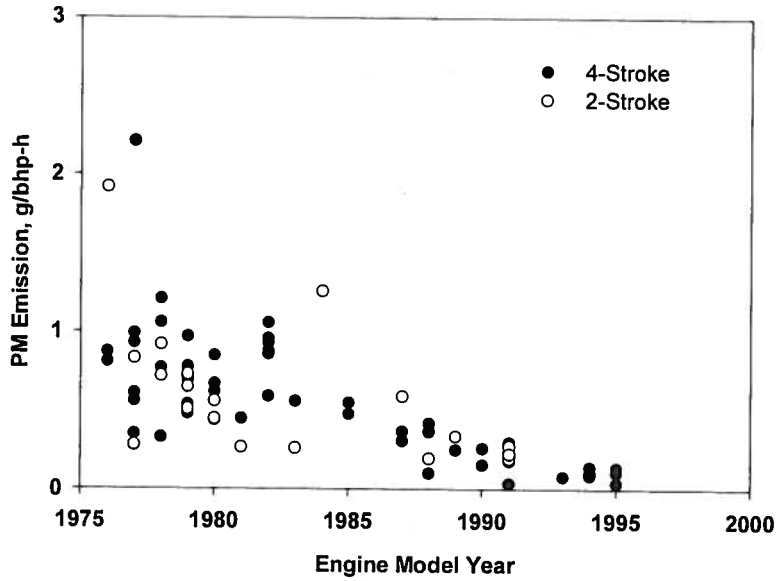

Figure 2-27. Comparison of two- and four-stroke engine diesel PM emissions from engine dynamometer studies.

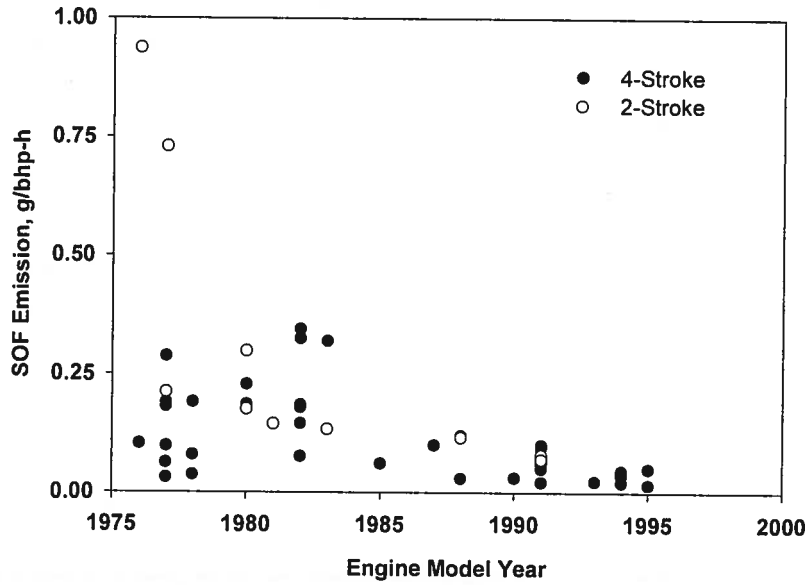

Figure 2-28. Diesel engine dynamometer SOF emissions from two- and four-stroke engines. SOF obtained by dichloromethane extraction in most studies.

Source: Data are from Table 2-8.

of dioxin emission factors are presented. PAH and nitro-PAH emission factors are discussed in Section 2.2.8.2.

2.2.7.1. *Aldehyde Emissions*

Among the gaseous components emitted by diesel engines, the aldehydes are particularly important because they constitute an important fraction of the gaseous emissions and they are probable carcinogens that also produce noncancer health effects. Formaldehyde makes up the majority of the aldehyde emissions (65% to 80%), with acetaldehyde being the second most abundant aldehyde in HD diesel emissions. Total aldehyde emissions reported from chassis dynamometer testing suggest that aldehyde emissions have declined since 1980; however, only two tests reported aldehydes from engines made after 1985 (Figure 2-29). Engine dynamometer studies also suggest a downward trend in the emissions of aldehydes in the time period from 1976 to 1994 (Figure 2-30). Engine dynamometer studies report aldehyde emission levels of 150–300 mg/bhp-hr for late 1970s engines with no significant effect of turbocharging, or IDI versus DI. High-pressure fuel injection may have resulted in a marginal increase in aldehyde emissions (Springer, 1979). By comparison, 1991 model year engines (DI, turbocharged) exhibited aldehyde emissions in the 30–50 mg/bhp-hr range (Mitchell et al., 1994).

2.2.7.2. *Dioxin and Furans*

Ballschmiter et al. (1986) reported detecting polychlorinated dibenzo-p-dioxins (CDDs) and polychlorinated dibenzofurans (CDFs) in used motor oil and thus provided some of the first evidence that CDDs and CDFs might be emitted by the combustion process in diesel-fueled engines. Incomplete combustion and the presence of a chlorine source in the form of additives in the oil or the fuel were speculated to lead to the formation of CDDs and CDFs. Since 1986, several studies have been conducted to measure or estimate CDD/CDF concentrations in emissions from diesel-fueled vehicles. These studies can be characterized as direct measurements from the engine exhaust and indirect measurements from the sampling of air within transportation tunnels.

Table 2-11 is a summary of various CDD/CDF emission characterization studies reported in the United States and Europe for diesel-fueled cars and trucks. Hagenmaier et al. (1990) reported an emission factor for LD diesel vehicles of 24 pg TEQ per liter of diesel fuel consumed. TEQ, or the toxic equivalency factor, rates each dioxin and furan relative to that of 2,3,7,8-TCDD, which is arbitrarily assigned a TEQ of 1.0 based on animal assays. Schwind et al. (1991) and Hutzinger et al. (1992) studied emissions of CDDs/CDFs from German internal combustion engines running on commercial diesel fuels and reported a range of CDD/CDF emission rates across the test conditions (in units of pg TEQ per liter of diesel fuel consumed) of 10–130 pg TEQ/L for diesel car exhaust and 70–81 pg TEQ/L for diesel truck exhaust.

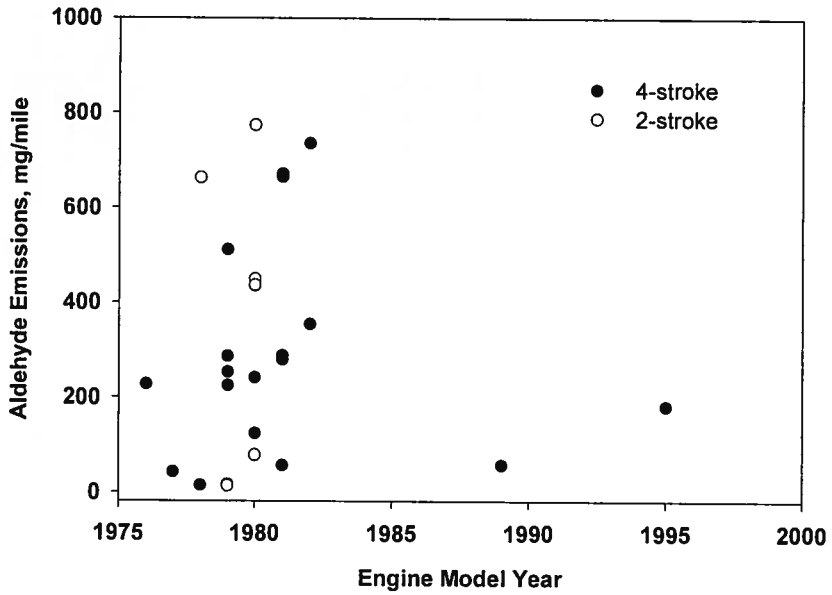

Figure 2-29. Diesel engine aldehyde emissions measured in chassis dynamometer studies.

Source: Data are from Warner-Selph and Dietzmann, 1984; Schauer et al., 1999; Unnasch et al., 1993.

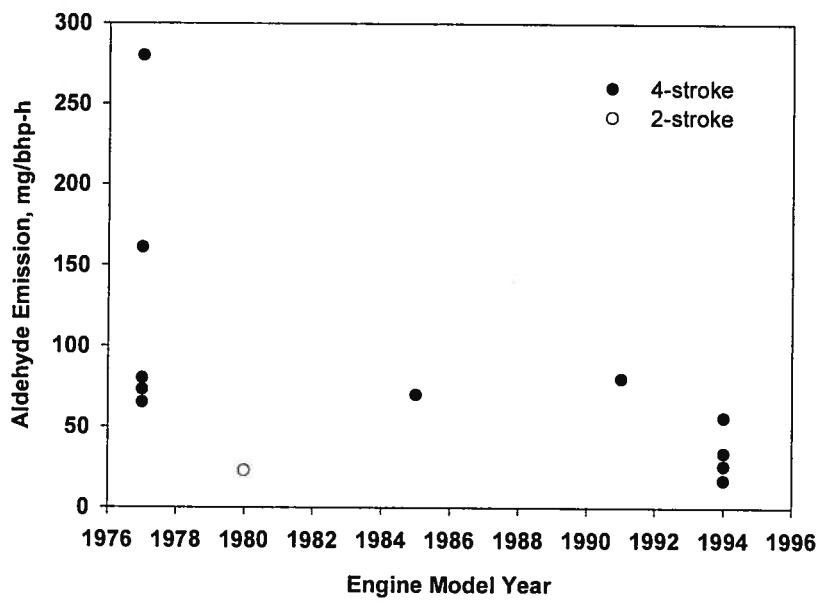

Figure 2-30. Diesel engine aldehyde emissions from engine dynamometer studies.

Source: Data from Table 2-8.

Table 2-11. Summary of CDD/CDF emissions from diesel-fueled vehicles

Study	Country	Vehicle tested	Number of test vehicles	Emission factor (pg TEQ/km driven)	Driving cycle; sampling location
CARB, 1987; Lew, 1996	United States	Diesel truck	1	663–1,300	6-hr dynamometer test at 50 km/hr
Marklund et al., 1990	Sweden	Diesel truck	1	not detected (<18)[a]	U.S. Federal mode 13 cycle; before muffler
Hagenmaier et al., 1990	Germany	Diesel car	1	2.4[a]	Comparable to FTP-73 test cycle; in tailpipe
Hagenmaier, 1994	Germany	Diesel bus	1	not detected (< 1 pg/L)	On-the-road testing
Oehme et al., 1991 (tunnel study)	Norway	—	(b)	520[c] 38[c] avg = 280 9,500[c] 720[c] avg = 5,100	Cars moving uphill (3.5% incline) at 60 km/hr Cars moving downhill (3.5% decline) at 70 km/hr Trucks moving uphill (3.5% incline) at 60 km/hr Trucks moving downhill (3.5% decline) at 70 km/hr
Schwind et al., 1991 Hutzinger et al., 1992	Germany	Diesel car Diesel truck	1 1	5.0–13[a] 13–15[a]	Various test conditions (i.e., loads and speeds) Various test conditions (i.e., loads and speeds)
Gertler et al., 1996 (tunnel study)	United States	Diesel trucks	(d)	mean = 172	Mean of seven 12-hour samples
Gullett and Ryan, 1997	United States	Diesel truck	1	mean - 29.0	Mean of five sample routes

[a]Results reported were in units of pg TEQ/liter of fuel. For purposes of this table, the fuel economy factor used by Marklund et al. (1990), 10 km/L or 24 miles/gal, was used to convert the emission rates into units of pg TEQ/km driven for the cars. For the diesel-fueled truck, the fuel economy factor reported in CARB (1987a) for a 1984 heavy-duty diesel truck, 5.5 km/L (or 13.2 miles/gal), was used.

[b]Tests were conducted over portions of 4 days, with traffic rates of 8,000-14,000 vehicles/day. Heavy-duty vehicles (defined as vehicles over 7 meters in length) ranged from 4% to 15% of total.

[c]Emission factors are reported in units of pg Nordic TEQ/km driven; the values in units of I-TEQ/km are expected to be about 3% to 6% higher.

[d]Tests were conducted over 5 days with heavy-duty vehicle rates of 1,800-8,700 vehicles per 12-hour sampling event. Heavy-duty vehicles accounted for 21% to 28% of all vehicles.

In 1994, Hagenmaier reported CDD/CDF emissions from a diesel-fueled bus and found no detectable levels in the exhaust (at a detection limit of 1 pg/L of fuel consumed) for individual congeners. In 1987, the California Air Resources Board (CARB) produced a draft report of a HD engine tested under steady-state conditions indicating a TEQ emission factor of 7,290 pg/L of fuel burned (or 1,300 pg/km driven) if nondetected values are treated as one-half the detection limit. Treating nondetected values as zeros yields a TEQ concentration equivalent to 3,720 pg/L of fuel burned (or 663 pg/km driven) (Lew, 1996). Norbeck et al. (1998c) reported emission factors for dioxin and furans from a Cummins L10 HD diesel engine running on pre-1993 fuel of 0.61 pg/L and 0.41 pg/L for the same engine running on reformulated fuel. The low emission factors reported by Norbeck et al. (1998c) were attributed to losses of dioxin and furan compounds to the dilution tunnel walls.

EPA has directly sampled the exhaust from a HD diesel truck for the presence and occurrence of CDDs/CDFs (Gullett and Ryan, 1997). The average of five tests (on highway and city street driving conditions) was 29.0 pg TEQ/km with a standard deviation of 38.3 pg TEQ/km; this standard deviation reflects the 30-fold variation in the two city driving route tests.

Tunnel studies are an indirect means of measuring contaminants that may be associated with emissions from cars and trucks. In these studies, scrapings of carbonaceous matter from the interior walls of the transportation tunnel or the tunnel air are sampled and analyzed for the target contaminants. Several European studies and one recent U.S. study evaluated CDD/CDF emissions from vehicles by measuring the presence of CDDs/CDFs in tunnel air. This approach has the advantage of allowing random sampling of large numbers of vehicles passing through the tunnel, including a range of ages and maintenance levels. The disadvantage of this approach is that it relies on indirect measurements (rather than tailpipe measurements), which may introduce unknown uncertainties into the interpretation of results.

Oehme et al. (1991) reported the emission rates associated with HD diesel trucks as follows: uphill = 9,500 pg TEQ/km; downhill = 720 pg TEQ/km; mean = 5,100 pg TEQ/km. The mean values are the averages of the emission rates corresponding to the two operating modes: vehicles moving uphill on a 3.5% incline at an average speed of 37 mi/hr and vehicles moving downhill on a 3.5% decline at an average speed of 42 mi/hr.

Wevers et al. (1992) measured the CDD/CDF content of air samples taken during the winter of 1991 inside a tunnel in Antwerp, Belgium. The results obtained indicated that the tunnel air had a dioxin TEQ concentration about twice as high as the outside air (80.3 fg TEQ/m^3 for tunnel air vs. 35 fg TEQ/m^3 for outside air for one set of measurements and 100 fg TEQ/m^3 for tunnel air vs. 58 fg TEQ/m^3 for outside air for a second set of measurements).

During October/November 1995, Gertler et al. (1996, 1998) measured CDDs/CDFs in the Fort McHenry Tunnel in Baltimore, Maryland. The emission factors calculated, assuming that all CDDs/CDFs emitted in the tunnel were from HD vehicles, are presented in Table 2-12. The average TEQ emission factor was reported to be 172 pg TEQ/km. The major uncertainties in the study were tunnel air volume measurement, sampler flow volume control, and analytical measurement of CDDs/CDFs (Gertler et al., 1996, 1998).

The relative strengths of the Gertler et al. (1996; 1998) study include: (1) The study is a recent study conducted in the United States and thus reflects current U.S. fuels and technology; (2) virtually no vehicle using the tunnel used leaded gasoline, which is associated with past emissions of CDDs and CDFs from gasoline-powered vehicles; (3) the tunnel walls and streets were cleaned 1 week before the start of sampling, and in addition, the study analyzed road dust and determined that resuspended road dust contributed only about 4% of the estimated emission factors; and (4) HD vehicles made up, on average 25.7% of vehicles using the tunnel.

Using the emissions factor from the Gertler et al. studies, the EPA Office of Research and Development's dioxin source emission inventory estimates that 33.5 g of dioxin TEQ (total 2,3,7,8-TCDD equivalents) were emitted from HD U.S. trucks in 1995. This is a very small contribution (1.2%) compared with the national annual emission of 2,800 g CDDs/CDFs.

2.2.8. Physical and Chemical Composition of Diesel Exhaust Particles

DPM is defined by the measurement procedures summarized in Title 40 CFR, Part 86, subpart N. This definition and the basic characteristics of DPM have been summarized in Section 2.2.2. As described there, DE particles are aggregates of primary spherical particles that consist of solid carbonaceous material and ash and contain adsorbed organic and sulfur compounds (sulfate) combined with other condensed material. The organic material includes unburned fuel, engine lubrication oil, and low levels of partial combustion and pyrolysis products.

The organic material is absorbed to the EC core and is also found in heterogeneously nucleated aerosol. This fraction of the DPM is frequently quantified as the SOF (i.e., the fraction that can be extracted by an organic solvent). Because of the toxicological significance of the organic components associated with DPM, it is important to understand, to the extent possible, the historical changes in the composition of SOF and potential changes in the fraction of SOF associated with DPM.

Various researchers have attempted to apportion the SOF to unburned oil and fuel sources by thermogravimetric analysis and have found that the results vary with test cycle and engine (Abbass et al., 1991; Wachter, 1990). Kittelson (1998) estimates that a typical composition of

Table 2-12. Baltimore Harbor Tunnel Study: estimated CDD/CDF emission factors for HD vehicles

Congener/congener group	Run-specific emission factors							Mean emission factors (pg/km)
	Run no. 2 (pg/km)	Run no. 3 (pg/km)	Run no. 5 (pg/km)	Run no. 6 (pg/km)	Run no. 8 (pg/km)	Run no. 9 (pg/km)	Run no. 10 (pg/km)	
2,3,7,8-TCDD	24.5	61.6	0.0	21.2	37.8	40.1	54.9	34.3
1,2,3,7,8-PeCDD	40.2	20.6	15.4	5.6	38.4	0.0	83.0	29.0
1,2,3,4,7,8-HxCDD	18.2	25.2	46.5	8.3	64.5	0.0	123	40.8
1,2,3,6,7,8-HxCDD	37.5	28.2	64.3	19.6	153	71.1	186	80.0
1,2,3,7,8,9-HxCDD	53.6	56.5	91.6	48.4	280	126	370	147
1,2,3,4,6,7,8-HpCDD	0	401	729	111	2,438	963	2,080	960
OCDD	0	3,361	3,382	1,120	9,730	5,829	7,620	4,435
2,3,7,8-TCDF	0	94.3	67.6	152.8	155.8	73.4	61.7	86.5
1,2,3,7,8-PeCDF	0	48.9	72.6	23.6	53.3	0.0	43.3	34.5
2,3,4,7,8-PeCDF	24.5	75.7	131	46.6	85.0	63.9	108	76.4
1,2,3,4,7,8-HxCDF	15.4	139	204	93.8	124	164	166	129
1,2,3,6,7,8-HxCDF	0.3	75.1	73.7	51.0	61.3	54.4	95.5	58.8
1,2,3,7,8,9-HxCDF	27.7	14.8	75.6	0	20.6	37.2	63.5	34.2
2,3,4,6,7,8-HxCDF	15.2	82.5	152	55.7	93.0	86.8	111	85.2
1,2,3,4,6,7,8-HpCDF	12.6	280	445	154	313	354	308	267
1,2,3,4,7,8,9-HpCDF	0	58.5	60.8	31.1	25.0	2.3	34.9	30.4
OCDF	0	239	401	175	416	534	370	305
Total 2,3,7,8-CDD	174	3,954	4,328	1,335	12,743	7,028	10,515	5,725
Total 2,3,7,8-CDF	95.7	1,108	1,684	784	1,347	1,371	1,362	1,107
Total TEQ	73.8	175	170	96	235	153	303	172
Total TCDD	245	0	140	165	311	109	97.3	152
Total PeCDD	110	21.9	83.3	35.6	174	0.0	165	84.2
Total HxCDD	677	0	753	54.5	2,009	1,666	2,971	1,162
Total HpCDD	0	802	1,498	142	5,696	1,933	4,377	2,064
Total OCDD	0	3361	3,382	1,120	9,730	5,829	7,620	4,435
Total TCDF	0	901	1,314	656	2,416	1,007	687	997
Total PeCDF	124	119	1,152	78.4	1,055	282	626	491
Total HxCDF	136	319	852	67.6	444	719	619	451
Total HpCDF	0	223	814	144	513	354	637	384
Total OCDF	0	239	401	175	416	534	370	305
Total CDD/CDF	1,291	5,987	10,390	2,638	22,766	12,434	18,168	10,525
HD vehicles as % of total vehicles	21.2	22.0	22.6	34.0	28.8	24.2	27.4	25.7

Notes:
(1) Listed values are based on the difference between the calculated chemical mass entering the tunnel and the mass exiting the tunnel.
(2) All calculated negative emission factors were set equal to zero.
(3) All CDD/CDF emissions were assumed to result from heavy-duty diesel-fueled vehicles. The table presents in the last row the percent of total traffic that was heavy-duty vehicles.

Source: Gertler et al., 1996.

SOF is about one-fourth unburned fuel and three-fourths unburned engine lubrication oil. Partial combustion and pyrolysis products represented a very small fraction of the SOF on a mass basis (Kittelson, 1998), which is confirmed in numerous other studies.

A number of investigators have tried to separate the organic fraction into various classes of compounds. Schuetzle (1983) analyzed the dichloromethane extract of DPM from a LD diesel engine and found that approximately 57% of the extracted organic mass is contained in the nonpolar fraction. About 90% of this fraction consists of aliphatic HCs from approximately C_{14} to about C_{40} (Black and High, 1979; Pierson and Brachaczek, 1983). PAHs and alkyl-substituted PAHs account for the remainder of the nonpolar mass. The moderately polar fraction (~9% w/w of extract) consists mainly of oxygenated PAH species, substituted benzaldehydes, and nitrated PAH. The polar fraction (~32% w/w of extract) is composed mainly of n-alkanoic acids, carboxylic and dicarboxylic acids of PAH, hydroxy-PAH, hydroxynitro-PAH, and nitrated N-containing heterocyclic compounds (Schuetzle, 1983; Schuetzle et al., 1985).

Rogge et al. (1993) reported the composition of the extractable portion of fine DPM emitted from two HD diesel trucks (1987 model year). The DPM filters were extracted twice with hexane, then three times with a benzene/2-propanol mixture. The extract was analyzed by capillary gas chromatography/mass spectrometry (GC/MS) before and after derivatization to convert organic acids and other compounds having an active H atom to their methoxylated analogues. Unidentified organic compounds made up 90% of the eluted organic mass and were shown to be mainly branched and cyclic HCs. From the mass fraction that was resolved as discrete peaks by GC/MS, ~42% were identified as specific organic compounds. Most of the identified resolved organic mass (~60%) consisted of n-alkanes, followed by n-alkanoic acids (~20%). PAH accounted for ~3.5% and oxy-PAH (ketones and quinones) for another ~3.3%.

The distribution of the emissions between the gaseous and particulate phases is determined by the vapor pressure of the individual species, by the amount and type of the DPM present (adsorption surface available), and by the temperature (Ligocki and Pankow, 1989). Two-ring and smaller compounds (e.g., naphthalene) exist primarily in the gas phase, whereas five-ring and larger compounds (e.g., benzo[a]pyrene) are almost completely adsorbed on the particles. Three- and four-ring compounds are distributed between the two phases. The vapor pressures of these intermediate PAHs can be significantly reduced by their adsorption on various surfaces. Because of this phenomenon, the amount and type of DPM present play an important role, together with temperature, in the vapor-particle partitioning of semivolatile organic compounds (SOCs).

The measurements of gas/particulate phase distribution are often accomplished by using a high-volume filter followed by an adsorbent such as polyurethane foam (PUF), Tenax, or XAD-2 (Cautreels and Van Cauwenberghe, 1978; Thrane and Mikalsen, 1981; Yamasaki et al., 1982).

The pressure drop behind a high-volume filter or cascade impactor can contribute to volatilization of the three- to five-ring PAHs from the PM proportional to their vapor pressures. The magnitude of this blow-off artifact depends on a number of factors, including sampling temperature and the volume of air sampled (Van Vaeck et al., 1984; Coutant et al., 1988). Despite these problems from volatilization, measurements with the high-volume filters followed by a solid adsorbent have provided most estimates of vapor-particle partitioning of SOCs in ambient air, as well as insights into the factors influencing SOC adsorption onto aerosols. Significant fractions of phenanthrene, anthracene, and their alkylated derivatives, along with fluoranthene and pyrene, exist in the gas phase. PAHs with molecular weight greater than that of pyrene are typically not observed on PUF samples. During the collection of particulate organic compounds, adsorption of semivolatile PAHs can also occur, as well as chemical transformation of the semivolatile compounds (Schauer et al., 1999; Cantrell et al., 1988; Feilberg et al., 1999; Cautreels and Van Cauwenberghe, 1978).

Most of the sulfur in the fuel is oxidized to SO_2, but a small amount (1% to 4%) is oxidized to sulfuric acid in the exhaust. Sulfate emissions are roughly proportional to sulfur in the fuel. Since the reduction of the allowable sulfur content in diesel fuel in 1993, sulfate emissions have declined from roughly 10% of the DPM mass to around 1%. Particulate emissions from numerous vehicles tested using low-sulfur fuel were found to have a sulfate content of only about 1% (Yanowitz et al., 1999). Water content is on the order of 1.3 times the amount of sulfate (Wall et al., 1987).

Metal compounds and other elements in the fuel and engine lubrication oil are exhausted as ash. Hare (1977) examined 1976 Caterpillar 3208 and Detroit Diesel Corporation 6V-71 engines and found the most abundant elements emitted from the 6V-71 engine were silicon, copper, calcium, zinc, and phosphorus. From the Caterpillar engine the most abundant elements were lead, chlorine, manganese, chromium, zinc, and calcium. Calcium, phosphorus, and zinc were present in the engine lubrication oil. The two-stroke 6V-71 engine had higher engine lubrication oil emissions and therefore emitted higher levels of zinc, calcium, and phosphorus than the Caterpillar 3208 engine. Other elements may have been products of engine wear or contaminants from the exhaust system. Springer (1979), in his study of 1977 Mack ETAY(B)673A and Caterpillar 3208 (EGR) engines, found that calcium was the most abundant metallic element in DPM samples, with levels ranging from 0.01 to 0.29 wt% of the DPM. Phosphorus and silica were the next most abundant elements reported, and sodium, iron, nickel, barium, chromium, and copper were either present at very low levels or were below detection limits. Roughly 1 wt% of the total DPM was represented by the analyzed metals. There was no consistent difference in metal emissions between the engines tested by Springer or between modes. Springer tested both engines on a 13-mode steady-state test. Dietzmann and co-workers

(1980) examined metal emission rates from four HD vehicles tested using the UDDS chassis cycle. For the single two-stroke engine tested (1977 Detroit Diesel Corporation 8V-71), calcium, phosphorus, and zinc emission rates were more than 10 times higher than metal levels observed for three 1979 model year four-stroke engines because of higher engine lubrication oil emissions. Metals accounted for 0.5% to 5% of total DPM, depending on engine model. In addition to these studies, other source profiles for HD diesel engine emissions report levels of chromium, manganese, mercury compounds, and nickel at levels above the detection limit (Cooper et al., 1987).

In more recent studies, Hildemann and co-workers (1991) examined metals in DPM from the same two 1987 trucks (four-stroke engines) studied by Rogge and co-workers (1993). Aluminum, silicon, potassium, and titanium were the only metals observed at statistically significant levels. Taken together these made up less than 0.75 wt% of total DPM mass. Lowenthal and co-workers (1994) also report metals emission rates for a composite sample of several diesel vehicles. The most abundant metals were zinc, iron, calcium, phosphorus, barium, and lanthanum. Together these represented less than 0.3% of total DPM mass, with an emissions rate of 3.3 mg/mi. Norbeck and co-workers (1998b) report engine transient test emissions of metals for a 1991 Cummins L10 engine. Silicon, iron, zinc, calcium, and phosphorus were observed and together made up about 0.5% of total DPM, with an emissions rate of 1.2 mg/bhp-hr.

2.2.8.1. *Organic and EC Content of Particles*

2.2.8.1.1. ***Measurement of the organic and EC fraction.*** Various methods have been used to quantify the organic fraction of DPM. The most common method has been Soxhlet extraction with an organic solvent. Following extraction, the solvent can be evaporated and the mass of extracted material (the SOF) determined, or alternatively the PM filter is weighed before and after extraction and the extracted material can be further analyzed to determine concentrations of individual organic compounds. Vacuum oven sublimation is used to measure a comparable quantity, the volatile organic fraction (VOF), which can be further speciated by GC with a flame ionization detector. Other methods have also been employed, including thermal methods, microwave extraction, sonication with an organic solvent, supercritical fluid extraction, thermogravimetric analysis, and thermal desorption GC. Abbass et al. (1991) compared various methods, including vacuum oven sublimation and 8 hours of Soxhlet extraction, with 4:1 benzene/methanol solvent for determination of SOF and found reasonably good agreement between the two methods. The VOF value was typically 10% higher; however, this variation was less than the coefficient of variation between measurements using the same method.

Levson (1988) reviewed literature regarding the extraction efficiency of various solvents and found contradictory results in many cases. He concluded that there is strong evidence that the most commonly used solvent, dichloromethane, leads to poor recoveries of higher molecular weight PAH. More recently, Lucas et al. (1999) reported the effect of varying dichloromethane/benzene ratios in the solvent (from 25% to 100% dichloromethane) and changing extraction times and found that the most effective extraction (i.e., the largest extracted mass) utilized a 70% dichloromethane/30% benzene mixture and extraction times several times longer than the commonly used 8-hour extraction period. Extractions of 70 hours using pure dichloromethane were found to result in about twice as much SOF as extractions of only 12 hours. Between 6 and 24 hours of extraction time (the typical range of extraction times used), the SOF recovered increased by about one-third. Using the most effective extraction conditions (Soxhlet, 70 hours, 70:30 dichloromethane:benzene ratio), Lucas et al. (1999) were able to extract more than 90% of the total particulate mass.

Other researchers have investigated the relative quantities of mass removed by sequential extraction by polar, moderately polar, and nonpolar solvents. The extracted nonpolar fraction (cyclohexane) ranged from 56% to 90% of the SOF, the moderately polar (dichloromethane) from 6% to 22%, and the polar fraction (acetonitrile) from 4% to 29% (Dietzmann et al., 1980). Water and sulfate are not soluble in cyclohexane or dichloromethane but are soluble in acetonitrile.

Although the reports on the extraction efficiencies for PAHs are in part contradictory, it appears that Soxhlet extraction and the binary solvent system composed of aromatic solvent and alcohol yield the best recovery of PAHs, as determined by C-B[*a*]P^{14} (benzo[a]pyrene) spiking experiments (Schuetzle and Perez, 1983). Limited recovery studies have shown that there is little degradation or loss of diesel POM on the HPLC column. More than 90% of the mass and 70% to 100% of the Ames *S. typhimurium*-active material injected onto the column has been recovered (Schuetzle et al., 1985).

Two thermal methods of organic and EC analysis include thermal optical reflectance (TOR) and thermal optical transmittance (TOT). The extractable portion of total carbon, although commonly used as a measure of organic compound content, is not equivalent to the OC fraction as measured by TOR or TOT. In addition, methodological differences between TOR and TOT also give rise to significant differences in the fraction of total carbon reported as organic and EC (Birch, 1998; Norris et al., 2000; Chow et al., 2000). Although total carbon reported using TOR or TOT provides results that are comparable (within 10%) (Norris et al., 2000) the EC content of samples analyzed by TOR is higher than that measured by TOT. This difference is primarily attributed to the temperature used to evolve carbon from the quartz filter onto which it is collected. In an analysis of urban $PM_{2.5}$ samples, Norris et al. (2000) found that

the EC content of samples analyzed by TOR was a factor of two higher than the EC content of the same samples analyzed by TOT. Experiments are ongoing to test specific source materials (including DPM) because some of the difference between methods appears to depend on the type of OC present on the sample.

The analytical technique used to measure OC and EC can have a significant effect on the quantity of reported. In the discussion that follows, every effort has been made to compare only studies using comparable methods and to state the analysis method employed.

2.2.8.1.2. ***Trends in SOF emissions.*** SOF emission values are highly dependent on the test cycle used. Various studies have shown that SOF generally increases at light engine loads and high engine speeds because these conditions lead to low exhaust temperatures, where fuel and oil are not as effectively oxidized (Scholl et al., 1982; Kittelson, 1998; Springer, 1979; Schuetzle and Perez, 1983; Martin, 1981b; Shi et al., 2000). These conditions are more typically observed in LD diesel vehicle applications, and thus DPM from these vehicles typically has a higher SOF component than HD diesel vehicles (Norbeck et al., 1998c). Acceleration modes normally cause increased emission of EC and an increase in total DPM emissions, whereas organic components are more dominant when motoring (Wachter, 1990). Additionally, cold-start test emissions of SOF have been shown to be approximately 25% higher than hot-start emissions (Wachter, 1990).

The quantity of sulfur in diesel fuel has been suggested to have a role in the quantity of SOF emitted (Sienicki et al., 1990; Tanaka et al., 1998). Sienicki et al. (1990) reported an approximate 25% increase in SOF when sulfur concentrations are increased from 0.08% to 0.33%. The cause is unclear but several explanations have been put forth, including increased absorption of organic compounds from the vapor phase onto the DPM by sulfates or sorbed sulfuric acid. Alternatively, it has been proposed that the measured SOF may include some sulfate, so that the apparent increase in organic material is due instead to sulfate. Other fuel effects include an increase in SOF emissions with a higher T90 (or T95) and with an increase in aromatic content (Barry et al., 1985; Sienicki et al., 1990; Tanaka et al., 1998; Rantanen et al., 1993).

Figures 2-31 and 2-32 show SOF emissions as a function of year for transient emissions tests on chassis and engines, respectively. Both figures suggest a significant decline in SOF emissions of approximately a factor of 5 since about 1980. The highest SOF emissions are for two-stroke engines built in the 1970s (up to approximately 1.2 g/mi). These data indicate that SOF emission factors for newer model year vehicles are lower than SOF emission factors for pre-1990 model year vehicles and that this decrease is similar to that observed for emissions of total DPM by model year. In a recent test of six pre-1976 HDDVs, Fritz et al. (2001) reported the

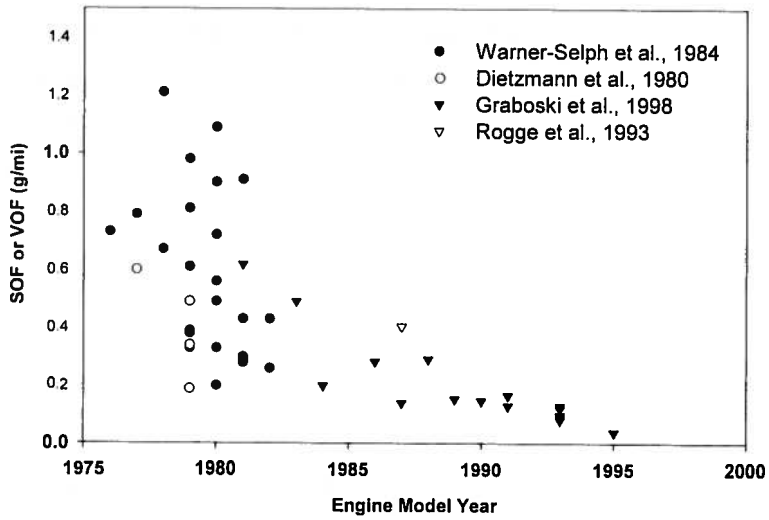

Figure 2-31. Trend in SOF emissions based on chassis dynamometer testing of HD diesel vehicles. Warner-Selph and co-workers: dichloromethane for 8 hours. Dietzman and co-workers: hexane followed by dichloromethane, extraction times not reported. Graboski and co-workers: VOF by vacuum sublimation at 225° C for 2.5 to 3 hours. Rogge and co-workers: cyclohexane followed by a benzene/2-propanol mixture that may extract significantly more organic matter.

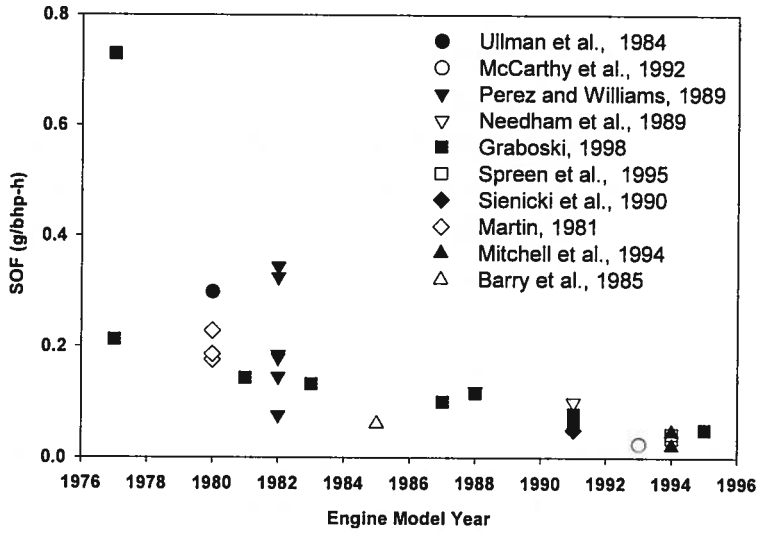

Figure 2-32. Trend in SOF emissions for transient engine dynamometer testing of HD diesel engines. Various extraction methods used; see Table 2-8.

volatile organic fraction (VOF) ranged from 0.4 g/mi to 4.5 g/mi. These data highlight the wide range in emission rates for of OC, as have been observed for total PM.

Steady-state testing conducted on late-1970s engines reported SOF at levels between 0.1 and 0.9 g/bhp-hr, whereas engines from the late 1980s and 1990s all emitted 0.03 g/bhp-hr or less (Table 2-8). Hori and Narusawa (1998) measured emissions from engines produced two decades apart, using identical analytical procedures, and found that SOF emission factors and the percentage contribution of SOF to DPM were lower in the new engine compared with the old engine, under all tested engine load and speed conditions and with different fuels. The authors reported that the decrease in SOF was due to lower emissions of both lubricating oil and unburned fuel. To meet the 1991 and 1994 U.S. emission standards, SOF emission rates would need to be reduced from the levels of the previous decade, although one may expect differences in SOF fractions of DPM with transient cycles used to determine compliance with emission standards verus steady-state conditions used in earlier test programs (Kawatani et al., 1993; Wachter, 1990). Finally, in the past three decades, for economic reasons engine manufacturers have made efforts to reduce oil consumption and increase the fuel efficiency of diesel engines, both of which would be expected to reduce SOF emissions. Problems in achieving SOF reductions from two-stroke engines were one factor leading to the phaseout of these engines for on-road use during the 1990s. No data are available prior to 1976 on SOF emissions from HD diesel vehicles. The engine technology changes that occurred between the mid-1950s and mid-1970s (high-pressure direct injection and turbocharging, primarily) might be expected to increase the efficiency of combustion and thereby reduce fuel-related SOF. SOF emissions levels in the mid- to late 1970s may be used as a conservative (low) estimate of SOF emissions during the preceding two decades.

The fraction of DPM attributed to SOF from chassis dynamometer studies also shows a decreasing trend over time, from SOFs that ranged up to approximately 50% in the 1980s to 20% SOF or less in the 1990s (Figure 2-33). The recent study by Fritz et al. (2001) reported the fraction of DPM attributed to VOF from 10% to 60% for HDDVs of model years 1951-1974. The wide range in SOF as a percent of DPM displayed in Figure 2-33 is suspected to result from factors such as engine deterioration and test cycle. The vehicle emissions data reported in Figure 2-33 do not overrepresent buses that are likely to emit DPM with a greater fraction of SOF than other vehicles. Figure 2-34 presents SOF as a fraction of DPM from the same engine dynamometer studies reported in Figure 2-32. These data do not reflect a downward trend in SOF as a fraction of DPM. Because similar extraction methods were used in reports of the SOF in both the chassis and engine dynamometer studies, this does not appear to be a source of the wide variability observed in the fraction of SOF reported. In some of the engine studies, improved air:fuel ratio control was tested in an attempt to lower carbonaceous DPM formation.

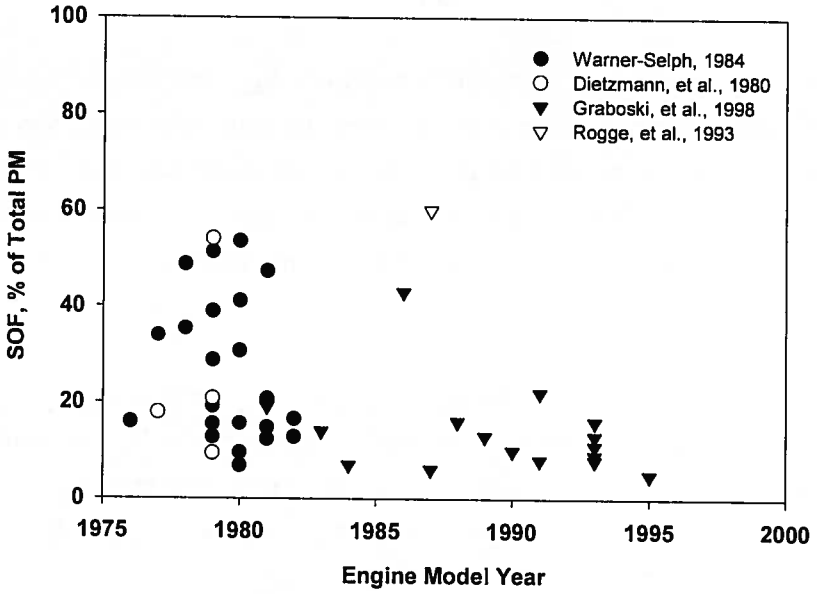

Figure 2-33. Trend in SOF emissions as a percent of total PM based on chassis dynamometer testing of HD diesel vehicles. Warner-Selph and co-workers: dichloromethane for 8 hours. Dietzman and co-workers: hexane followed by dichloromethane, extraction times not reported. Graboski and co-workers: VOF by vacuum sublimation at 225° C for 2.5 to 3 hours. Rogge and co-workers: cyclohexane followed by a benzene/2-propanol mixture that may extract significantly more organic matter.

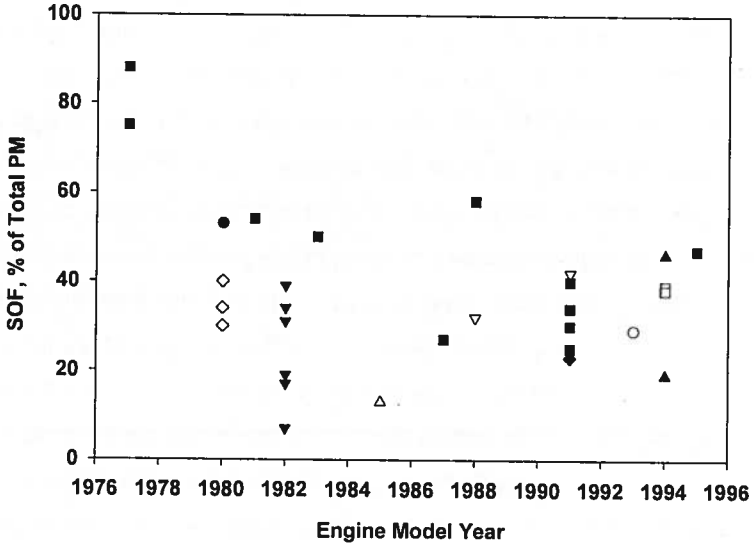

Figure 2-34. Trend in SOF emissions as a percentage of total PM from engine dynamometer testing. Data are from Table 2-8. (See Figure 2-32 for figure key.)

Therefore, substantial differences in SOF as a percent of total DPM could be the result of different engine technology or test conditions. The engine dynamometer results presented in Figures 2-32 and 2-34 are from new, or relatively new, engines, that is, engines with no deterioration, whereas the older engines tested on a chassis dynamometer may have experienced significant deterioration that would increase SOF emissions as a percent of DPM. One of the main differences suspected for the lack of a decreasing trend in the percent of SOF in the engine dynamometer studies is the test cycle used. The engine dynamometer tests typically include test modes, such as high speed and low load, or low-speed lugging modes, that produce much higher SOF relative to DPM than the driving cycles used on the chassis tests.

It appears that as a fraction of total DPM, SOF from new model year HD diesel vehicles is lower than that from older (pre-1990) HD diesel vehicles. However, as with total DPM emissions, a wide range in the fraction of SOF can be observed under different driving conditions and from vehicles with extensive engine wear. In general, DPM emissions have a lower fraction of organic matter compared to gasoline PM (Table 2-13). Recent testing of HD engines at the Desert Research Institute suggests that the OC fraction of DPM is approximately 19%, whereas earlier studies reported in the U.S. EPA SPECIATE database suggest a slightly higher organic fraction of DPM from HD diesel vehicles, ranging from 21% to 36%. The SPECIATE database represents older vehicles that, as discussed above, tend to have higher SOF emissions. The OC emissions from LD diesel vehicles recently reported by Norbeck et al. (1998c) and those reported by the U.S. EPA SPECIATE suggest that LD diesel vehicles emit DPM with a slightly higher organic content than that from HD diesel vehicles, ranging from 22% to 43%. Gasoline engine PM emissions have recently been analyzed at the Desert Research Institute by Fujita et al. (1998) and Watson et al. (1998) for hot stabilized, visibly smoking vehicles, and cold-starts. These data all indicate that LD gas vehicles emit PM with a higher fraction of organic matter than diesel vehicles, with the highest organic content measured from smoking and high-emitting gasoline vehicles (averaging 76% OC). One new finding from the data reported by Fujita et al. (1998) is the roughly equivalent emission of organic and EC from cold-start emissions of gasoline vehicles. Additional information is needed to characterize a range of OC for DPM from smoking and high-emitting diesel vehicles as well as cold-start HD diesel vehicles.

2.2.8.1.3. ***Trends in EC content.*** Because EC is a major component of the chemical source profile of DE, it is commonly used to determine the contribution of diesel vehicles to ambient PM samples (i.e., in source apportionment via chemical mass balance modeling). EC is not, strictly speaking, a regulated pollutant, and so EC emissions are not routinely measured in tests of diesel vehicles and engines. The scant data available on measured EC emissions from HD

Table 2-13. Organic and elemental carbon fractions of diesel and gasoline engine PM exhaust

Engine type	% OC	% Elemental carbon
HD diesel engines[a]	19 ± 8	75 ± 10
HD diesel engines (SPECIATE)[b]	21-36	52-54
LD diesel engines[c]	30 ± 9	61 ± 16
LD diesel engines (SPECIATE)[b]	22-43	51-64
Gasoline engines (hot stabilized)[a]	56 ± 11	25 ± 15
Gasoline engines (smoker and high emitter)[a,c]	76 ± 10	7 ± 6
Gasoline engines (cold start)[a]	46 ± 14	42 ± 14

[a] Fujita et al., 1998, and Watson et al., 1998.
[b] U.S. EPA SPECIATE database.
[c] Norbeck et al., 1998c.

diesel vehicles are plotted in Figure 2-35. Different analytical methods were employed for these studies, making the comparison of emission rates difficult. Results from the three studies, all performed on HD trucks, suggest a decline in EC emission rates by model year since the early 1980s. In a study conducted in 1992, four HD vehicles of unknown vintage were tested and a combined EC emission rate of 0.81 g/mi was reported, which is consistent with the 1990 timeframe in Figure 2-35 (Lowenthal et al., 1994). EC as a percentage of total DPM in these studies ranged from 30% to 90%, most likely as a result of different testing cycles and different engines and different analytical methods.

Figure 2-36 presents these data as EC fraction of total fine PM. The EC content of DPM varied widely in the 1980s from approximately 20% to 90%, whereas in more recent years, the data suggest a smaller range in the EC fraction, from approximately 50% to 90% (with one data point at 30%). Recent emission profiles for HD diesel vehicles suggest that 75% ± 10% of the DPM is attributable to EC, whereas approximately 25% of gasoline PM is composed of EC, except for PM emissions during gasoline vehicle cold-starts, which were found to have an EC content of approximately 42% (Table 2-13). These data also provide evidence that newer model year HD engines generally emit DPM that is more rich in EC than older HD engines.

2.2.8.2. *PAHs and Nitro-PAH Emissions*

PAHs, nitro-PAHs, and oxidized derivatives of these compounds have attracted considerable attention because of their known mutagenic and, in some cases, carcinogenic

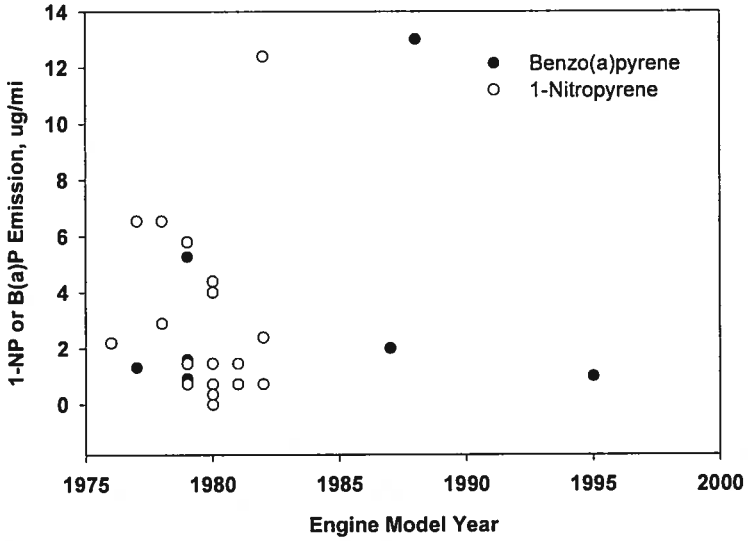

Figure 2-35. EC emission rates for diesel vehicles.

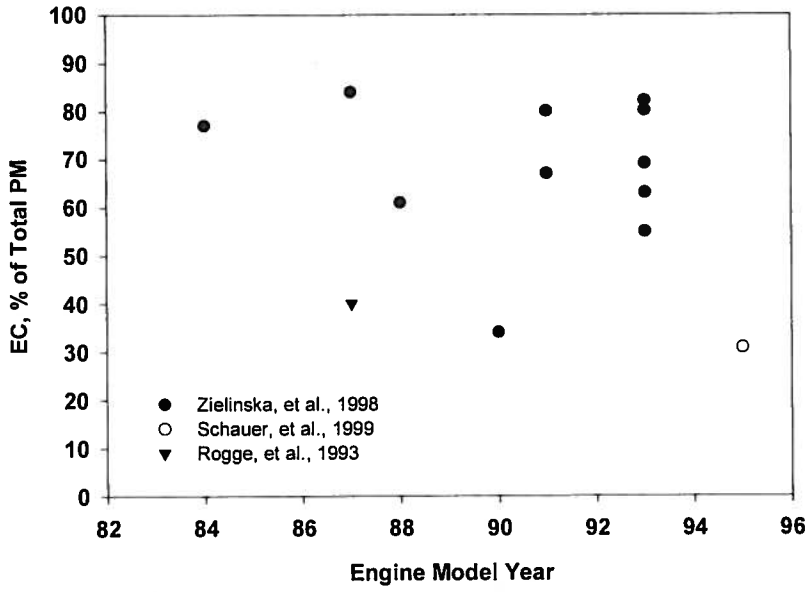

Figure 2-36. EC content as percent of fine PM for DPM samples obtained in chassis dynamometer studies.

character (National Research Council, 1982). In this section, PAH and nitro-PAH concentrations and emission rates and trends in emissions over time are presented.

2.2.8.2.1. ***PAHs identified in DE.*** At least 32 PAHs have been identified in the exhaust of LD diesel vehicles and HD diesel vehicles (Table 2-14) (Watson et al., 1998; Zielinska et al., 1998). Table 2-15 lists the PAHs and thioarenes identified in three LD diesel vehicles' DPM extracts, reported as ng/g of DPM (Tong et al., 1984). SOF fractions accounted for 11% to 15% of the total DPM mass for the LD diesel vehicles reported by Tong et al. (1984), which is lower than the LD diesel vehicles organic fraction reported by Norbeck et al. (1998c) in Table 2-13. Among the PAHs reported by Watson et al. (1998) and Zielinska et al. (1998), the higher molecular weight compounds (pyrene through coronene) that are expected to partition to the particle phase have emission rates from HD diesel vehicles ranging from below detection limits up to 0.071 mg/mi. HD diesel vehicle emission rates for the lower molecular weight PAHs ranged up to 2.96 mg/mi for dimethylnaphthalenes. In general, among the vehicles tested, PAH emission rates were higher for LD diesel vehicles compared with HD diesel vehicles. Table 2-16 presents emission rates of four representative particle-phase PAHs from HD diesel vehicles, LD diesel vehicles, and gasoline (with and without catalytic converter) engines. Emission rates for benzo[a]pyrene were higher in diesel emissions compared with gasoline emissions, except for the report by Rogge et al. (1993), who used extraction methods different from those in other studies (discussed above).

2.2.8.2.2. ***Nitro-PAHs identified in DE.*** Positive isomer identification for 16 nitro-PAHs has been made utilizing the GC retention times of authentic standards and low- and high-resolution mass spectra as identification criteria. These include 1-nitropyrene; 2-methyl-1-nitronaphthalene; 4-nitrobiphenyl; 2-nitrofluorene; 9-nitroanthracene; 9-methyl-10- nitroanthracene; 2-nitroanthracene; 2-nitrophenanthrene; 1-methyl-9-nitroanthracene; 1-methyl-3-nitropyrene; 1-methyl-6-nitropyrene; 1-methyl-8-nitropyrene; 1,3-, 1,6-, and 1,8-dinitropyrene; and 6-nitrobenzo[a]pyrene. In addition, two nitrated heterocyclic compounds were identified, 5- and 8-nitroquinoline. Forty-five additional nitro-PAHs were tentatively identified in this diesel particulate extract (Paputa-Peck et al., 1983). The concentration of nitro-PAHs adsorbed on diesel particles varies substantially from sample to sample. Usually 1-nitropyrene is the predominant component, and concentrations ranging from 7 to 165 μg/g of particles are reported (Levson, 1988).

Table 2-17 gives the approximate concentrations of several of the abundant nitro-PAHs quantified in the early 1980s LD diesel particulate extracts (with the exception of

Table 2-14. Emission rates of PAH (mg/mi) from LD and HD diesel vehicles

PAH	Light-duty diesel	Heavy-duty diesel
Naphthalene	5.554 ± 0.282	2.451 ± 0.154
2-Menaphthalene	3.068 ± 0.185	2.234 ± 0.152
1-Menaphthalene	2.313 ± 0.134	1.582 ± 0.103
Dimethylnaphthalenes	5.065 ± 0.333	2.962 ± 0.488
Biphenyl	0.743 ± 0.041	0.505 ± 0.037
2-Methylbiphenyl	0.203 ± 0.015	0.049 ± 0.024
3-Methylbiphenyl	1.048 ± 0.063	0.401 ± 0.036
4-Methylbiphenyl	0.447 ± 0.028	0.144 ± 0.021
Trimethylnaphthalenes	6.622 ± 0.563	1.940 ± 0.221
Acenaphthylene	0.422 ± 0.024	0.059 ± 0.087
Acenaphthene	0.096 ± 0.008	0.030 ± 0.040
Phenanthrene	1.411 ± 0.072	0.084 ± 0.011
Fluorene	0.442 ± 0.038	0.066 ± 0.022
Methylfluorenes	1.021 ± 0.091	0.071 ± 0.055
Methylphenanthrenes	1.115 ± 0.064	0.124 ± 0.069
Dimethylphenanthrenes	0.637 ± 0.047	0.090 ± 0.096
Anthracene	0.246 ± 0.025	0.052 ± 0.016
9-Methylanthracene	0.013 ± 0.002	0.434 ± 0.082
Fluoranthene	0.213 ± 0.014	0.044 ± 0.026
Pyrene	0.245 ± 0.020	0.071 ± 0.017
Methyl(pyrenes/fluoranthenes)	0.548 ± 0.045	0.022 ± 0.082
Benzonaphthothiophene	0.002 ± 0.002	0.001 ± 0.027
Benz[a]anthracene	0.020 ± 0.005	0.066 ± 0.046
Chrysene	0.029 ± 0.005	0.009 ± 0.021
Benz[b+j+k]fluoranthene	0.056 ± 0.005	0.009 ± 0.022
Benzo[e]pyrene	0.019 ± 0.003	0.010 ± 0.014
Benzo[a]pyrene	0.013 ± 0.004	0.013 ± 0.044
Indeno[1,2,3-cd]pyrene	0.010 ± 0.003	0.001 ± 0.037
Dibenzo[a]anthracene	0.002 ± 0.003	0.000 ± 0.053
Benzo[b]chrysene	0.001 ± 0.002	0.001 ± 0.027
Benzo[ghi]perlyne	0.018 ± 0.004	0.013 ± 0.048
Coronene	0.006 ± 0.006	0.001 ± 0.095

Table 2-15. Polycyclic aromatic hydrocarbons identified in extracts of diesel particles from LD diesel engine exhaust

Compound	Molec. wt.	Concentration ng/mg extract
Acenaphthylene	152	30
Trimethylnaphthalene	170	140–200
Fluorene	166	100–168
Dimethylbiphenyl	182	30–91
C_4 -Naphthalene	184	285–351
Trimethylbiphenyl	196	50
Dibenzothiophene	184	129–246
Phenanthrene	178	2,186–4,883
Anthracene	178	155–356
Methyldibenzothiophene	198	520–772
Methylphenanthrene	192	2,028–2,768
Methylanthracene	192	517–1,522
Ethylphenanthrene	206	388–464
4H-Cyclopenta[*def*]phenanthrene	190	517–1,033
Ethyldibenzothiophene	212	151–179
2-Phenylnaphthalene	204	650–1,336
Dimethyl(phenanthrene/anthracene)	206	1,298–2,354
Fluoranthene	202	3,399–7,321
Benzo[*def*]dibenzothiophene	208	254–333
Benzacenaphthylene	202	791–1,643
Pyrene	202	3,532–8,002
Ethylmethyl (phenanthrene/anthracene)	220	590–717
Methyl(fluoranthene/pyrene)	216	1,548–2,412
Benzo[*a*]fluorene/benzo[*b*]fluorene	216	541–990
Benzo[*b*]naphtho[2,1-*d*]thiophene	234	30–53
Cyclopentapyrene	226	869–1,671
Benzo[*ghi*]fluoranthene	226	217–418
Benzonaphthothiophene	234	30–126
Benz[*a*]anthracene	228	463–1,076
Chrysene or triphenylene	228	657–1,529
1,2-Binapthyl	254	30–50
Methylbenz[*a*]anthracene	242	30–50
3-Methylchrysene	242	50–192
Phenyl(phenanthrene/anthracene)	254	210–559
Benzo[*j*]fluoranthene	252	492–1,367
Benzo[*b*]fluoranthene	252	421–1,090
Benzo[*k*]fluoranthene	252	91–289
Benzo[*e*]pyrene	252	487–946
Benzo[*a*]pyrene	252	208–558
Benzo[*ah*]anthracene	278	50–96
Indeno[1,2,3-[*cd*]pyrene	276	30–93
Benzo[*ghi*]perylene	276	443–1,050
Dibenzopyrene	302	136–254

Source: Tong et al., 1984.

Table 2-16. Emission rates of particle-bound PAH (μg/mi) from diesel and gasoline engines

PAH	Diesel engines					Gasoline engines			
	HDD			LDD		Noncatalyst		Catalyst	
	(a)	(b)	(c)	(a)	(d)	(c)	(e)	(a)	(c)
Pyrene	71	17.6	36.2	245	66	49.6	45	248	4.0
Fluoranthene	44	27.2	20.8	213	50	77.3	32	196	3.6
Benzo[a]pyrene	13	<0.1	2.1	13	NA	69.6	3.2	1.0	3.0
Benzo[e]pyrene	10	0.24	4.2	19	NA	73.3	4.8	1.0	3.6

(a) Watson et al., 1998 included gas-phase PAH .
(b) Westerholm et al., 1991.
(c) Rogge et al., 1993.
(d) Smith, 1989; 1986 Mercedes Benz.
(e) Alsberg et al., 1985.

3-nitrobenzanthrone, reported recently) in μg/g of particles. Concentrations for some of the nitro-PAHs identified range from 0.3 μg/g for 1,3-dinitropyrene to 8.6 μg/g for 2,7-dinitro-9-fluorenone and 75 μg/g for 1-nitropyrene. More recent nitro-PAH and PAH data for HD diesel engines are reported in units of g/bhp-hr or mass/volume of exhaust, making it impossible to directly compare them to the older data (Norbeck et al., 1998b; Bagley et al., 1996, 1998; Baumgard and Johnson, 1992; Opris et al., 1993; Hansen et al., 1994; Harvey et al., 1994; Kantola et al., 1992; Kreso et al., 1998; McClure et al., 1992; Pataky et al., 1994).

2.2.8.2.3. ***PAH and nitro-PAH emission changes over time.*** It is difficult to compare PAH emissions from different studies because not all investigators analyze for total PAH or the same suite of PAH compounds. Most studies have reported emissions of B[*a*]P or 1-nitropyrene (1-NP) because of their toxicological activity. The results of chassis dynamometer studies in which B[*a*]P or 1-NP were measured are displayed in Figure 2-37. Dietzmann and co-workers (1980) examined four vehicles equipped with late 1970s turbocharged DI engines. Emissions of B[*a*]P from particle extracts ranged from 1.5 to 9 μg/mi. No relationship between engine technology (one of the engines was two-stroke) and B[*a*]P emissions was observed. Rogge and co-workers (1993) reported total particle-associated PAH and B[*a*]P emissions from two 1987 model year trucks (averaged together, four-stroke and turbocharged engines). The total particle-phase PAH emission rate was 0.43 mg/mi and the B[*a*]P emission rate was 2.7 μg/mi. Particle-phase PAH in the Rogge et al. (1993) study accounted for approximately 0.5% of total DPM mass. Schauer and co-workers (1999) recently reported a particle-phase PAH emission rate of 1.9 mg/mi (accounting for about 0.7% of total DPM mass) for a 1995 MD turbocharged and aftercooled truck. B[*a*]P emissions were not reported, but emissions of individual species of similar

Table 2-17. Concentrations of nitro-PAHs identified in LD diesel particulate extracts

Nitro-PAH[a]	Concentration (µg/g of particles)
4-nitrobiphenyl	2.2
2-nitrofluorene	~1.8
2-nitroanthracene	4.4
9-nitroanthracene	1.2
9-nitrophenanthrene	1.0
3-nitrophenanthrene	4.1
2-methyl-l-nitroanthracene	8.3
1-nitrofluoranthene	1.8
7-nitrofluoranthene	0.7
3-nitrofluoranthene	4.4
8-nitrofluoranthene	0.8
1-nitropyrene	18.9; 75[b]
6-nitrobenzo[a]pyrene	2.5
1,3-dinitropyrene[b]	0.30
1,6-dinitropyrene[b]	0.40
1,8-dinitropyrene[b]	0.53
2,7-dinitrofluorene[c]	4.2; 6.0
2,7-dinitro-9-fluorenone[c]	8.6; 3.0
3-nitrobenzanthrone[d]	0.6 to 6.6

[a]From Campbell and Lee (1984) unless noted otherwise. Concentrations recalculated from µg/g of extract to µg/g of particles using a value of 44% for extractable material (w/w).
[b]From Paputa-Peck et al, 1983.
[c]From Schuetzle, 1983.
[d]From Enya et al., 1997 (Isuzu Model 6HEL 7127cc).

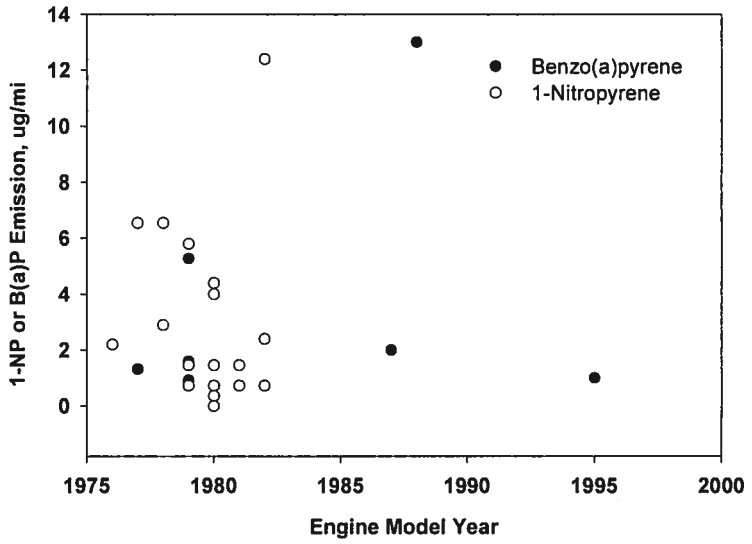

Figure 2-37. Diesel engine emissions of benzo[*a*]pyrene and 1-nitropyrene measured in chassis dynamometer studies.

Source: Schuetzle and Perez, 1983; Zielinska et al., 1988; Kado et al., 1996; Dietzmann et al., 1980; Warner-Selph and Dietzmann, 1984; Rogge et al., 1993; Schauer et al., 1999.

molecular weight were approximately 10 μg/mi. Schauer et al. (1999) also reported a gas-phase PAH emission rate of 6.9 mg/mi for the same truck. Measurements of particle- and gas-phase PAHs conducted for the Northern Front Range Air Quality Study in Colorado (Zielinska et al., 1998) showed an average B[*a*]P emission rate of 13 μg/mi for 15 vehicles ranging from 1983 to 1993 model years. The combined gas- and particle-phase PAH emission rate reported for the NFRAQS study was 13.5 mg/mi. B[*a*]P emissions from chassis studies are summarized in Figure 2-37. Zielinska (1999) reports a decreasing trend in particle-associated DE PAH from 11 measurements made on vehicles from model year 1984 to 1993 with a low correlation coefficient of 0.29.

B[*a*]P emissions reported from diesel engine dynamometer studies are summarized in Figure 2-38. Springer (1979) compared B[*a*]P emissions from naturally aspirated and turbocharged engines and found that naturally aspirated engines emitted about 1 μg B[*a*]P/bhp-hr, and DI and IDI engines emitted about 0.15 μg B[*a*]P/bhp-hr (Table 2-8). The difference between 1 and 0.15 μg/bhp-hr could not be attributed to specific technology changes. The majority of engine test data indicate that B[*a*]P emissions have generally ranged from approximately 1 to 4 μg/bhp-hr over the past 25 years.

Emissions reported for 1-NP from diesel engines tested by chassis dynamometer range from 0.1 to 12 μg/mi (Figure 2-37), and diesel engine dynamometer studies report 1-NP emission factors ranging from 1 to 4 μg/bhp-hr (Figure 2-38). Too few measurements are available to discern trends in the emission rates of these compounds.

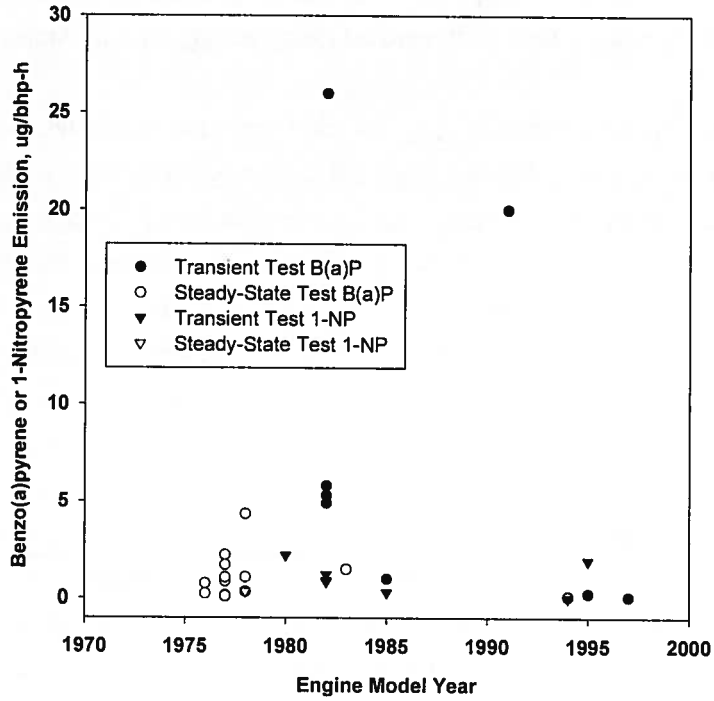

Figure 2-38. Diesel engine dynamometer measurements of benzo[*a*]pyrene and 1-nitropyrene emissions from HD diesel engines.

Source: Data are from Table 2-8.

As discussed in Section 2.2.4, Williams et al. (1987) and Andrews et al. (1998) of the University of Leeds have demonstrated that the solvent-extractable PAH from diesel particulate originates primarily in the fuel. PAH molecules are relatively refractory, so a significant fraction survives the combustion process and is exhausted as DPM. These studies have been confirmed by other research groups (Crebelli et al., 1995; Tancell et al., 1995) that included the use of isotopic labeling of fuel PAH. Additionally, engine oil was found to be a reservoir for PAH that originates in the fuel. Pyrosynthesis of PAH occurs during very high temperature conditions in a diesel engine, and under these conditions many of the DPM and other pyrolysis products are ultimately oxidized before exiting the cylinder. Thus, pyrogenic formation of PAH is thought to contribute a small fraction of the total PAH in diesel engine exhaust. As discussed above, fuel

PAH content is expected to have slowly increased over a 30-year period until 1993, after which PAH content of diesel fuel is expected to have remained constant. Increasing use of catalytic cracking over time may lead to increasing proportions of PAH in distillates; however, fuel standards limit the aromaticity of fuel to 35% (Section 2.2.4).

Recently, Norbeck et al. (1998a) reported on the effect of fuel aromatic content on PAH emissions. Three diesel fuels were used in a Cummins L10 engine: pre-1993 fuel containing 33% aromatic HC and 8% PAH; low aromatic fuel containing a maximum content of 10% aromatic HC and maximum of 1.4% PAH; and a reformulated fuel containing 20% to 25% aromatic HC and 2% to 5% PAH. The investigators found that emission rates for the low-molecular-weight PAHs (PAHs with three or fewer rings) were significantly lower when the engine was tested using the low aromatic fuel compared to when the engine was run on the pre-1993 or reformulated fuel (Table 2-18). Although emission rates reported for several higher molecular weight (particle-associated) PAHs were lower (ranging from 4% to 28% lower) for the low aromatic fuel compared with the other two fuels, the differences were not statistically significant except for coronene.

On the basis of these limited data it is difficult to draw a precise, quantitative conclusion regarding how PAH, B[*a*]P, or 1-NP emissions have changed over time and in response to fuel and engine changes. A decrease in the emissions of PAH from post-1990 model year vehicles and engines compared with pre-1990 vehicles and engines is suggested by the data; however, the data also suggest that differences in a vehicle's engine type and make, general engine condition, fuel composition, and test conditions can influence the emission levels of PAH.

2.2.8.3. *Particle Size*

Figure 2-39 shows a generic size distribution for diesel particulate based on mass and particle number. Approximately 50% to 90% of the number of particles in DE are in the ultrafine size range (nuclei-mode), with the majority of diesel particles ranging in size from 0.005-0.05 μm and the mode at about 0.02 μm. These aerosol particles are formed from exhaust constituents and consist of sulfuric acid droplets, ash particles, condensed organic material, and primary carbon spherules (Abdul-Khalek et al., 1998; Baumgard and Johnson, 1996). Although it accounts for the majority of particles, ultrafine DPM accounts for only 1% to 20% of the mass of DPM.

Approximately 80% to 95% of diesel particle mass is in the size range from 0.05 to 1.0 μm, with a mean particle diameter of about 0.2 μm. The EC core has a high specific surface area of approximately 30 to 50 m^2/g (Frey and Corn, 1967), and Pierson and Brachaczek (1976) report

that after the extraction of adsorbed organic material, the surface area of the diesel particle core

Table 2-18. Average emission rates for polycyclic aromatic hydrocarbons for different fuel types (units are µg/bhp-hr)

PAH	**Pre-1993 diesel fuel** Cetane No. >40 Aromatic 33% v. PAH 8% wt.	**Low aromatic diesel fuel** Cetane No. >48 Aromatic 10% v. PAH 1.4% wt.	**Reformulated diesel blend** Cetane No. 50-55 Aromatic 20%-25% v. PAH 2%-5% wt.
2,3,5-trimethyl naphthalene	283.68 ± 5.27	14.77 ± 2.42	56.21 ± 2.82
Phenanthrene	336.71 ± 9.08	160.92 ± 15.54	220.73 ± 52.68
Anthracene	38.89 ± 1.43	18.54 ± 2.13	26.16 ± 6.86
Methylphenanthrenes/anthracenes	331.32 ± 16.07	25.17 ± 1.41	111.98 ± 28.74
Fluoranthene	128.45 ± 7.60	132.36 ± 18.30	123.07 ± 26.21
Pyrene	193.03 ± 16.51	211.19 ± 37.35	206.82 ± 39.04
Benzo[c]phenanthrene	3.03 ± 0.24	1.74 ± 0.14	1.54 ± 0.26
Benzo[ghi]fluoranthene	24.84 ± 2.68	18.93 ± 2.14	16.94 ± 2.31
Cyclopenta[cd]pyrene	21.44 ± 4.11	26.15 ± 3.12	21.25 ± 3.46
Benz[a]anthracene	16.42 ± 1.67	10.57 ± 1.15	10.96 ± 2.42
Chrysene + triphenylene	17.36 ± 1.66	10.38 ± 0.54	12.20 ± 2.72
Benzo[b+j+k]fluoranthene	31.05 ± 4.17	23.17 ± 1.98	29.18 ± 7.93
Benzo[e]pyrene	16.71 ± 2.72	14.55 ± 1.34	18.99 ± 5.58
Benzo[a]pyrene	20.46 ± 3.27	16.48 ± 1.56	20.59 ± 5.75
Perylene	4.32 ± 0.88	3.71 ± 0.74	4.18 ± 1.16
Indeno[1,2,3-cd]fluoranthene	0.34 ± 0.07	0.21 ± 0.02	0.17 ± 0.00
Benzo[c]chrysene	0.29 ± 0.05	0.18 ± 0.05	0.14 ± 0.04
Dibenz[a,h]anthracene	0.93 ± 0.05	0.55 ± 0.10	0.67 ± 0.09
Indeno[1,2,3-cd]pyrene	19.45 ± 2.71	14.04 ± 1.99	22.16 ± 9.11
Dibenz[a,h+a,c]anthracene	1.54 ± 0.15	0.87 ± 0.12	1.48 ± 0.67
Benzo[b]chrysene	0.40 ± 0.01	0.15 ± 0.05	0.27 ± 0.05
Benzo[ghi]perylene	49.17 ± 9.63	39.81 ± 7.22	60.74 ± 26.60
Coronene	9.49 ± 3.13	4.93 ± 0.47	7.48 ± 1.59
Dibenzo[a,l]pyrene	2.84 ± 0.45	1.25 ± 0.15	2.31 ± 0.48
Dibenzo[a,e]pyrene	1.10 ± 0.29	0.61 ± 0.06	1.13 ± 0.15
Dibenzo[a,i]pyrene	0.91 ± 0.21	0.27 ± 0.09	0.71 ± 0.15
Dibenzo[a,h]pyrene	1.33 ± 0.25	0.75 ± 0.07	0.84 ± 0.20

Source: Norbeck et al., 1998a.

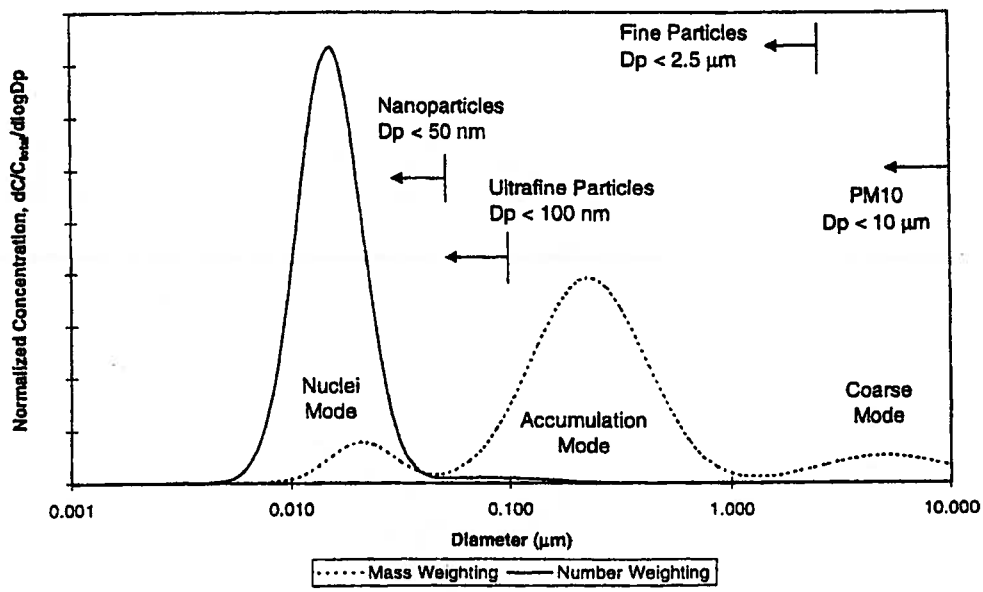

Figure 2-39. Particle size distribution in DE.

Source: Kittelson, 1998.

is approximately 90 m^2/g. Because these particles have a very large surface area per gram of mass, it makes them excellent carriers for adsorbed inorganic and organic compounds; potentially enhancing penetration of such compounds to lower portions of the respiratory tract upon inhalation. In addition, ultrafine aerosols can also reach the same areas of the lung.

Considerable caution is required when reporting particle size measurements from diesel engine exhaust because dilution conditions during the measurement process significantly affect size distributions (i.e., the size distribution is largely a function of how it was measured), and DPM size distributions obtained in dilution tunnel systems may not be relevant to size distributions resulting from the physical transformation of engine exhaust in the atmosphere. Measurements made on diluted DE typically show higher numbers of nuclei-mode particles than do measurements made on raw exhaust because of condensation to form nuclei-mode aerosol upon cooling of the exhaust. To understand particle size distributions emitted from diesel engines, investigators employ various dilution techniques, none of which have been standardized. Dilution ratio, sampling temperature, humidity, relative concentrations of carbon and volatile matter, and other sampling factors can therefore have a large impact on the number and makeup of nuclei-mode particles (Abdul-Khalek et al., 1999; Shi and Harrison, 1999; Lüders

et al., 1998; Brown et al., 2000). Dilution air temperature and humidity can have a large effect on particle number and size distribution, especially in the size range below 0.05 μm (also referred to as nanoparticles). Shi and Harrison (1999) report that a high dilution ratio and high relative humidity favor the production of ultrafine particles in diesel engine exhaust. Abdul-Khalek et al. (1998) report that an increase in the residence time of the exhaust during dilution resulted in an increase in the number of particles in exhaust. Khatri et al. (1978) report increased gas-phase HC condensation to DPM with a decrease in dilution air temperature. Some studies report no peak in diesel particles in the ultrafine size range (Kleeman et al., 2000). Kittelson (2000) reports that nanoparticle formation can be prevented by an oxidizing catalyst, which burns organic components of the exhaust, making them unavailable for nucleation or condensation to form an aerosol.

Experiments conducted in a dilution tunnel represent the atmospheric behavior of DE only under the conditions specific to the dilution tunnel and do not represent the full range of atmospheric conditions. Gertler (1999) demonstrated an increase in 0.02 μm particles as the fraction of diesel vehicles in the Tuscarora Mountain tunnel increased from 13% to 78%. These data suggest that the mode at 0.02 μm for ultrafine DPM from DE is evidenced under some real-world conditions.

Several groups have shown that decreasing sulfur content decreases the number of nuclei-mode particles measured in the exhaust, assuming temperature is low enough and residence time is long enough for nucleation and condensation of sulfate aerosol and water in the dilution tunnel (Baumgard and Johnson, 1992, 1996; Opris et al., 1993; Abdul-Khalek et al., 1999). The application of this finding to real-world conditions is difficult to predict, as the number of nuclei-mode particles formed from sulfate and water in the atmosphere will be determined by atmospheric conditions, not by dilution tunnel conditions. With all other factors held constant, it appears that reducing fuel sulfur content reduces the number of sulfate nuclei-mode particles. Thus, the reduction in on-road fuel sulfur content that occurred in 1993 reduced the amount of sulfur dioxide and sulfate available for particle formation. As discussed above, the contribution of sulfate to total DPM mass ranges from 1% to 5% and is therefore not a substantial portion of DPM mass.

More controversial is the suggestion that the DPM emission size distribution from newer technology engines (1991 and later) may be shifted to a much higher number concentration of nuclei-mode particles, independent of fuel sulfur content (Kreso et al., 1998; Abdul-Khalek et al., 1998; Baumgard and Johnson, 1996; Bagley et al., 1996). For example, Kreso and co-workers (1998) compared emissions from a 1995 model year engine with measurements made on 1991 and 1988 model year engines in earlier studies (Bagley et al., 1993, 1996). Nuclei-mode particles made up 40% to 60% of the number fraction of DPM emissions for the 1988 engine and

97%+ of the DPM from the 1991 and 1995 engines. Number concentrations were roughly two orders of magnitude higher for the newer engines. SOF made up 25% to 30% of DPM mass in the 1988 engine and 40% to 80% of DPM mass for the newer engines. Total DPM mass was significantly reduced for the newer engines. It was suggested that increased fuel injection pressure leads to improved fuel atomization and evaporation, in turn leading to smaller primary carbonaceous particles. Dilution conditions (relatively low temperature, low primary dilution ratio, long residence time of more than 3 seconds) strongly favor the formation of nucleation products. The 1991 and 1988 engines were tested with 100 ppm sulfur fuel whereas the 1995 engine was tested with 310 ppm sulfur fuel, which may confound the results to some extent.

The results of Kreso and co-workers (1998) and of Bagley and co-workers (1993, 1996) have been called into question because the high level of SOF emitted by the 1991 engine, particularly at high-load test modes, was inconsistent with SOF values measured for other engines using similar types of technology (Last et al., 1995; Ullman et al., 1995). Kittelson (1998) notes that there is far less carbonaceous DPM formed in newer engines compared with older engines. Accumulation-mode particles may have provided a high surface area for adsorption of sulfate and unburned organic compounds. In the absence of this surface area for adsorption, higher number concentrations of small particles are formed from nucleation of HCs and sulfuric acid.

A study performed at EPA by Pagan (1999) suggested that increased injection pressure can lead to the formation of more nuclei-mode particles in the exhaust. Particle size distributions were measured for diluted exhaust from an engine in which injection pressure could be varied from roughly 35 to 110 MPa (about 5,000–16,000 psi), comparable to pressures obtained with injection technology introduced in the 1980s. The dilution system and particle size measurement setup were identical in all experiments, removing some of the uncertainty in earlier studies that compared engine tests performed years apart. The results showed a clear increase in the number of nuclei-mode particles and a decrease in the number of accumulation-mode particles as injection pressure was increased. This shift did not occur, however, at high engine speeds and loads, but only at low to intermediate speeds and loads. The increase in number concentration of nuclei-mode particles was much lower than the two orders of magnitude increase reported by Kreso et al. (1998) or Bagley et al. (1996). One must use caution in applying the results of Pagan to modern high-injection pressure diesel engines with turbocharging/charge-air cooling because the engine used by Pagan was a naturally aspirated engine to which high-pressure common rail injection was applied. This would likely preclude this particular engine from meeting current on-highway PM or NO_x standards. Although some studies have suggested that increased injection pressure can lead to elevated ultrafine DPM number counts, Kittelson et al.

(1999) cite a German study that reported a decrease in ultrafine DPM number and mass with increasing injection pressure.

Although the majority of particles in DE from modern on-road diesel engines are in the ultrafine size range, evidence regarding a change in the size distribution over time is unclear. To understand the size distribution of DPM to which people are exposed will require measurements under conditions that more closely resemble ambient conditions.

2.3. ATMOSPHERIC TRANSFORMATION OF DIESEL EXHAUST

Primary diesel emissions are a complex mixture containing hundreds of organic and inorganic constituents in the gas and particle phases, the most abundant of which are listed in Table 2-19. The more reactive compounds with short atmospheric lifetimes will undergo rapid transformation in the presence of the appropriate reactants, whereas more stable pollutants can be transported over greater distances. A knowledge of the atmospheric transformations of gaseous and particulate components of diesel emissions and their fate is important in assessing environmental exposures and risks. This section describes some of the major atmospheric transformation processes for gas-phase and particle-phase DE, focusing on the primary and secondary organic compounds that are of significance for human health. For a more comprehensive summary of the atmospheric transport and transformation of diesel emissions, see Winer and Busby (1995).

2.3.1. Gas-Phase Diesel Exhaust

Gas-phase DE contains organic and inorganic compounds that undergo various chemical and physical transformations in the atmosphere, depending on the abundance of reactants and meteorological factors such as wind speed and direction, solar radiation, humidity, temperature, and precipitation. Gaseous DE will react primarily with the following species (Atkinson, 1988):

- Sunlight, during daylight hours
- Hydroxyl (OH) radical, during daylight hours
- Ozone (O_3), during daytime and nighttime
- Hydroperoxyl (HO_2) radical, typically during afternoon/evening hours
- Gaseous nitrate (NO_3) radicals or dinitrogen pentoxide (N_2O_5), during nighttime hours
- Gaseous nitric acid (HNO_3) and other species such as nitrous acid (HONO) and sulfuric acid (H_2SO_4).

Table 2-19. Classes of compounds in diesel exhaust

Particulate phase		Gas phase	
Heterocyclics, hydrocarbons (C_{14}-C_{35}), and PAHs and derivatives:		Heterocyclics, hydrocarbons (C_1-C_{10}), and derivatives:	
Acids	Cycloalkanes	Acids	Cycloalkanes, Cycloakenes
Alcohols	Esters	Aldehydes	Dicarbonyls
Alkanoic acids	Halogenated cmpds.	Alkanoic acids	Ethyne
n-Alkanes	Ketones	n-Alkanes	Halogenated cmpds.
Anhydrides	Nitrated cmpds.	n-Alkenes	Ketones
Aromatic acids	Sulfonates	Anhydrides	Nitrated cmpds.
	Quinones	Aromatic acids	Sulfonates
			Quinones
Elemental carbon		Acrolein	
Inorganic sulfates and nitrates		Ammonia	
Metals		Carbon dioxide, carbon monoxide	
Water		Benzene	
		1,3-Butadiene	
		Formaldehyde	
		Formic acid	
		Hydrogen cyanide, hydrogen sulfide	
		Methane, methanol	
		Nitric and nitrous acids	
		Nitrogen oxides, nitrous oxide	
		Sulfur dioxide	
		Toluene	
		Water	

Sources: Mauderly, 1992, which summarized the work of Lies et al., 1986; Schuetzle and Frazier, 1986; Carey, 1987; Zaebst et al., 1988, updated from recent work by Johnson, 1993; McDonald, 1997; Schauer et al., 1999.

The major loss process for most of the DE emission constituents is oxidation, which occurs primarily by daytime reaction with OH radical (Table 2-20). For some pollutants, photolysis, reaction with O_3, and reactions with NO_3 radicals during nighttime hours are also important removal processes. The atmospheric lifetimes do not take into consideration the potential chemical or biological importance of the products of these various reactions. For example, the reaction of gas-phase PAHs with NO_3 appears to be of minor significance as a PAH loss process, but it is more important as a route of formation of mutagenic nitro-PAHs. The reaction products for some of the major gaseous DE compounds are listed in Table 2-21 and are discussed briefly below.

2.3.1.1. *Organic Compounds*

The organic fraction of diesel is a complex mixture of compounds, very few of which have been characterized. The atmospheric chemistry of several organic constituents of DE (which are also produced by other combustion sources) has been studied. A few of these

Table 2-20. Calculated atmospheric lifetimes for gas-phase reactions of selected compounds present in automotive emissions with important reactive species

Compound	Atmospheric lifetime resulting from reaction with:				
	OH[a]	O_3[b]	NO_3[c]	HO_2[d]	hν[e]
NO_2	1.3 days	12 h	24 min	2 h	2 min
NO	2.5 days	1 min	1.2 min	20 min	—
HNO_3	110 days	—	—	—	—
SO_2	16 days	>200 years	>1.4×10[4] years	>600 years	—
NH_3	90 days	—	—	—	—
Propane	12 days	>7,000 years	—	—	—
n-Butane	5.6 days	>4,500 years	3.6 years	—	—
n-Octane	1.9 days	—	1.2 years	—	—
Ethylene	1.9 days	9 days	1.2 years	—	—
Propylene	7 h	1.5 days	6 days	—	—
Acetylene	19 days	6 years	>5.6 years	—	—
Formaldehyde	1.9 days	>2 - 104 years	84 days	23 days	4 h
Acetaldehyde	0.6 day	>7 years	20 days	—	60 h
Benzaldehyde	1.2 days	—	24 days	—	—
Acrolein	0.6 day	60 days	—	—	—
Formic acid	31 days	—	—	—	—
Benzene	11 days	600 years	>6.4 years	—	—
Toluene	2.5 days	300 years	3.6 years	—	—
m-Xylene	7 h	75 years	0.8 years	—	—
Phenol	6 h	—	8 min	—	—
Naphthalene[f]	6.8 h	>80 days	1.5 years	—	—
2-Methylnaphthalene[f]	2.8 h	>40 days	180 days		—
1-Nitronaphthalene[f]	2.3 days	>28 days	1 8 years		1.7 h
Acenaphthene[f]	1.5 h	>30 days	1.2 h	—	—
Acenaphthylene[f]	1.3 h	~43 min	6 min	—	—
Phenanthrene[f]	11.2 h	41 days	4.6 h	—	—
Anthracene[f]	8.6 h	—	—	—	—
Fluoranthene[f]	~2.9 h	—	~1 year	—	—
Pyrene[f]	~2.9 h	—	~ 120 days	—	—

[a] For 12-h average concentration of OH radical of 1.6×10^{6} molecule/cm^3 (Prinn et al., 1992).
[b] For 24-h average O_3 concentration of 7×10^{11} molecule/cm^3.
[c] For 12-h average NO_3 concentration of 5×10^{8} molecule/cm^3 (Atkinson, 1991).
[d] For 12-h average HO_2 concentration of 10^{8} molecule/cm^3.
[e] For solar zenith angle of 0°.
[f] Lifetimes from Arey (1998), for 12-h concentration of OH radical of 1.9×10^{6} molecule/cm^3.

Source: Winer and Busby, 1995, unless noted otherwise.

Table 2-21. Major components of gas-phase diesel engine emissions, their known atmospheric transformation products, and the biological impact of the reactants and products

Gas-phase emission component	Atmospheric reaction products	Biological impact
Carbon dioxide	—	Major contributor to global warming.
Carbon monoxide	—	Highly toxic to humans; blocks oxygen uptake.
Oxides of nitrogen	Nitric acid, ozone	Nitrogen dioxide is a respiratory tract irritant and major ozone precursor. Nitric acid contributes to acid rain.
Sulfur dioxide	Sulfuric acid	Respiratory tract irritation. Contributor to acid rain.
Hydrocarbons:		
Alkanes ($\leq C_{18}$)	Aldehydes, alkyl nitrates, ketones	Respiratory tract irritation. Reaction products are ozone precursors (in the presence of NO_x).
Alkenes ($\leq C_4$) (e.g., 1,3-butadiene)	Aldehydes, ketones	Respiratory tract irritation. Some alkenes are mutagenic and carcinogenic. Reaction products are ozone precursors (in the presence of NO_x).
Aldehydes:		
Formaldehyde	Carbon monoxide, hydroperoxyl radicals	Formaldehyde is a probable human carcinogen and an ozone precursor (in the presence of NO_x).
Higher aldehydes (e.g., acetaldehyde, acrolein)	Peroxyacyl nitrates	Respiratory tract and eye irritation; causes plant damage.
Monocyclic aromatic compounds (e.g., benzene, toluene)	Hydroxylated and hydroxylated-nitro derivatives[a]	Benzene is toxic and carcinogenic in humans. Some reaction products are mutagenic in bacteria (Ames assay).
PAHs ($\leq$4 rings) (e.g., phenanthrene, fluoranthene)[b]	Nitro-PAHs (4 rings)[c]	Some of these PAHs and nitro-PAHs are known mutagens and carcinogens.
Nitro-PAHs (2 and 3 rings) (e.g., nitronaphthalenes)	Quinones and hydroxylated-nitro derivatives	Some reaction products are mutagenic in bacteria (Ames assay).

[a]Some reaction products expected to partition into the particle phase.
[b]Nitro-PAHs with more than two rings will partition into the particle phase.
[c]PAHs containing four rings are usually present in both the vapor and particle phases.

Source: Health Effects Institute, 1995.

2.3.1.1. *Organic Compounds*

The organic fraction of diesel is a complex mixture of compounds, very few of which have been characterized. The atmospheric chemistry of several organic constituents of DE (which are also produced by other combustion sources) has been studied. A few of these reactions and their products are discussed below. For a complete summary of the atmospheric chemistry of organic combustion products, see Seinfeld and Pandis (1998).

Acetaldehyde forms peroxyacetyl nitrate (via formation of peroxyl radicals and reaction with NO_2), which has been shown to be a direct-acting mutagen toward *S. typhimurium* strain TA100 (Kleindienst et al., 1985) and is phytotoxic. Benzaldehyde, the simplest aromatic aldehyde, forms peroxybenzoyl nitrate or nitrophenols following reaction with oxides of nitrogen (Table 2-21).

For those PAHs present in the gas phase, reaction with the OH radical is the major removal route, leading to atmospheric lifetimes of a few hours in daylight. The gas-phase reaction of PAHs containing a cyclopenta-fused ring such as acenaphthene, acenaphthylene, and acephenanthrylene with the nitrate radical may be an important loss process during nighttime hours. Relatively few data are available concerning the products of these gas-phase reactions. It has been shown that in the presence of NO_x, the OH radical reactions with naphthalene, 1- and 2-methylnaphthalene, acenaphthylene, biphenyl, fluoranthene, pyrene, and acephenanthrylene lead to the formation of nitroarenes (Arey et al., 1986; Atkinson, 1986; Atkinson et al., 1990; Zielinska et al., 1988, 1989a; Arey, 1998). In addition, in a two-step process involving OH radical reaction and NO_2 addition, 2-nitrofluoranthene and 2-nitropyrene can be formed and eventually partition to the particle phase, as will other nitro-PAHs.

The addition of the NO_3 radical to the PAH aromatic ring leads to nitroarene formation (Sweetman et al., 1986; Atkinson et al., 1987, 1990; Zielinska et al., 1989a). The gas-phase reactions of NO_3 radical with naphthalene, 1- and 2-methylnaphthalene, acenaphthene, phenanthrene, anthracene, fluoranthene, and pyrene produce, in general, the same nitro-PAH isomers as the OH radical reaction, but with different yields (Arey et al., 1989; Sweetman et al., 1986; Atkinson et al., 1987, 1990; Zielinska et al., 1986, 1989a). For example, the same 2-nitrofluoranthene is produced from both OH radical and NO_3 gas-phase reactions, but the reaction with NO_3 produces a much higher yield. The production of several nitroarene compounds has been studied in environmental chambers (Arey et al., 1989; Zielinska et al., 1990; Atkinson and Arey, 1994; Arey, 1998; Feilberg et al., 1999), and generally the same nitro-PAH isomers formed from reaction with OH and NO_3 radicals are observed in ambient air samples. Secondary formation of nitroarenes through the gas-phase reactions of the 2-, 3-, and 4-ring PAHs is the major source for many of the nitroarenes observed in ambient air (Pitts et al., 1985a-c; Arey et al., 1986; Zielinska et al., 1988). Photolysis is the major removal pathway for

nitroarenes with lifetimes of approximately 2 hours (Feilberg et al., 1999; Nielsen and Ramdahl, 1986).

2.3.1.2. *Inorganic Compounds*

SO_2 and oxides of nitrogen (primarily NO) are emitted from diesel engines. SO_2 is readily oxidized by the OH radical in the atmosphere, followed by formation of the HO_2 radical and HSO_3, which rapidly reacts with water to form H_2SO_4 aerosols. Because SO_2 is soluble in water, it is scavenged by fog, cloud water, and raindrops. In aqueous systems, SO_2 is readily oxidized to sulfate by reaction with hydrogen peroxide (H_2O_2), O_3, or O_2 in the presence of a metal catalyst (Calvert and Stockwell, 1983). Sulfur emitted from diesel engines is predominantly (~98%) in the form of SO_2, a portion of which will form sulfate aerosols by the reaction described above. Nonroad equipment, which typically uses fuel containing 3,300 ppm sulfate, emits more SO_2 than on-road diesel engines, which use fuels currently containing an average of 340 ppm sulfur because of EPA regulations effective in 1993 decreasing diesel fuel sulfur levels. EPA estimates that mobile sources are responsible for about 7% of nationwide SO_2 emissions, with diesel engines contributing 74% of the mobile source total (the majority of the diesel SO_2 emissions originate from nonroad engines) (U.S. EPA, 1998b).

NO is also oxidized in the atmosphere to form NO_2 and particulate nitrate. The fraction of motor vehicle NO_x exhaust converted to particulate nitrate in a 24-hour period has been calculated using a box model to be approximately 3.5% nationwide, a portion of which can be attributed to DE (Gray and Kuklin, 1996). EPA estimates that in 1997, mobile sources were responsible for about 50% of nationwide NO_x emissions, with diesel engines being responsible for approximately one-half of the mobile source total (U.S. EPA, 1998b).

2.3.1.3. *Atmospheric Transport of Gas-Phase DE*

Gas-phase DE can be dry deposited, depending on the deposition surface, atmospheric stability, and the solubility and other chemical properties of the compound. Dry deposition of organic species is typically on the order of weeks to months, with dry deposition velocities of approximately 10^{-4} cm/sec (Winer and Busby, 1995). In contrast, inorganic species such as SO_2 and nitric acid have relatively fast deposition rates (0.1–2.5 cm/sec) and will remain in the atmosphere for shorter time periods compared with the organic exhaust components. Some gas-phase species will also be scavenged by aqueous aerosols and potentially deposited via precipitation. These processes can greatly reduce the atmospheric concentration of some vapor-phase species. Atmospheric lifetimes for several gas-phase components of DE are on the order of hours or days, during which time atmospheric turbulence and advection can disperse these pollutants widely.

2.3.2. Particle-Phase Diesel Exhaust

Particle-associated DE is composed of primarily carbonaceous material (organic and EC) with a very small fraction composed of inorganic compounds and metals. The OC fraction adsorbed on DPM is composed of high-molecular-weight compounds, such as PAHs, which are generally more resistant to atmospheric reactions than PAHs in the gas phase. The EC component of DE is inert to atmospheric degradation, whereas the PAH compounds are degraded by reaction with the following species:

- Sunlight, during daytime hours
- O_3, during daytime and nighttime
- NO_3 and N_2O_5, during nighttime hours
- OH and HO_2
- NO_2, during nighttime and daytime hours
- H_2O_2
- HNO_3 and other species such as HONO and H_2SO_4.

Because many of the PAH derivatives formed by reaction with some of the reactants listed above have been found to be highly mutagenic, a brief discussion of PAH photolysis, nitration, and oxidation follows. Some of the major degradation products from particulate DE and their biological impact are listed in Table 2-22.

2.3.2.1. *Particle-Associated PAH Photooxidation*

Laboratory studies of photolysis of PAHs adsorbed on 18 different fly ashes, carbon black, silica gel, and alumina (Behymer and Hites, 1985, 1988) and several coal stack ashes (Yokely et al., 1986; Dunstan et al., 1989) have shown that the extent of photodegradation of PAHs depends very much on the nature of the substrate to which they are adsorbed. The dominant factor in the stabilization of PAHs adsorbed on fly ash was the color of the fly ash, which is related to the amount of carbon black present. It appears that PAHs were stabilized if the carbon black content of the fly ash was greater than approximately 5%. On black substrates, half-lives of PAHs studied were on the order of several days (Behymer and Hites, 1988). The environmental chamber studies of Kamens et al. (1988) on the daytime decay of PAHs present on residential wood smoke particles and on gasoline internal combustion emission particles showed PAH half-lives of approximately 1 hour at moderate humidities and temperatures. At very low angle sunlight, very low water vapor concentration, or very low temperatures, PAH daytime half-lives increased to a period of days. The presence and

Table 2-22. Major components of particle-phase diesel engine emissions, their known atmospheric transformation products, and the biological impact of the reactants and products

Particle-phase emission component	Atmospheric reaction products	Biological impact
Elemental carbon	—	Nuclei adsorb organic compounds; size permits transport deep into the lungs (alveoli)
Inorganic sulfate and nitrate	—	Respiratory tract irritation
Hydrocarbons (C_{14}-C_{35})	Little information; possibly aldehydes, ketones, and alkyl nitrates	Unknown
PAHs (≥4 rings) (e.g., pyrene, benzo[a]pyrene)	Nitro-PAHs (≥4 rings)[a] Nitro-PAH lactones	Larger PAHs are major contributors of carcinogens in combustion emissions. Many nitro-PAHs are potent mutagens and carcinogens.
Nitro-PAHs (≥3 rings) (e.g., nitropyrenes)	Hydroxylated-nitro derivatives	Many nitro-PAHs are potent mutagens and carcinogens. Some reaction products are mutagenic in bacteria (Ames assay).

[a]Nitro-PAHs with more than two rings will partition into the particle phase.
Source: Health Effects Institute, 1995.

composition of an organic layer on the aerosol seems to influence the rate of PAH photolysis (Jang and McDow, 1995; McDow et al., 1994; Odum et al., 1994).

Because of limited understanding of the mechanisms of these complex heterogeneous reactions, it is currently impossible to draw any firm conclusion concerning the photostability of particle-bound PAHs in the atmosphere. Because DPM contains a relatively high quantity of EC, it is reasonable to speculate that PAHs adsorbed onto these particles might be relatively stable under standard atmospheric conditions, leading to an anticipated half-life of 1 or more days.

2.3.2.2. *Particle-Associated PAH Nitration*

Since 1978, when Pitts et al. (1978) first demonstrated that B[*a*]P deposited on glass-fiber filters exposed to air containing 0.25 ppm NO_2 with traces of HNO_3 formed nitro-B[*a*]P, numerous studies of the heterogeneous nitration reactions of PAHs adsorbed on a variety of substrates in different simulated atmospheres have been carried out (Finlayson-Pitts and Pitts, 1986). PAHs deposited on glass-fiber and Teflon-impregnated glass-fiber filters react with gaseous N_2O_5, yielding their nitro derivatives (Pitts et al., 1985b,c). The most abundant isomers formed were 1-NP from pyrene, 6-nitro-B[*a*]P from B[*a*]P, and 3-nitroperylene from perylene.

The formation of nitro-PAHs during sampling may be an important consideration for DPM collection because of the presence of NO_2 and HNO_3 (Feilberg et al., 1999). However, Schuetzle (1983) concluded that the artifact formation of 1-NP was less than 10% to 20% of the 1-NP present in the diesel particles if the sampling time was less than 23 min (one FTP cycle) and if the sampling temperature was not higher than 43 °C. The formation of nitroarenes during ambient high-volume sampling conditions has been reported to be minimal, at least for the most abundant nitropyrene and nitrofluoranthene isomers (Arey et al., 1988).

DPM contains a variety of nitroarenes, with 1-NP being the most abundant among identified nitro-PAHs. The concentration of 1-NP was measured in the extract of particulate samples collected at the Allegheny Mountain Tunnel on the Pennsylvania Turnpike as 2.1 ppm and ~5 ppm by mass of the extractable material from diesel and SI vehicle PM, respectively. These values are much lower than would be predicted on the basis of laboratory measurements for either diesel or SI engines (Gorse et al., 1983). Several nitroarene measurements have been conducted in airsheds heavily affected by motor vehicle emissions (Arey et al., 1987; Atkinson et al., 1988; Zielinska et al., 1989a,b; Ciccioli et al., 1989, 1993). Ambient PM samples were collected at three sites in the Los Angeles Basin during two summertime periods and one wintertime period. Concentrations of 1-NP ranged from 3 pg/m^3, to 60 pg/m^3, and 3-nitrofluoranthene was also present in DPM at concentrations ranging from not detectable to 70 pg/m^3.

2.3.2.3. *Particle-Associated PAH Ozonolysis*

Numerous laboratory studies have shown that PAHs deposited on combustion-generated fine particles and on model substrates undergo reaction with O_3 (Katz et al., 1979; Pitts et al., 1980, 1986; Van Vaeck and Van Cauwenberghe, 1984; Finlayson-Pitts and Pitts, 1986). The dark reaction toward O_3 of several PAHs deposited on model substrates has been shown to be relatively fast under simulated atmospheric conditions (Katz et al., 1979; Pitts et al., 1980, 1986). Half-lives on the order of 1 to several hours were reported for the more reactive PAHs, such as B[*a*]P, anthracene, and benz[a]anthracene (Katz et al., 1979).

The reaction of PAHs deposited on diesel particles with 1.5 ppm O_3 under high-volume sampling conditions has been shown to be relatively fast, and half-lives on the order of 0.5 to 1 hour have been reported for most PAHs studied (Van Vaeck and Van Cauwenberghe, 1984). The most reactive PAHs include B[*a*]P, perylene, benz[a]anthracene, cyclopenta[cd]pyrene, and benzo[ghi]perylene. The benzofluoranthene isomers are the least reactive of the PAHs studied, and benzo[e]perylene is less reactive than its isomer B[*a*]P. The implications of this study for the high-volume sampling ambient POM are important: reaction of PAHs with O_3 could possibly occur under high-volume sampling conditions during severe photochemical smog

episodes, when the ambient level of O_3 is high. However, the magnitude of this artifact is difficult to assess from available data.

2.3.2.4. *Atmospheric Transport of DE Particulate Matter*

Ultrafine particles emitted by diesel engines undergo nucleation, coagulation, and condensation to form fine particles. DPM can be removed from the atmosphere by dry and wet deposition. Particles of small diameter (<1 μm), such as DPM, are removed less efficiently than larger particles by wet and dry deposition and thus have longer atmospheric residence times. Dry deposition rates vary depending on the particle size. Because of their small size, DE particles have residence times of several days (dry deposition velocities of approximately 0.01 cm/sec) (Winer and Busby, 1995). Diesel particulates may be removed by wet deposition if they serve as condensation nuclei for water vapor deposition or are scavenged by precipitation in- or below-cloud.

In a study designed to assess the atmospheric concentrations and transport of DE particles, Horvath et al. (1988) doped the sole source of diesel fuel in Vienna with an organometallic compound of the heavy earth element dysprosium. The authors found that in some of the more remote sampling areas, DPM composed more than 30% of the particulate mass, indicating that DPM can be dispersed widely.

2.3.3. Diesel Exhaust Aging

Primary DE is considered "fresh," whereas "aged" DE is considered to have undergone chemical and physical transformation and dispersion over a period of a day or two. Laboratory dilution tunnel measurements represent a homogeneous environment compared to the complex and dynamic system into which real-world DE is emitted. The physical and chemical transformation of DE will vary depending on the environment into which it is emitted. In an urban or industrial environment, DE may enter an atmosphere with high concentrations of oxidizing and nitrating radicals, as well as nondiesel organic and inorganic compounds that may influence the toxicity, chemical stability, and atmospheric residence time.

In general, secondary pollutants formed in an aged aerosol mass are more oxidized, and therefore have increased polarity and water solubility (Finlayson-Pitts and Pitts, 1986). Kamens et al. (1988) reported that photooxidation of particle-bound PAH is enhanced as relative humidity is increased. Weingartner et al. (1997a) and Dua et al. (1999) have reported that unlike many other types of particles, diesel particles do not appear to undergo hygroscopic growth once emitted to the atmosphere and may even shrink in size to some extent under increasing relative humidity conditions. Weingartner et al. (1997a) evaluated the hygroscopic growth of diesel particles and found that freshly emitted diesel particles demonstrated minimal hygroscopic

growth (2.5%), whereas aged particles subjected to UV radiation and ozonolysis exhibited somewhat greater but still minimal hygroscopic growth. An increase in the sulfur content of diesel fuel has also been observed to result in somewhat greater water condensation onto diesel particles. To the extent that DE components are oxidized or nitrated in the atmosphere, they may be removed at rates different from their precursor compounds and may exhibit different biological reactivities. Data suggesting that minimal hygroscopic growth of DPM occurs also has implications for the dosimetry of these particles in the lung because the smaller particles will reach the lowest airways of the lung, whereas growth of the particle would result in deposition in the upper airways. The dosimetry of DPM is discussed in Chapter 3.

In a recent experiment, the biological activity of DPM exposed to 0.1 ppm ozone for 48 hours was compared with that of DPM not exposed to ozone (Ghio et al., 2000). Instillations of the ozonated DPM in rat lung resulted in an increase in biological activity (neutrophil influx, increased protein, and lactate dehydrogenase activity) compared with DPM that had not been treated with ozone. These data suggest that ambient levels of ozone can alter DPM constituents causing an increase in toxicity compared with nonozonated DPM.

In addition to changes in particle composition with aging, particle size distributions may vary depending on aggregation and coagulation phenomena in the aging process. People in vehicles, near roadways (e.g., cyclists, pedestrians, people in nearby buildings), and on motorcycles will be exposed to more fresh exhaust than the general population. In some settings where emissions are entrained for long periods through meteorological or other factors, exposures would be expected to include both fresh and aged DE. The complexities of transport and dispersion of emission arising from motor vehicles have been the subject of extensive modeling and experimental studies over the past decades and have been summarized by Sampson (1988); exposures to DPM are discussed in the next section of this chapter.

The major organic constituents of DE and their potential degradation pathways described above provide evidence for (1) direct emission of PAHs, (2) secondary formation of nitroarenes, and (3) secondary sulfate and nitrate formation. Because nitro-PAH products are often more mutagenic than their precursors, the formation, transport, and concentrations of these compounds in an aged aerosol mass are of significant interest.

2.4. AMBIENT DIESEL EXHAUST CONCENTRATIONS AND EXPOSURES

2.4.1. Diesel Exhaust Gases in the Ambient Atmosphere

Although emissions of several DE components have been measured, few studies have attempted to elucidate the contribution of diesel-powered engines to atmospheric concentrations of these components. The emission profile of gaseous organic compounds is different for diesel and SI vehicles; the low-molecular-weight aromatic HCs and alkanes ($<C_9$) are more

characteristic of SI engine emissions, whereas the heavier alkanes (>C_{10}) and aromatic HCs (such as naphthalene, methyl- and dimethyl- naphthalenes, methyl- and dimethyl-indans) are more characteristic of diesel engine emissions. These differences were the basis for apportionment of gasoline- and diesel-powered vehicle emissions to ambient nonmethane hydrocarbon (NMHC) concentrations in the Boston and Los Angeles (South Coast Air Basin) urban areas.

The chemical mass balance receptor model (described below) was applied to ambient samples collected in these areas, along with appropriate fuel, stationary, and area source profiles (Fujita et al., 1997). The average of the sum of NMHC attributed to DE, gasoline-vehicle exhaust, liquid gasoline, and gasoline vapor was 73% and 76% for Boston and the South Coast Air Basin (SoCAB), respectively. The average source contributions of DE to NMHC concentrations were 22% and 13% for Boston and the SoCAB, respectively. Diesel vehicles emit lower levels of NMHC in the exhaust compared with gasoline vehicles. The relative contribution of DE clearly depends on several factors, including fleet composition, sampling location (e.g., near a bus station vs. near a highway or other sources), and the contribution from point and area sources. The contribution of DE to ambient NMHC showed large variations among sampling sites in the Boston area. The source apportionment in the Fujita et al. (1997) study indicates that mobile vehicle-related emissions account for the majority of ambient NMHC in the two urban areas studied, and the results can likely be extrapolated to other urban areas with similar source compositions. Other source apportionment methods such as those used by Henry et al. (1994) have been applied to speciated HC data to separate the mobile source direct emission from gasoline evaporative emissions. This method uses a combination of graphical analysis (Graphical Ratio Analysis for Composition Estimates, GRACE) and multivariate receptor modeling methods (Source Apportionment by Factors with Explicit Restrictions, SAFER) and was not used to identify the diesel engine contribution to the HCs measured.

2.4.2. Ambient Concentrations of DPM

Because DPM is chemically complex, an assessment of ambient DPM concentrations relies primarily on (1) studies that collect ambient samples and adequately characterize their chemical composition, or (2) modeling studies that attempt to recreate emissions and atmospheric conditions. Ambient concentrations of DPM also have been reported from studies using surrogate species. The results of these studies are summarized below. Studies conducted in Europe and Japan were reviewed, but for the most part were not included because of questions surrounding the applicability of measurements in locations that use different diesel technology and control measures from those in the United States.

2.4.2.1. *Source Apportionment Studies*

Receptor models are used to infer the types and relative contributions of sources to pollutant measurements made at a receptor site. Receptor models assume that the mass is conserved between the source and receptor site and that the measured mass of each pollutant is a sum of the contributions from each source. Receptor models are referred to as "top-down" in contrast to "bottom-up" methods, which use emission inventory data, activity patterns, and dispersion modeling from the source to predict concentrations at a receptor site.

The most commonly used receptor model for quantifying concentrations of DPM at a receptor site is the chemical mass balance (CMB) model. Input to the CMB model includes measurements of PM mass and chemistry made at the receptor site as well as measurements made of each of the source types suspected to impact the site. Because of problems involving the elemental similarity between diesel and gasoline emission profiles and their co-emission in time and space, chemical molecular species that provide markers for separation of these sources have been identified (Lowenthal et al., 1992). Recent advances in chemical analytical techniques have facilitated the development of sophisticated molecular source profiles, including detailed speciation of PM-associated organic compounds that allow the apportionment of PM to gasoline and diesel sources with increased confidence. CMB analysis that uses speciation of organic compounds in the source profiles is typically referred to as extended species CMB. Older studies that made use of only EC, total OC, trace elements, and major ions in the source profiles (conventional CMB) have been published and are summarized here, but they are subject to more uncertainty. It should be noted that because receptor modeling is based on the application of source profiles to ambient measurements, estimates of DPM concentration generated by this method include the contribution from on-road and nonroad sources to the extent the source profiles are similar (which would include military sources depending on the sampling locations and fleet composition). In addition, this method identifies sources of primary emissions of DPM only, and the contribution of secondary aerosols is not attributed to sources.

The CMB model has been used to assess concentrations of DPM in areas of California, Phoenix, Denver, and Manhattan (Table 2-23). DPM concentrations reported by Schauer et al. (1996) for samples collected in California in 1982 ranged from 4.4 $\mu g/m^3$ in west Los Angeles to 11.6 $\mu g/m^3$ in downtown Los Angeles. The average contribution of DPM to total $PM_{2.5}$ mass ranged from 13% in Rubidoux to 36% in downtown Los Angeles. As mentioned above, this model accounts for primary emissions of DPM only; the contribution of secondary aerosol formation (both acid and organic aerosols) is not included. In sites downwind from urban areas, such as Rubidoux in this study, secondary nitrate formation can account for a substantial fraction of the mass (25% of the fine mass measured in Rubidoux was attributed to secondary nitrate), a portion of which comes from DE (Gray and Kuklin, 1996).

Table 2-23. Ambient DPM concentrations reported from chemical mass balance modeling

Reference	Location	Year of sampling	Location type	Diesel $PM_{2.5}$ $\mu g/m^3$ mean, (range)	Average DPM % of total PM (range)	Source profile used
Schauer et al., 1996	West LA, CA	1982, annual average (~60 samples at each site)	Urban	4.4	18	EC, OCS, elements
	Pasadena, CA		Urban	5.3	19	
	Rubidoux, CA		Urban	5.4	13	
	Los Angeles, CA		Urban	11.6	36	
Chow et al., 1991	West Phoenix, AZ	1989-90, winter 11 days at each site	Urban	13 (max. 22)	18	EC, OCT, MI, elements
	Central Phoenix, AZ		Urban	13 (max. 16)	20	
	South Scottsdale, AZ		Urban	10 (max. 12)	17	
	Estrella Park, AZ		Nonurban	5	9	
	Gunnery Park, AZ		Nonurban	3	10	
	Pinnacle Peak, AZ		Nonurban	2	12	
California EPA, 1998a	California, 6 air basins	1988-92, annual	Urban[c]	1.8–3.6[a]	[b]	EC, OCT, MI, elements
	California, 9 air basins		Nonurban[c]	0.2–2.6[a]	[b]	EC, OCT, MI, elements
Wittorff et al., 1994	Manhattan, NY	1993, spring 3 days	Urban	29.2(13.2–46.7)[a]	53 (31–68)	EC, OCT, MI, elements
Maricopa Association of Governments, 1999	Phoenix, AZ	1994–95, winter 12 days	Urban	2.4 (0–5.3)	15 (0–27)	EC, OCS, MI, elements
Fujita et al., 1998	Welby, CO	1996–97, winter 60 days	Urban	1.7 (0–7.3)	10 (0–26)	EC, OCS, MI, elements
	Brighton, CO		Suburban	1.2 (0–3.4)	10 (0–38)	

[a]PM_{10}.
[b]Not available.
[c]Urban air basins are qualitatively defined as those areas that are moderately or largely urbanized, and nonurban air basins are those areas that are largely nonurban, but may have one or more densely populated areas.
Abbreviations: EC: Elemental carbon; OCT: OC total; OCS: OC species; MI: Major ions including nitrate, sulfate, chloride and, in some cases, ammonium, sodium, potassium.

The California Environmental Protection Agency (Cal EPA) reported ambient DPM concentrations for 15 air basins in California based on ambient measurements taken statewide from 1988 to 1992 (Cal EPA, 1998a). Cal EPA used CMB analysis of ambient measurements from the San Joaquin Valley (1988-89), South Coast (1986), and San Jose (winters for 1991–92 and 1992–93) to determine mobile source contributions and then applied the California 1990 PM_{10} emissions inventory to determine the fraction of mobile source PM_{10} attributable to diesel emissions. The results of this analysis indicate that annual average basin-wide levels of direct DPM may be as low as 0.2 $\mu g/m^3$ and may range up to 2.6 $\mu g/m^3$ for basins that are largely nonurban but may have one or more densely populated areas (such as Palm Springs in the Salton Sea basin). DPM concentrations for air basins that are moderately or largely urbanized ranged from 1.8 $\mu g/m^3$ to 3.6 $\mu g/m^3$.

Two studies using CMB analysis that report DPM concentrations have been conducted in the Phoenix area. A wintertime study in 1989–90 reported DPM concentrations for nonurban areas ranging from 2 $\mu g/m^3$ to 5 $\mu g/m^3$ and DPM concentrations for central and south Phoenix urban areas ranging from 10 $\mu g/m^3$ to 13 $\mu g/m^3$ (Chow et al., 1991). Chow et al. (1991) reported that DPM levels on single days can range up to 22 $\mu g/m^3$ at the central Phoenix site. A more recent study conducted from November 1994 through March 1995 reported DPM concentrations for Phoenix averaging 2.4 $\mu g/m^3$ and reaching 5.3 $\mu g/m^3$ (Maricopa Association of Governments, 1999). The extended species CMB was used for this study, providing a more confident identification of DPM separate from gasoline PM emissions than the earlier Phoenix study. DPM accounted for an average 15% of ambient $PM_{2.5}$, and gasoline PM accounted for an average of 52% of ambient $PM_{2.5}$ in the 1994–95 Phoenix study.

In a recently published study designed to investigate the ability of a new type of factor analysis, positive matrix factorization, to separate sources contributing to the urban aerosol in Phoenix, Ramadan et al. (2000) report their success in separating the DE PM from other motor vehicle PM. Fine PM samples were collected by two different types of samplers in Phoenix, one set collected from March 1995 through June 1998 and a second set from June 1996 through June 1998. Elemental and OC were analyzed using TOT. Particles of DE origin were identified by their high EC content in addition to specific trace elements, including manganese, sulfur, and iron. DPM concentrations exceeding 5 $\mu g/m^3$ were reported for winter months during the study period. The investigators concluded that motor vehicles, vegetative burning, and HD DE were the three major sources contributing to ambient fine PM in Phoenix, with higher contributions in the winter than in summer.

During the winter of 1997, a study assessed DPM concentrations at two urban sites in the Denver area (Fujita et al., 1998). The Northern Front Range Air Quality Study (NFRAQS), initiated to assess the sources of the "brown cloud" observed along Colorado's Front Range,

conducted air quality sampling during the winter of 1996, summer of 1996, and winter of 1997. For a 60-day period from December 1996 through January 1997, ambient samples collected at two urban Denver sites were analyzed for OC species for use in the extended-species CMB. The average DPM concentrations reported for the urban site at Welby, CO, and the suburban site at Brighton, CO, were 1.7 $\mu g/m^3$ and 1.2 $\mu g/m^3$, respectively. During the study period, DPM concentrations exceeded 5 $\mu g/m^3$ on two occasions in Welby, with reported DPM concentrations of 5.7 $\mu g/m^3$ and 7.3 $\mu g/m^3$. DPM accounted for an average of 10% of ambient $PM_{2.5}$, and gasoline PM accounted for an average of 27% of ambient $PM_{2.5}$.

One of the major claims from the NFRAQS was a substantial contribution of EC from gasoline-powered vehicles, mainly from cold-start and high-emitting vehicles. At the Welby site, the contribution of diesel and gasoline emissions to EC measurements was 52% and 42%, respectively. At the Brighton site, the contribution of diesel and gasoline emissions to EC measurements was 71% and 26%, respectively. The findings from the NFRAQS are compelling and suggest the need for further investigations to quantify the contribution from cold-start and high-emitting vehicle emissions for both gasoline and diesel vehicles. Geographical, temporal, and other site-specific parameters that influence PM concentrations, such as altitude, must be considered when extrapolating the NFRAQS findings to other locations.

In addition to the need for urban and rural average DPM concentrations, an assessment of potential health effects resulting from DPM exposure includes an assessment of people in environments with potentially elevated levels of DPM. Limited data are available to allow a characterization of DPM concentrations in "hotspots" such as near heavily traveled roadways, bus stations, train stations, and marinas. Only one CMB study has attempted to apportion PM measured in an urban hotspot. Wittorff et al. (1994) reported results of conventional CMB performed on PM samples collected in the spring of 1993 over a 3-day period at a site adjacent to a major bus stop on Madison Avenue in midtown Manhattan. Buses in this area idle for as long as 10 minutes, and PM emissions are augmented by the elevated levels of DPM emitted during acceleration away from the bus stop (discussed in Section 2.2.5). DPM concentrations reported from this study ranged from 13.0 $\mu g/m^3$ to 46.7 $\mu g/m^3$. This study attributed, on average, 53% of the PM_{10} to DE. The DPM concentrations resulting from the source apportionment method used in this study require some caution because the CMB model overpredicted PM_{10} concentrations by an average 30%, which suggests that additional sources of the mass were not accounted for in the model. The relevance of the Manhattan bus stop concentrations and potential exposure for large urban populations provide strong motivation for further studies in the vicinity of such hotspots.

In summary, source apportionment studies of ambient samples collected before 1990 suggest that seasonal and annual average DPM concentrations for nonurban areas ranged from 2

μg/m^3 to 5 μg/m^3. DPM concentrations reported from CMB studies for urban areas in the pre-1990 timeframe ranged from 4.4 μg/m^3 to 13 μg/m^3, with concentrations on individual days ranging up to 22 μg/m^3. Source apportionment applied to ambient measurements taken in 1990 or later suggest that seasonal or annual average DPM levels in suburban/nonurban locations can range from 0.2 μg/m^3 to 2.6 μg/m^3, with maximum reported values ranging up to 3.4 μg/m^3. DPM concentrations reported from CMB studies in urban areas during 1990 or later range from 1.7 μg/m^3 to 3.6 μg/m^3, with maximum concentrations up to 7.3 μg/m^3. The highest DPM concentrations reported from CMB analysis of ambient measurements were those in the vicinity of a bus stop in midtown Manhattan, which ranged from 13.2 μg/m^3 to 46.7 μg/m^3.

2.4.2.2. *EC Surrogate for DPM*

EC is a major component of DE, contributing approximately 50% to 85% of diesel particulate mass, depending on engine technology, fuel type, duty cycle, engine lubrication oil consumption, and state of engine maintenance (Graboski et al., 1998b; Zaebst et al., 1991; Pierson and Brachaczek, 1983; Warner-Selph and Dietzmann, 1984). In urban ambient environments, DE is one of the major contributors to EC, with other potential sources including spark-engine exhaust; combustion of coal, oil, or wood; charbroiling; cigarette smoke; and road dust. Although cold-start emissions from gasoline combustion vehicles were reported to be an important source of EC in wintertime samples collected in two cities in the Denver area (Fujita et al., 1998), it is currently unclear to what extent these results are transferable to other locations. It is noteworthy that the EC content of the cold-start emissions from gasoline combustion vehicles was lower than that from diesel combustion engines in the same study by almost a factor of 2.

Fowler (1985) evaluated several components of DE and concluded that EC is the most reliable overall measure of ambient DE exposure. Because of the large portion of EC in DPM, and the fact that DE is one of the major contributors to EC in many ambient environments, DPM concentrations can be bounded using EC measurements. Surrogate calculations of DPM have been based on the fraction of ambient EC measured in a sample that is attributable to diesel engine exhaust and the fraction of the diesel particle mass accounted for by EC. In the recent Multiple Air Toxics Exposure Study in the South Coast Air Basin (MATES-II, SCAQMD, 2000), EC measurements were used to estimate DPM concentrations by the following relationship: approximately 67% of fine EC in the ambient air in the Los Angeles area originates from diesel engine exhaust (Gray, 1986), and the average EC fraction of diesel particles measured was 64%. Therefore, in the MATES-II study, the South Coast Air Quality Management District calculated DPM concentrations from EC measurements by multiplying a measured EC concentration by 67% and dividing by the fraction of DPM mass accounted for by EC of 64%, for example, DPM concentration = (EC * 0.67)/0.64, or DPM = EC * 1.04 (not

appreciably different from EC≈DPM). This calculation, used in the MATES-II study, relies on data collected in the 1982 timeframe and may not accurately represent the current day contributions of diesel engines to the ambient EC inventory. Using a 1998 emissions inventory for the South Coast Air Basin, it is now estimated that a more appropriate conversion from EC to DPM is to multiply EC by 1.24 (MATES-II, SCAQMD, 2000).

An alternative calculation can be derived using data from recent studies in Colorado and Arizona (Fujita et al., 1998; Maricopa Association of Governments, 1999). The fraction of EC attributable to DE can be estimated from detailed source profiles applied to a CMB model as discussed above. The contribution of diesel engines to EC averaged 68% ± 20% for Brighton, CO, and 49% ± 26% at Welby, CO, as part of the winter 1996-1997 NFRAQS. In Phoenix, diesel engine exhaust was estimated to account for approximately 46% ± 22% of the ambient EC. For some environments, such as certain occupational settings in which diesel engines are in proximity to workers, all the EC may realistically be attributed to DE as a reasonable upper bound estimate of DPM concentrations.

As discussed in Section 2.2, the EC content of DPM can vary widely depending on engine type, load conditions, and the test cycle. However, typical profiles for HD and LD diesel engines have been determined and the typical EC fraction of DPM ranges from approximately 52% to 75%.

Ambient EC attributed to DE in the studies described above ranges from 46% to 68%. A lower-bound estimate of DPM from ambient EC measurements in areas with similar source contributions to those in the Phoenix and Denver areas can be derived using the equation:

$$DPM = (EC * 0.46)/0.75 \text{ or } DPM = EC * 0.62$$

An upper-bound estimate uses the equation:

$$DPM = (EC * 0.68)/0.52 \text{ or } DPM = EC * 1.31$$

Using the average of the ranges provides the equation:

$$DPM = EC * 0.89.$$

Clearly the choice of a point estimate can provide a surrogate calculation of DPM that can vary by at least a factor of two. Although a recommended surrogate DPM calculation method is not provided here, the surrogate DPM calculation is used to illustrate the usefulness of

this approach for estimating DPM in the absence of a more sophisticated receptor modeling analysis for locations where fine PM EC concentrations are available.

One source of variability in EC concentrations reported for ambient studies is the measurement method used to quantify EC. As discussed in Section 2.2.8.1, EC and OC are operationally defined. Ambient samples are typically analyzed for EC using thermal optical reflectance or thermal optical transmittance. The measurement technique used in the NFRAQS and Phoenix studies was TOR, which, as discussed in Section 2.2.8.2, often results in higher EC levels compared to TOT analyses.

Table 2-24 provides a lower- and upper-bound DPM estimate from annual average EC concentrations for three urban areas, in addition to DPM concentrations reported from EC measurements for the MATES- II (SCAQMD, 2000). Under an EPA research grant with the Northeastern States for Coordinated Air Use Management (NESCAUM), $PM_{2.5}$ samples were collected every 6 days for 1 year (1995) in Boston (Kenmore Square), MA, and Rochester, NY, and were analyzed for EC using TOT (Salmon et al., 1997). DPM concentrations were estimated to be in the range from 0.8 $\mu g/m^3$ to 1.7 $\mu g/m^3$ in Boston, and from 0.4 $\mu g/m^3$ to 0.8 $\mu g/m^3$ in Rochester (Table 2-24).

Table 2-24. Ambient diesel particulate matter concentrations from elemental carbon measurements in urban locations

Reference	Year of sampling	Location	$DPM_{2.5}$ $\mu g/m^3$ lower-upper bound range (point estimate)[a]	DPM % of total PM
Salmon et al., 1997	1995, annual	Boston, MA	0.8–1.7 (1.1)	6-12
		Rochester, NY	0.4-0.8 (0.5)	3-6
Sisler, 1996	1992-1995, annual	Washington, DC	0.9-2.2 (1.5)	4-12
		MATES II [c]	Diesel $PM_{2.5}$ $\mu g/m^3$ avg± std dev.	
South Coast Air Quality Management District, 1999	1995-6, annual	Anaheim, CA	2.4 ± 1.8	[b]
		Burbank, CA	3.3 ± 1.9	[b]
		Los Angeles, CA	3.5 ± 1.9	[b]
		Fontanta, CA	3.4 ± 2.3	[b]
		Huntington Park, CA	4.5 ± 2.4	[b]
		Long Beach, CA	2.5 ± 1.7	[b]
		Pico Rivera, CA	4.4 ± 2.2	[b]
		Rubidoux, CA	3.4 ± 2.0	[b]

[a] Lower-bound range: DPM=EC*0.62; upper-bound range: DPM=EC*1.31; point estimate: DPM=EC*0.89.
[b] Not available.
[c]The Multiple Air Toxics Exposure Study in the South Coast Air Basin reported DPM calculated from EC concentrations as DPM=EC*1.04. Standard deviations are reported.

The Interagency Monitoring of Protected Visual Environments (IMPROVE) project being conducted by the National Park Service includes an extensive aerosol monitoring network mainly in rural or remote areas of the country (national parks, national monuments, wilderness areas, national wildlife refuges, and national seashores), and also in Washington, DC (Sisler, 1996). $PM_{2.5}$ samples, collected from March 1992 through February 1995 twice weekly for 24-hour duration at 43 sites (some co-located in the same rural park area), were analyzed for a suite of chemical constituents, including EC (using TOR). EC concentrations in these rural locations may have EC source contributions quite different from those in the urban areas in which the fraction of EC attributable to DE has been reported. The lack of information regarding EC sources in these rural locations makes the application of the EC surrogate highly uncertain. It is noteworthy that annual average EC concentrations in the rural and remote regions reported as part of the IMPROVE network range from 0.1 $\mu g/m^3$ for Denali National Park, AK, to 0.9 $\mu g/m^3$ for the Lake Tahoe, CA, area. In Washington, DC, the annual average EC concentration of 1.7 $\mu g/m^3$ is estimated as an annual average DPM concentration of 1.4 $\mu g/m^3$.

The annual average EC measurements in Washington, DC, suggest that the DPM concentrations are in the range from 1.0 $\mu g/m^3$ to 2.2 $\mu g/m^3$, accounting for 5% to 12% of ambient $PM_{2.5}$. Seasonally averaged data for the Washington, DC, site indicate that EC concentrations and, by extension, DPM concentrations peak in the autumn and winter (2.0 $\mu g/m^3$ and 0.9 $\mu g/m^3$ EC, respectively).

DPM concentrations reported recently as part of the MATES-II study at eight locations ranged from 2.4 $\mu g/m^3$ to 4.5 $\mu g/m^3$. DPM concentrations at Huntington Park and Pico Rivera, CA, were higher than other DPM concentrations in the South Coast Air Basin, perhaps because of higher diesel truck traffic, proximity to nonroad diesel sources, or nondiesel sources of EC, including gasoline vehicle traffic.

In a recent study of the trends in fine particle and EC concentrations in Southern California, Christoforou et al. (2000) report that EC concentrations measured in 1993 were 29%-40% of EC concentrations measured in 1982 at four urban Los Angeles sites. The authors credit lower PM emission rates from on-road diesel engines as well as cleaner-burning diesel fuel for the observed EC decrease. The extent to which nonroad diesel equipment impacts a given site will influence the trend in ambient EC concentrations because fewer regulations have been promulgated to control the PM emissions from these engines.

2.4.2.3. *Dispersion Modeling Results*

Dispersion models estimate ambient levels of PM at a receptor site on the basis of emission factors for the relevant sources and parameters that simulate atmospheric processes such as the advection, mixing, deposition, and chemical transformation of compounds as they are

transported from the source to the receptor site(s). Cass and Gray (1995), Gray and Cass (1998), and Kleeman and Cass (1998) have applied dispersion models to the South Coast Air Basin to estimate DPM concentrations. The models used by these investigators applied emission factors from 1982 and consequently are representative of concentrations prior to the implementation of DPM emission controls. In addition to offering another approach for estimating ambient DPM concentrations, dispersion models can provide the ability to distinguish on-highway from nonroad diesel source contributions and have presented an approach for quantifying the concentrations of secondary aerosols from DE.

Cass and Gray (1995) used a Lagrangian particle-in-cell model to estimate the source contributions to atmospheric fine carbon particle concentrations in the Los Angeles area, including diesel emission factors from on-highway and off-highway sources. Their dispersion model indicates that for 1982, the annual average ambient concentrations of DPM ranged from 1.9 $\mu g/m^3$ in Azusa, CA, to 5.6 $\mu g/m^3$ in downtown Los Angeles (Table 2-25). The contribution of on-highway sources to DPM ranged from 63.3% in downtown Los Angeles to 89% in west Los Angeles. Of the on-highway diesel contribution, the model predicted that for southern California, HD trucks made up the majority (85%) of the DPM inventory, and overall they contributed 66% of the DPM in the ambient air. Nonroad sources of DE include pumping stations, construction sites, shipping docks, railroad yards, and heavy equipment repair facilities. Cass and Gray (1995) also report that wintertime peaks in DPM concentrations can reach 10 $\mu g/m^3$.

Table 2-25. Ambient diesel particulate matter concentrations from dispersion modeling

Reference	Location	Year of sampling	Location type	$DPM_{2.5}$ g/m^3 (mean)	DPM % of total PM
Cass and Gray, 1995	Azusa, CA	1982, annual	Nonurban	1.4[a]	5
	Lennox, CA	1982, annual	Nonurban	3.8[a]	13
	Anaheim, CA	1982, annual	Urban	2.7[a]	12
	Pasadena, CA	1982, annual	Urban	2.0[a]	7
	Long Beach, CA	1982, annual	Urban	3.5[a]	13
	Downtown LA, CA	1982, annual	Urban	3.5[a]	11
	West LA, CA	1982, annual	Urban	3.8[a]	16
Kleeman and Cass, 1998	Claremont, CA	18-19 Aug 1987	Nonurban	2.4 (4.0)[a,b]	8 (6)[b]
Kleeman et al., 2000	Long Beach, CA	24 Sept 1996	Urban	1.9(2.6)[b]	8 (7)[b]
	Fullerton, CA	24 Sept 1996	Nonurban	2.4(3.9)[b]	9 (8)[b]
	Riverside, CA	25 Sept 1996	Suburban	4.4(13.3)[b]	12 (13)[b]

[a] On-road diesel vehicles only; all other values are for on-road plus nonroad diesel emissions.
[b] Value in parentheses includes secondary DPM (nitrate, ammonium, sulfate and hydrocarbons) attributable to atmospheric reactions of primary diesel emissions of NO_X, SO_2 and hydrocarbons. For the fraction of ambient PM attributable to DPM, the value in parenthesis reports total DPM (primary plus secondary) as a fraction of total ambient PM (primary plus secondary).

Kleeman and Cass (1998) developed a Lagrangian model that examines the size and chemical evolution of aerosols, including gas-to-particle conversion processes during transport. This model was applied to one well-characterized episode in Claremont, CA, on August 27-28, 1987. The model provided reasonable predictions of PM_{10} (overpredicting PM_{10} by 13%), EC, and OC, and it adequately reconstructed the size distribution of the aerosols. The model indicated that on August 27-28, 1987, the $PM_{2.5}$ concentration was 76.7 $\mu g/m^3$, 13.2% (10.1 $\mu g/m^3$) of which was attributable to diesel engine emissions. This estimate includes secondary aerosol formation for sulfate, ammonium, nitrate, and organic compounds, which accounted for 4.9 $\mu g/m^3$ of the total estimated DPM mass. The secondary organic aerosol was estimated to be 1.1 $\mu g/m^3$, or 31% of the total secondary aerosol mass, with the remainder composed of nitrate, ammonium, and sulfate aerosols.

Dispersion modeling estimates of diesel PM concentrations from on-highway and nonroad sources have recently been developed as part of the EPA National Air Toxics Assessment (NATA) National Scale Assessment. This assessment uses the Assessment System for Population Exposure Nationwide (ASPEN) dispersion model to estimate ambient concentrations for the year 1996. The NATA national scale assessment reports concentrations of DPM and 32 additional urban air toxic compounds at the county, State, and national level (NATA, 2001).

ASPEN makes a number of simplifying assumptions in order to model concentrations on a nationwide scale. For instance, concentration estimates at the census tract level were estimated using modeling assumptions to allocate emissions from the county level, and the model is very sensitive to the assumptions used. In addition, dispersion of emissions from nonpoint sources (e.g., on-highway and nonroad vehicles) was treated simplistically. For resident tracts that have radii greater than 0.3 km, non-point-source ambient concentrations are estimated on the basis of five pseudo-point sources. The average concentration for the census tract is determined by spatially averaging the ambient concentrations associated with the receptors defined for the five pseudosources that fall within the bounds of the tract. Other limitations include the following: terrain impacts on dispersion were not included; the study relied on long-term climate summary data, and no long-range transport was included for DPM (medium-range transport for DPM, within 300 km, was included). Because of the limitations, the results are most meaningfully interpreted when viewed over large geographic areas. The 1996 results from ASPEN compare well (generally within a factor of 1.5) with estimated concentrations from EC measurements and receptor modeling, as well as data from other dispersion modeling studies. The complete results of the assessment are available at http://www.epa.gov/ttn/uatw/nata.

Table 2-26 presents 25th percentile, average, and 75th percentile nationwide concentrations from the 1996 National-Scale Assessment as well as the contribution of on-road and nonroad DE the sources to the nationwide average. The national average DPM concentration reported in the National-Scale Assessment is 2.1 $\mu g/m^3$, of which nonroad sources are estimated to contribute 67% and on-road sources contribute the remainder. Less than 2% of the nationwide DE inventory is attributed to point sources, and these were not included in the modeling as part of National-Scale Assessment. A wide range in average State-specific ambient DPM concentrations was reported by the National-Scale Assessment with the lowest values for mainly rural States with few DE sources, such as Wyoming (annual average of 0.2 $\mu g/m^3$), and the highest values for States with large urban centers such as New York (annual average of 5.4 $\mu g/m^3$).

Table 2-26. Nationwide ambient diesel particulate matter concentrations for 1996 from the National Air Toxics Assessment National-Scale Assessment dispersion modeling

Location	25th percentile, DPM_{10} mg/m^3	Average, DPM_{10} mg/m^3	75th percentile, DPM_{10} mg/m^3	Contribution to average from on-road sources, DPM_{10} mg/m^3	Contribution to average from nonroad sources, DPM_{10} mg/m^3
Nationwide	0.9	2.1	2.5	0.6	1.4
All urban counties	1.2	2.4	2.7	0.7	1.7
All rural counties	0.4	0.7	1.0	0.3	0.5

Source: NATA, 2001. Data available at http://www.epa.gov/ttn/uatw/nata.

2.4.3. Exposures to Diesel Exhaust

Ultimately, it is personal exposure that determines health impacts. In the following sections, modeled average exposures and some information reflecting potential exposures for those who spend a large portion of their time outdoors are presented. Occupational exposures to DPM are summarized for the variety of workplaces in which diesel engines are used. These occupational exposures are placed into context with equivalent environmental exposures to understand the potential for overlap in average occupational and average ambient exposures. Because DE is a mixture of particles and gases, one must choose a measure of exposure (i.e., dosimeter); $\mu g/m^3$ of DPM has historically been used in many studies as the dosimeter for the entire DE mixture.

2.4.3.1. *Occupational Exposure to DE*

The National Institute for Occupational Safety and Health (NIOSH, 1988) estimates that approximately 1.35 million workers are occupationally exposed to DE emissions. Such workers emissions include mine workers, railroad workers, bus and truck drivers, truck and bus maintenance garage workers, loading dock workers, firefighters, heavy equipment operators, and farm workers.

Measurements of DPM exposure in occupational environments have included respirable particulate (<3.5 μm), smoking-corrected respirable particulate, combustible respirable particulate, and EC, among other methods. The measurement method used in each of the studies discussed below is listed in Table 2-27. Occupational exposures to DPM as well as breathing zone concentrations of DPM have been described in some detail by Watts (1995), Groves and Cain (2000), Hammond (1998), the World Health Organization (1996), and Birch and Cary (1996) and are briefly, but not comprehensively, summarized here.

The highest occupational exposures to DPM are for workers in coal mines and noncoal mines using diesel-powered equipment. These exposures, reported by several investigators, range from approximately 10 $\mu g/m^3$ to 1,280 $\mu g/m^3$ (Table 2-27). Rogers and Whelan (1999) report exposures to specific DPM-associated PAHs (including naphthalene, fluorene, phenanthrene, pyrene, and benz[a]anthracene) for mine workers using diesel fuels containing low and high levels of sulfur, aliphatic, and aromatic compounds. Results of this study indicate that the composition of DPM to which workers were exposed varies considerably based on engine condition, fuel, and other operating parameters. Mine worker exposures to PAH compounds were highest for naphthalene, ranging from 1,312 μg/g to 3,228 μg/g of organics, and exposures were lowest for benz[a]anthracene, ranging from less than 3 μg/g up to 18 μg/g of organics.

Other investigators have reported DPM-associated PAH concentrations that do not necessarily represent personal exposures but are a snapshot of short periods of elevated concentration that make up a portion of a worker's daily exposure. Bagley et al. (1991, 1992) reported levels of B[*a*]P ranging from below the detection limit of 0.05 ng/m^3 to 61 ng/m^3 collected only during periods of mining activity. Watts (1995) reported DPM concentrations in four mines collected during significant diesel activity, ranging from 850 $\mu g/m^3$ to 3,260 $\mu g/m^3$. Heino (1978) reports DPM concentrations for locomotive engineers reaching 2,000 $\mu g/m^3$.

In a study of four railroads, Woskie et al. (1988) reported concentrations of respirable dust (corrected for cigarette smoke particulate) that ranged from 39 $\mu g/m^3$ for engineers/firers to 134 $\mu g/m^3$ for locomotive shop workers and 191 $\mu g/m^3$ for hostlers. Woskie et al. (1988) also reported smoking-corrected respirable dust for railroad clerks (17 $\mu g/m^3$), who are considered to be not exposed to DE. Although these exposures may have included nondiesel PM (background

Table 2-27. Occupational exposure to DPM

Author	Year of sample	Location/job type, typical work schedule of 8 hours	n	Sample type	Range in DPM, μg/m³
Gangal and Dainty, 1993[a]	NA	Noncoal mine workers	~200	RCD	100–900
Säverin, 1999	1992	Noncoal mine workers	255[b]	RTC	38–1,280
Rogers and Whelan, 1999	1990-99	Coal mine workers	>1,300	DPSMM	10–640
Haney, 1990[a]	1980s	Coal mine workers (five mines)	NA	SJI	180–1,000
Ambs, 1991a[a]	NA	Coal mine workers (four mines)	NA	PDEAS	750–780
Woskie et al., 1988	3-years in mid-1980s	Railroad engineer/frier	128	ARP	39–73
		Railroad braker/conductor	158	ARP	52–191
		Railroad shop workers	176	ARP	114–134
Groves and Cain, 2000	NA	Railway repair	64	EC(U)	7-50
Froines et al., 1987	1985	Firefighters (two stations)	238	TSP	63–748
NIOSH, 1992[a]	NA	Firefighters (three stations)	18	EC(T)	6–70
Birch and Cary, 1996	NA	Firefighters	NA	EC(U)	20–79
	NA	Fire station employees (four stations)	NA	EC(U)	4–52
Birch and Cary, 1996	NA	Airport ground crew	NA	EC(U)	7–15
	NA	Public transit workers	NA	EC(U)	15–98
NIOSH, 1990	1990	Diesel forklift dockworkers	24	EC(T)	12–61
Zaebst et al., 1991	1990	Dockworkers	75	EC(T)	9–20
		Mechanics	80	EC(T)	5–28
		Long- and short-haul truckers	128	EC(T)	2–7
Groves and Cain, 2000	NA	Bus garage/repair	53	EC(U)	7-217
		Forklift trucks	27	EC(U)	7-403
Kittelson et al., 2000	1999-2000	Bus drivers	39	EC(T)	1–3
		Parking ramp attendants	12	EC(T)	2 ± 0.4

[a] Cited in Watts (1995). NA: not available.
[b] Personal exposure and area samples were not reported separately for this study.
RCD: respirable combustible dust; RTC: respirable total carbon SPM: submicrometer PM; DPSMM: diesel particulate submicron mass (two-stage impaction sampler used to separate PM by size); EC(T): elemental carbon analyzed by TOT; EC(R) elemental carbon analyzed by TOR; EC(U) elemental carbon analyzed by colouremetric method or method not reported; SJI: single-jet impactor agreed within 10% with simultaneous PDEAS measurements; PDEAS: personal DE aerosol sampler collects DPM <0.8 μm, SPM: particulate matter; ARP: respirable particulate adjusted to remove the influence of cigarette smoke; TSP: total suspended particulate matter.

respirable dust levels have been estimated to have contributed approximately 10 μg/m^3 to 33 μg/m^3 for this study), the majority of the respirable PM is believed to have originated from diesel locomotive emissions. Groves and Cain (2000) reported EC exposures among railway repair workers averaging 21 μg/m^3 with a range from 7-50 μg/m^3. DPM exposures reported for firefighters operating diesel engine vehicles range from 4 μg/m^3 to 748 μg/m^3, which also encompasses the range of DPM exposures reported for airport ground crew and public transportation system personnel (7 μg/m^3 to 98 μg/m^3).

Studies reporting DE exposure among fire station employees typically report particulate levels below 100 μg/m^3 (ranging from 4 μg/m^3 to 79 μg/m^3) (NIOSH, 1992; Birch and Cary, 1996). In a study by Froines et al. (1987), DPM exposures for firefighters in two stations ranged from 39 μg/m^3 to 73 μg/m^3. Birch and Cary (1996) also reported DPM exposures for airport ground crew and public transit workers, ranging from 7 μg/m^3 to 15 μg/m^3 for airport ground crews and 15 μg/m^3 to 98 μg/m^3 for public transit workers. Dock workers using diesel-powered forklifts have been reported to have DPM exposures ranging from 6 μg/m^3 to 403 μg/m^3 (NIOSH, 1990; Zaebst et al., 1991; Groves and Cain, 2000). In studies by NIOSH (1990) and Fowler (1985), the organic material measured accounted for about one-half to almost all of the carbonaceous DPM exposures, providing evidence that some pieces of nonroad equipment (forklifts and construction equipment) emitted DPM with a significant OC fraction in the 1980s and early 1990s.

Zaebst et al. (1991) also reported DPM exposures for mechanics, road drivers, and local drivers for 8-hour shifts at each of six large hub truck terminals. Residential background and highway background samples at fixed sites were also collected during warm-weather and cold-weather periods, and the geometric mean for DPM concentrations ranged from 1 μg/m^3 to 5 μg/m^3. DPM exposures for road and local truckers in warm- and cold-weather periods ranged from 2 μg/m^3 to 7 μg/m^3, whereas exposure levels for mechanics were reported between 5 μg/m^3 and 28 μg/m^3 (geometric means).

Kittelson et al. (2000) are measuring DPM exposures for bus drivers, parking garage attendants, and mechanics using TOT to quantify EC. Personal exposures for bus drivers on four different routes range from 1 μg/m^3 to 3 μg/m^3 and exposure among parking ramp attendants averaged 2 μg/m^3. These results are preliminary, and data for the mechanics have not yet been analyzed. This study will also characterize PAH compounds to which these workers are exposed.

Bus garage workers have also been assessed for exposure to DE using urinary excretion of 8-oxo-2'-deoxyguanosine (Loft et al., 1999). Other biomarkers of DE exposure in occupational workers have included measurements of urinary 1-hydroxypyrene, adducts of DNA

and hemoglobin, and 8-hydroxyguanosine in lung tissue (Nielsen et al., 1996; Tokiwa et al., 1999; Zwirner-Baier and Neumann, 1999; Hara et al., 1997).

To estimate an environmental exposure that is equivalent to an occupational lifetime exposure, the fraction of lifetime worker inhalation exposure (calculated as the amount of air breathed on the job multiplied by the typical amount of time spent on the job) is calculated relative to 70-year lifetime inhalation exposure: (10 m^3/shift/20 m^3/day) * (5 days/7 days) * (48 weeks/52 weeks) * (45-year career/70-year lifetime) = 0.21. Using this calculation, 21% of an annual average occupational lifetime exposure is roughly equivalent to a 70-year annual average lifetime environmental exposure. The equivalent environmental exposures for the occupational exposures presented in Table 2-28 range from 0.6 $\mu g/m^3$ to 14 $\mu g/m^3$ for truckers, dock workers, and mechanics, and from 2 $\mu g/m^3$ to 269 $\mu g/m^3$ for miners. The low end of the range of environmental equivalent exposures for several of the occupational settings overlaps with average modeled exposures and with ambient concentrations of DPM in urban areas in the 1990–1996 timeframe. The overlap between some occupational exposures and environmental exposures, as well as the small difference between occupational environmental equivalent exposures and environmental exposures, is a significant concern and suggests the potential for significant risk in the general population. The possible magnitude of the cancer risk in the general population is discussed in Chapter 8, Section 8.3.

Table 2-28. Ranges of occupational exposure to DPM by job category with estimates of equivalent environmental exposures

Year of sampling	Occupations	Occupational DPM, $\mu g/m^3$	Environmental equivalent[a] exposure, $\mu g/m^3$
1980s and 1990s	Miners	10–1,280	2–269
1980s	Railroad workers	39–191	8–40
1985 and later	Firefighters	4–748	1–157
NA	Airport crew, public transit workers	7–98	2–21
1990	Dockworkers, mechanics	5–61	1–13
1990	Long- and short-haul truckers	2–7	0.4–2

[a]Environmental equivalent exposure is calculated as the occupational exposure * (10 m^3/shift / 20 m^3/day)* (5 days / 7days) * (48 weeks / 52 weeks) * (45 year career / 70 year lifetime), or occupational exposure * 0.21 (discussed in section 2.4.3.1.

2.4.3.2. *Ambient Exposure to DE*

Modeled estimates of population exposures to DPM integrate exposure in various indoor and outdoor environments and also account for the demographic distribution, time-activity

patterns, and DPM concentrations in various environments, including job-related exposures. Two modeling efforts have been developed to determine DPM exposures in the general population: the Hazardous Air Pollutant Exposure Model for Mobile Sources, version 3 (HAPEM-MS3) and the California Population Indoor Exposure Model (CPIEM). EPA has also developed version 4 of the HAPEM, which provides State-specific average exposures for DPM and 32 other urban air toxic compounds. The draft exposure assessment using HAPEM version 4 (HAPEM4) has been conducted as part of the National Air Toxics Assessment National-Scale Analysis described in Section 2.4.2.3 above and results are provided here.

2.4.3.2.1. ***The Hazardous Air Pollutant Exposure Model.*** To estimate population exposures to DPM, EPA has used HAPEM-MS3 (U.S. EPA, 1999b). This model provides national and urban-area-specific exposures to DPM from on-road sources only. HAPEM-MS3 is based on the CO probabilistic National Ambient Air Quality Standards (NAAQS) exposure model (pNEM/CO), which is used to estimate the frequency distribution of population exposure to CO and the resulting carboxyhemaglobin levels (Law et al., 1997). HAPEM simulates the CO exposure scenario of individuals in 22 demographic groups for 37 microenvironments. CO concentrations are based on ambient measurements made in 1990 and are related to exposures of individuals in a 10-km radius around the sampling site. DPM exposures are calculated as in Equation 2-5, using a ratiometric approach to CO.

$$DPM_{\mu g/m^3} = (CO_{\mu g/m^3} / CO_{g/mi}) \times DPM_{g/mi} \qquad (2\text{-}5)$$

Data provided to the model include CO monitoring data for 1990; time-activity data collected in Denver, Washington, DC, and Cincinnati from 1982 to 1985; microenvironmental data; and 1990 census population data. Motor vehicle DPM and CO emission rates reported by EPA (1999c) are used to calculate mobile-source DPM exposures, and exposures in future years are projected based on the increase in vehicle miles traveled. EPA's PART5 model is used to estimate DPM emission rates (g/mi) for the fleet as a whole in any given calendar year. PART5 is currently being modified to account for deterioration, actual in-use emissions, poor maintenance, and tampering effects, all of which increase emission factors. As a result, HAPEM-MS3 exposure estimates based on PART5 emission factors may underestimate true exposures from on-road sources. A comparison of PART5 HD diesel vehicle emission factors with those presented earlier in this chapter suggests that PART5 may underestimate HD diesel vehicle emissions by up to 50%.

HAPEM-MS3 assumes that the highway fleet (gasoline plus diesel) emissions ratio of CO to DPM can be used as an adjustment factor to convert estimated CO personal exposure to

DPM exposure estimates. This assumption is supported by the observation that even though gasoline vehicles emit the large majority of CO, gasoline and diesel highway vehicles travel on the same roadways. DPM and CO are both relatively long-lived atmospheric species (1–3 days) except under certain conditions (Seinfeld and Pandis, 1998); therefore, the model does not account for chemical and physical differences between the DPM and CO, and the model assumes that for the average person in a modeled air district, CO and DPM are well mixed. Exposure in microscale environments in which these assumptions may not be valid were not modeled.

A validation study conducted for the pNEM/CO model on which HAPEM-MS3 is based indicates that CO exposures for the population in the 5th percentile were overestimated by approximately 33%, whereas those with exposures in the 98th percentile were underestimated by about 30%. This validation study is considered applicable to the HAPEM-MS3 model. To address the underestimate of exposures for the most highly exposed, Brodowicz (1999) used CO concentrations relevant to the most highly exposed populations to determine DPM exposures for different demographic groups within this population; the results are discussed below.

Annual average DPM exposures from on-road vehicles and nonroad sources nationwide for the general population, rural and urban population, outdoor workers, and urban children are reported in Tables 2-29 and 2-30. The modeled annual average DPM exposure nationwide (urban and rural areas) in 1996 from on-road sources only was 0.8 $\mu g/m^3$. The modeled annual average exposure in urban areas for the same year was 0.8 $\mu g/m^3$, and the modeled exposure for rural areas was 0.4 $\mu g/m^3$. Among the demographic groups modeled, urban outdoor workers in general were found to have the highest average exposure to DPM, averaging 1.0 $\mu g/m^3$ from on-road sources in 1996. DPM exposures attributable to on-road sources are projected to decrease until approximately 2007 because of fleet turnover and the full implementation of Federal regulations that are currently in place. Full implementation of the recently finalized Heavy-Duty Engine and Vehicle Standards and Highway Diesel Fuel Sulfur Control Requirements would significantly lower DPM exposures from on-road sources in the post-2007 timeframe (U.S. EPA, 2000b).

Because diesel vehicle traffic, and therefore exposure to DPM, varies for different urban areas, HAPEM-MS3 was used to estimate annual average population exposures for 10 urban areas. Modeled 1996 DPM exposures in the cities ranged from 0.6 $\mu g/m^3$ in Chicago and St. Louis to 1.3 $\mu g/m^3$ in Phoenix (Table 2-31). In 1996, estimated average DPM exposure from on-road sources was higher than the national average in five cities: Atlanta, Minneapolis, New York, Phoenix, and Spokane. Nationally in 1996, 97% of DPM exposure from on-road vehicles was attributable to HD diesel vehicles, and the rest was generated mainly by LD diesel trucks.

Table 2-29. Annual average nationwide DPM exposure estimates (μg/m³) from on-road sources for rural and urban demographic groups in 1990, 1996, and 2007 using HAPEM-MS3

Demographic group	1990	1996	2007
50-State population	0.8	0.8	0.4
Rural population	0.5	0.4	0.2
Urban population	0.9	0.8	0.4
Urban outdoor workers	1.1	1.0	0.5
Urban children (0-17)	0.9	0.8	0.4

Source: U.S. EPA, 1999b, adjusted to reflect HDDV VMT described in U.S. EPA, 2000b.

Table 2-30. Draft annual average, 25th, and 75th percentile nationwide DPM exposure estimates (μg/m³) from on-road and nonroad sources for rural and urban counties in 1996 using HAPEM4

Demographic group	25th Percentile, DPM_{10} mg/m³	Average, DPM_{10} mg/m³	75th Percentile, DPM_{10} mg/m³	Contribution to average from on-road sources, DPM_{10} mg/m³	Contribution to average from nonroad sources, DPM_{10} mg/m³
Nationwide	0.6	1.4	1.8	0.5	0.9
Rural population	0.3	0.6	0.7	0.2	0.3
Urban population	0.8	1.6	2.0	0.5	1.1

Source: NATA, 2001. Data available at http://www.epa.gov/ttn/uatw/nata.

Because HAPEM-MS3 is suspected to underestimate exposures in highly exposed populations, 1990 CO concentrations relevant to the most highly exposed populations were used to determine 1990 DPM exposures for different demographic groups in this population. The highest DPM exposures ranged from 0.8 μg/m³ for outdoor workers in St. Louis to 2.0 μg/m³ for outdoor workers in Spokane and up to 4.0 μg/m³ for outdoor children in New York (Table 2-31). The highest exposed demographic groups were those who spend a large portion of their time outdoors. It is important to note that these exposure estimates are lower than the total exposure to DPM because they reflect only DPM from on-road sources and not exposure to nonroad DPM emissions.

Table 2-31. Annual average DPM exposures for 1990 and 1996 in the general population and among the highest exposed demographic groups in nine urban areas and nationwide from on-road sources only using HAPEM-MS3

Urban area	1990 Population average exposure, μg/m³	1996 Population average exposure, μg/m³	Highest DPM exposure in 1990, μg/m³ (demographic group experiencing this exposure)
Nationwide	*0.8*	*0.8*	*NA*
Atlanta, GA	0.8	0.9	NA
Chicago, IL	0.8	0.6	1.3 (outdoor workers)
Denver, CO	0.7	0.8	1.2 (outdoor workers)
Houston, TX	0.6	0.9	0.8 (outdoor workers)
Minneapolis, MN	1.0	1.0	1.5 (outdoor workers)
New York, NY	1.6	1.2	4.0 (outdoor children)
Philadelphia, PA	0.7	0.7	1.2 (outdoor children)
Phoenix, AZ	1.4	1.3	2.4 (nonworking men 18-44)
Spokane, WA	1.3	1.1	2.0 (outdoor workers)
St. Louis, MO	0.6	0.6	0.8 (outdoor workers)

NA - Not available.
Source: U.S. EPA, 1999b, adjusted to reflect HDDV VMT described in U.S. EPA, 2000b.

The HAPEM4 modeling approach provides exposure estimates from on-road and nonroad sources as well as point and area sources for pollutants other than DPM. In addition, HAPEM4 incorporates technical advancements over previous Agency exposure assessments. Instead of using a surrogate pollutant such as CO to estimate exposure, HAPEM4 uses census tract DPM concentrations provided by the ASPEN dispersion model described in Section 2.4.2.3 to estimate DPM exposure for individuals in each census tract in the United States. The exposure modeling results are aggregated to provide county, State, and nationwide exposure estimates. HAPEM4 also incorporates the latest data regarding time-activity patterns from the Consolidated Human Activity Database and the latest data available regarding penetration of PM to indoor environments. The results of this modeling approach are currently undergoing peer review and are therefore considered a draft and subject to change.

Nationwide exposure estimates from HAPEM4 are provided in Table 2-30. The draft National-Scale Assessment 1996 national average estimate of DPM exposure attributable to on-road and nonroad sources is 1.4 μg/m³. On-road sources are estimated to account for 0.5 μg/m³ and nonroad sources 0.9 μg/m³. The HAPEM-MS3 1996 exposure value of 0.8 μg/m³ and the

most recent draft National-Scale Assessment value of 0.5 μg/m^3 differ slightly as a result of the different modeling approaches. Both the HAPEM-MS3 and HAPEM4 exposure results support the risk perspective provided in Chapter 8, Section 8.3.

2.4.3.2.2. ***Personal exposures: microenvironments/hotspots.*** Personal monitoring for DPM exposure has focused on occupationally exposed groups, including railroad workers, mine workers, mechanics, and truck drivers. Although some studies have measured personal exposures to ambient PM, none have conducted detailed chemical analysis to quantify the portion of PM attributable to DE (e.g., using extended species CMB, discussed above). EC concentrations have been reported for some microenvironments and are discussed in this section. Microenvironmental exposures of significant concern include in-vehicle exposures such as school buses and passenger cars as well as near highways and in urban canyons. Because DPM from mobile sources is emitted into the breathing zone of humans, this source has a greater potential for human exposure (per kg of emissions) compared to combustion particulates emitted from point sources.

Recent EC measurements reported for enclosed vehicles driving on Sacramento roadways ranged from below detection limits up to 10 μg/m^3 and from 3 μg/m^3 to 40 μg/m^3 on Los Angeles roadways. Elevated levels of $PM_{2.5}$ and EC were observed when the vehicle being followed was powered by a HD diesel truck or bus (Cal EPA, 1998b). EC is also present in the exhaust of gasoline vehicles, so these measurements are likely to include some EC from gasoline vehicles. The SHEDS (Stochastic Human Exposure and Dose Simulation) model for PM predicts that although the typical person spends only about 5% of his or her time in a vehicle, this microenvironment can contribute on average 20% and as much as 40% of a person's total PM exposure (Burke et al., 2000).

The California Air Resources Board also collected EC near the Long Beach Freeway for 4 days in May 1993 and 3 days in December 1993 (Cal EPA, 1998a). Using emission estimates from their EMFAC7G model and EC and OC composition profiles for diesel and gasoline exhaust, tire wear, and road dust, CARB estimated the contribution of the freeway to DPM concentrations. For the 2 days of sampling in December 1993, DE from vehicles on the nearby freeway was estimated to contribute from 0.7 μg/m^3 to 4.0 μg/m^3 excess DPM above background concentrations, with a maximum of 7.5 μg/m^3.

In 1986, EC concentrations were measured in Glendora, CA, during a carbonaceous aerosol intercomparison study (Cadle and Mulawa, 1990; Hansen and Novakov, 1990). One technique used during the study reported EC concentrations in 1-minute intervals, reflecting the impact from diesel vehicles 50 m from the study site. The diesel vehicles were estimated to contribute up to 5 μg/m^3 EC above the background concentration.

In a study designed to investigate relationships between DE exposure and respiratory health of children in the Netherlands, EC measurements were collected in 23 schools located from 47 m to 377 m from a freeway and in 8 schools located at a distance greater than 400 m from a freeway (Brunekreef, 1999). EC concentrations in schools near freeways ranged from 1.1 $\mu g/m^3$ to 6.3 $\mu g/m^3$, with a mean of 3.4 $\mu g/m^3$, and EC concentrations in schools more than 400 m from freeways ranged from 0.8 $\mu g/m^3$ to 2.1 $\mu g/m^3$, with a mean of 1.4 $\mu g/m^3$. Brunekreef et al. (2000), using a reflectance method to report "soot" or carbonaceous particulate concentrations as a surrogate for EC, found a statistically significant increase in carbonaceous particle concentrations inside and outside of the schools with increasing truck traffic (predominantly diesel), with decreasing distance between the school and the highway, and with an increase in the percent of time the school was downwind of the highway. In additional studies in elderly subjects in Helsinki and Amsterdam, Janssen et al. (2000) reported that outdoor measurements of EC were highly correlated with indoor and personal exposure measurements of EC, supporting the position that short-term increases in outdoor EC concentrations are reflected in increased personal exposures even for those who spend much of their time indoors.

Although there is little quantitative information regarding personal exposure to DPM, certain exposure situations are expected to result in higher than average exposures. Those in the more highly exposed categories would generally include people living in urban areas in which diesel delivery trucks, buses, and garbage trucks frequent the roadways, but also included would be people living near freeways, bus stations, construction sites, train stations, marinas frequented by diesel-powered vessels, and distribution hubs using diesel truck transport. One study using the 1-hydroxypyrene biomarker of DE exposure reported exposure among most (76%) of the 26 adolescents sampled in Harlem (Northridge et al., 1999). In a follow-on study, Kinney et al. (2000) reported EC concentrations from personal monitors worn by study staff on sidewalks at four Harlem intersections that ranged from 1.5 $\mu g/m^3$ to 6 $\mu g/m^3$. The EC concentrations were found to be associated with diesel bus and truck counts such that spatial variations in sidewalk concentrations of EC were attributed to local diesel sources in Harlem.

In any situation in which diesel engines operate and a majority of time is spent outdoors, personal exposures to DE are expected to exceed average exposures. Because a large but currently undefined portion of DPM is emitted during acceleration, those living and working in the vicinity of sources operating in this transient mode could experience highly elevated levels of DPM. DPM enriched in soluble organic material (as opposed to EC) is emitted from LD vehicles, some nonroad equipment, on-road diesel engines during cold-start and motoring conditions, and poorly maintained vehicles. The potential health effects of acute exposures to elevated DPM levels as well as health effects resulting from chronic exposures are discussed in subsequent chapters in this document.

2.4.3.2.3. ***The California Population Indoor Exposure Model.*** CPIEM, developed under contract to the CARB, estimates Californians' exposure to DPM using distributions of input data and a Monte Carlo approach (Cal EPA, 1998a). This model uses population-weighted outdoor DPM concentrations in a mass balance model to estimate DPM concentrations in four indoor environments: residences, office buildings, schools, and stores/retail buildings. The model takes into account air exchange rates, penetration factors, and a net loss factor for deposition/removal. In four additional environments (industrial plants, restaurants/lounges, other indoor places, and enclosed vehicles), assumptions were made about the similarity of each of these spaces to environments for which DPM exposures had been calculated. Industrial plants and enclosed vehicles were assumed to have DPM exposures similar to those in the outdoor environment; restaurants/lounges were assumed to have DPM concentrations similar to stores; and other indoor places were assumed to have DPM concentrations similar to offices. The estimated DPM concentrations in the indoor and outdoor environments range from 1.6 $\mu g/m^3$ to 3.0 $\mu g/m^3$ (Table 2-32).

Table 2-32. Modeled and estimated concentrations of DPM in microenvironments for California for all sources

Microenvironment	Estimated mean DPM (stdev), $\mu g/m^3$
Residences	1.9 (0.9)
Offices	1.6 (0.7)
Schools	1.9 (0.8)
Stores/public/retail bldgs	2.1 (0.9)
Outdoor places	3.0 (1.1)
Industrial plants[a]	3.0 (1.1)
Restaurants/lounges[a]	2.1 (0.9)
Other indoor places[a]	1.6 (0.7)
Enclosed vehicles[a]	3.0 (1.1)

[a]Concentrations assumed based on similarity with modeled environments.
Source: California EPA, 1998a.

The DPM concentrations reported in Table 2-32 were used as input to CPIEM, and time-activity patterns for children and adults were used to estimate total indoor and total air exposures to DPM. Overall, total indoor exposures were estimated to be 2.0 ± 0.7 μg/m^3, and total air exposures (indoor and outdoor exposures) were 2.1 ± 0.7 μg/m^3 (Table 2-33). The South Coast Air Basin and the San Francisco Bay Area were also modeled using CPIEM, where total air exposures to DPM were estimated to be 2.5 ± 0.9 μg/m^3 and 1.7 ± 0.9 μg/m^3, respectively.

Table 2-33. Estimated indoor air and total air exposures to DPM in California in 1990

Exposed population	Total indoor exposure (stdev), μg/m^3	Total air exposure, (stdev), μg/m^3
All Californians	2.0 (0.7)	2.1 (0.8)
South Coast Air Basin	2.4 (0.9)	2.5 (0.9)
San Francisco Bay Area	1.7 (0.9)	1.7 (0.9)

Source: California EPA, 1998a.

Exposure estimates were also made by Cal EPA (1998a) for 1995, 2000, and 2010 using a ratiometric approach to 1990 exposures. Total air exposures reported for 1995 and projected for 2000 and 2010 were 1.5 μg/m^3, 1.3 μg/m^3, and 1.2 μg/m^3, respectively.

2.5. SUMMARY AND DISCUSSION

This chapter summarizes information regarding the history of the use of diesel engines, technological developments and their impact on emissions over time, Federal standards on DE, the chemical and physical character of DE, atmospheric transformations of DE, and ambient DE concentrations and exposures. The aspects of each of these topics that are most relevant to the discussion of health effects in later chapters of this document are summarized here. Because the majority of information regarding the chemical composition and historical changes in DE pertains to on-road diesel engines, these data are discussed in greater detail than diesel emissions from nonroad equipment. Where possible, nonroad emissions were discussed in Chapter 2 and are briefly summarized here.

2.5.1. History of Diesel Engine Use, Standards, and Technology

The use of diesel engines in the trucking industry began in the 1940s, and diesel engines slowly displaced gasoline engines among HD trucks, accounting for 36% of new HD truck sales in 1960, 85% of sales in 1970, and almost 100% of sales in 1997. It is estimated that in 2000, HD diesel vehicles will travel more than 224 billion miles (U.S. EPA, 2000b). In 1997, on-highway HD diesel engines contributed 66% of the $PM_{2.5}$ emitted by on-highway vehicles.

To understand changes in emissions over time, it is important to note the difference between model year emission trends and calendar year emission trends. Emission trends by model year refer to the year in which an engine was made; the emission rate is specific to the technology and regulations in effect for that year. Emissions in a specific calendar year refer to aggregate emissions due to the mix of model year engines on the road. Because of the time required for fleet turnover, emission rates for the on-road fleet in any calendar year are not as low as the most recent model year emission rate. In 1997, 40% of the HD vehicles on the road were at least 10 years old and traveled approximately 17% of total HD vehicle miles.

EPA set a smoke standard for on-road HD diesel engines beginning with the 1970 model year. In the ensuing years, standards for PM from diesel engines for on-road applications decreased from 0.6 g/bhp-hr in 1988 to 0.1 g/bhp-hr for trucks in 1994-1995 and 0.05 g/bhp-hr for buses in 1996-1997. Calendar year emission contributions of PM from diesel engines to national PM_{10} inventories reflect decreases expected to result from Federal regulations, because the emission factor models (MOBILE5 and PART5) used to provide emission estimates for mobile sources largely use engine test data required for certification. The U.S. EPA Trends Report estimates that PM_{10} emissions attributable to on-road diesel vehicles decreased 27% between 1980 and 1998. DPM emission factors (g/mi by model year) measured from in-use vehicles decreased on average by a factor of six from the mid-1970s to the mid-1990s.

It is important to note that in spite of the decreasing trend in DPM emission factors by model year, a wide range in emission factors from in-use testing is reported, even for newer model year HD vehicles (from less than 0.1 g/mi to more than 1 g/mi for model year 1996 vehicles). The high variability in DPM emissions within one model year has been attributed to deterioration[3] and differences in measurement methods and test conditions at the various testing facilities. Studies in which consistent testing methods were used suggest that deterioration (even for newer model year engines) causes some of the variability in emission factors, whereas other

[3]Deterioration includes increases in emission rates (g/bhp hr) due to normal wear as well as manufacturing defects and malfunctions such as retarded timing, fuel injector malfunction, smoke limiting mechanism problems, clogged air filter, wrong or worn turbocharger, clogged intercooler, engine mechanical failure, excess oil consumption, and electronics that have been tampered with or have failed.

studies clearly demonstrate the important influence of test conditions and driving protocols (e.g., aggressive driving) on DPM emission factors.

Even though significant reductions in DPM from diesel vehicle emissions for on-road applications have been realized, diesel engines (nonroad and on-road combined) are still significant contributors to 1998 inventories of particulate matter, contributing approximately 23% of $PM_{2.5}$ emissions (not including the contribution from natural and miscellaneous sources).

Technology innovations that impact diesel engine emissions have occurred in the years since 1960, in particular the advent of turbocharging with charge air cooling and direct-injection engines. The use of these new technologies tends to lower emissions from on-road diesel engines; until the late 1970s, however, engines were optimized for performance rather than emissions, so the effect on emissions prior to this time was small. The limited amount of data available indicates that on-road engines in the 1950 to 1975 timeframe had DPM emissions similar to, and in some cases higher than, those of the mid-1970 engines that were not yet controlled for particulates.

Few data are available to assess the changes in emission rates from locomotive, marine, or other nonroad diesel engine sources over time. It is expected that because the typical lifespan of a locomotive engine is at least 40 years and PM regulations for these engines do not take effect until 2000, PM emission rates by model year from locomotives are not likely to have changed substantially since the introduction of the diesel engine into the railroad industry in the early 1950s.

Particulate matter regulations for nonroad diesel equipment are not as stringent as PM regulations for on-road diesel engines. Although PM emissions have declined for on-road trucks, it is estimated that PM_{10} emissions from nonroad diesel engines increased 17% between 1980 and 1998. DPM emissions from nonroad diesel engines are expected to continue to increase from current levels in the absence of new regulations. No information is available regarding changes in the chemical composition of nonroad engine emissions over time.

2.5.2. Physical and Chemical Composition of Diesel Exhaust

Complete and incomplete combustion of fuel in the diesel engine results in the formation of a complex mixture of hundreds of organic and inorganic compounds in the gas and particle phases. Among the gaseous components of DE, the aldehydes are particularly important because of their health effects and because they are an important fraction of the gaseous emissions. Formaldehyde makes up a majority of the aldehyde emissions (65%-80%) from diesel engines, with the next most abundant aldehydes being acetaldehyde and acrolein. Other gaseous components of DE that are notable for their health effects include benzene, 1,3-butadiene, PAH, and nitro-PAH. Dioxin compounds have also been detected in trace quantities in DE and

currently account for 1.2% of the national inventory. Dioxin compounds are known to accumulate in certain foods, such as beef, poultry, and dairy products. It is unknown whether deposition of DE emissions has an impact on food chains in local areas.

DPM contains EC, OC, and small amounts of sulfate, nitrate, metals, trace elements, water, and unidentified compounds. DPM is typically composed of more than 50% to approximately 75% EC depending on the age of the engine, deterioration, HD versus LD, fuel characteristics, and driving conditions. The OC portion of DPM originates from unburned fuel, engine lubrication oil, and low levels of partial combustion and pyrolysis products and typically ranges from approximately 19% to 43%, although the range can be broader depending on many of the same factors that influence the EC content of DPM. Polyaromatic hydrocarbons generally constitute less than 1% of the DPM mass. Metal compounds and other elements in the fuel and engine lubrication oil are exhausted as ash and typically make up 1%-5% of the DPM mass. Elements and metals detected in DE include barium, calcium, chlorine, chromium, copper, iron, lead, manganese, mercury, nickel, phosphorus, sodium, silicon, and zinc. The composition of DPM contrasts strongly with the typical chemical composition of ambient $DPM_{2.5}$ that is dominated by sulfate for aerosols measured in the eastern United States and by nitrate, ammonium, and OC in the western United States.

Approximately 1% to 20% of the mass of DPM in DE is in the ultrafine size range (nuclei-mode), with the majority of particles ranging in size from 0.005 to 0.05 microns and having a mean diameter of about 0.02 microns. These particles account for 50%-90% of the number of particles. These ultrafine particles are largely composed of sulfate and/or sulfate with condensed OC.

Evidence regarding an increase in the number of ultrafine particles from new HD engines is inconclusive. The dilution conditions used to measure the size distribution of DE have a large impact on the number of ultrafine particles quantified. To understand the size distribution of DPM to which people are exposed will require measurements under conditions that more closely resemble ambient conditions.

Approximately 80%-95% of the mass of particles in DE is in the size range from 0.05-1.0 microns, with a mean particle diameter of about 0.2 microns, and therefore in the fine PM size range. Diesel particles in the 0.05-1.0 micron range are aggregates of primary spherical particles consisting of an EC core, adsorbed organic compounds, sulfate, nitrate, and trace elements. These particles have a very large surface area per gram of mass, which makes them an excellent carrier for adsorbed inorganic and organic compounds and, due to their small size, they can effectively reach the lower portions of the respiratory tract. The EC core has a high specific surface area of approximately 30-90 m^2/g.

Because of the potential toxicological significance of the organic components associated with DPM, it is important to understand, to the extent possible, the historical changes in the amount and composition of the DPM-associated organic fraction. The organic component of DPM has typically been characterized by extraction with organic solvents, although other techniques such as thermogravimetric methods have also been used. Results from studies using similar extraction methods were compared to characterize historical changes in the SOF emission rates, the percentage of DPM comprised by SOF, and the composition of SOF. Data from both engine and chassis dynamometer tests suggest that SOF emission rates have decreased by model year from 1975 to 1995. When expressed as a percentage of total DPM, the contribution of SOF to total DPM demonstrates a wide range of variability that may be attributed to different test cycles, different engine types, and different deterioration rates among the vehicles tested. Currently, LD diesel engines emit DPM with a higher fraction of SOF than do HD engines.

Chassis dynamometer tests demonstrate an overall decrease in the mass percentage contribution of SOF to DPM, ranging from 10% to 60% in the 1980s and ~5% to 20% in the 1990s. In contrast, engine dynamometer tests demonstrate that typically 10%-50% of DPM mass is soluble organic matter for engines in model years 1980-1995. The higher SOF fraction of DPM from 1990s model year engine dynamometer tests is attributed primarily to the differences in the engine and chassis dynamometer driving cycles. The engine dynamometer testing includes high- speed and low-load or low-speed lugging test modes in the engine Federal Test Procedure that produce DPM with a high SOF fraction.

The chassis dynamometer data are considered to reflect real-world trends in emissions from heavy HD vehicles by model year because vehicles from different model years, with different mileage and different levels of deterioration, are represented. Thus, it is expected that the percentage of SOF from new (1990 or later) model year heavy HD diesel vehicles is lower than that from older vehicles. This expectation is supported by data demonstrating an overall increase in the fraction of EC in the carbonaceous component of DPM. The important observation from the engine test data is that some driving modes occurring in real-world applications even with new (post-1990) engines may produce DPM with a high SOF component (up to 50%).

PAH and nitro-PAH are present in DPM from both new and older engine exhaust. There is no information to suggest that the overall PAH composition profile for DPM has changed. There are too few data to speculate on the changes in emissions of total PAH, nitro-PAH, or PAH and nitro-PAH components such as BaP and 1-NP. The data suggest that differences in a vehicle's engine type and make, general engine condition, fuel composition, and test conditions can influence the emissions levels of PAH. Some studies suggest that fuel composition is the most important determinant of PAH emissions. There is limited evidence that gas-phase PAH

emission rates increase with higher fuel PAH content and that some particle-phase PAH emission rates increase with higher fuel PAH content. These data suggest that during the period from 1960 to 1986, when the aromatic content of fuel increased, PAH emissions may have increased until the aromatic content of diesel fuel was capped in 1993. The aromatic content of nonroad diesel fuel is not federally regulated and is typically greater than 30%. PAH emissions from nonroad equipment would also be expected to vary with the PAH content of the fuel.

Currently, information regarding emission rates, chemical composition, and relative contribution of DPM from high-emitting HD diesel vehicles is not available and may significantly change the understanding of DPM composition to which people are exposed. Some studies have reported a substantial number of smoking diesel trucks in the in-use fleet. Although the correlation between smoke and particulate concentration varies with the driving cycle and measurement method, the results of smoke opacity tests suggest that high-emitting HD diesel vehicles may be important contributors to ambient DE and DPM concentrations.

The chemical composition of DPM to which people are currently exposed is determined by a combination of older and newer technology on-road and nonroad engines. Consequently, the decrease in the SOF of DPM by model year does not directly translate into a proportional decrease in DPM-associated organic material to which people are currently exposed. In addition, the impact from high-emitting and/or smoking diesel engines is not quantified at this time. Because of these uncertainties, the changes in DPM composition over time cannot presently be quantified. The data clearly indicate that toxicologically significant organic components of DE (e.g., PAHs, PAH derivatives, nitro-PAHs) were present in DPM and DE in the 1970s and are still present in DPM and DE as a whole.

Although a significant fraction of ambient DPM (over 50% is possible) is also emitted by nonroad equipment, there are no data available to characterize changes in the chemical composition of DPM from nonroad equipment over time.

Some analysts project that diesel engines will increase substantially in the LD fleet in coming years. Although LD engines currently emit DPM with higher SOF than HD engines of the same model year, recently promulgated Tier 2 standards will require control measures in the 2004-2007 timeframe that will reduce PM emissions from these vehicles. These control measures provide some assurance that even if LD diesel use increases, DPM emitted from these vehicles will likely have a smaller SOF component than such engines currently emit.

2.5.3. Atmospheric Transformation of Diesel Exhaust

An understanding of the physical as well as chemical transformations of DE in the atmosphere is necessary to fully understand the impact of this complex chemical mixture on human health. In the past two decades, data acquired from laboratory and ambient experiments

have provided information regarding the atmospheric loss processes and transformation of DE, but knowledge concerning the products of these chemical transformations is still limited. A recent study has suggested that DPM exposed to ambient levels of ozone is sufficiently altered to increase the rat lung inflammatory effect compared with DPM not exposed to ozone.

Studies investigating the chemical and physical changes of DE emissions suggest that there is little or no hygroscopic growth of primary diesel particles. This observation suggests that the small size of DPM particles might be maintained upon inhalation, particularly near the emission source, allowing these particles to reach the lower portions of the respiratory tract. Increased solubility can increase the removal efficiency of secondary diesel particles compared with their precursor compounds. Secondary aerosols from DE may also exhibit different biological reactivities from the primary particles. For example, there is evidence for nitration of some PAH compounds resulting in the formation of nitroarenes that are often more mutagenic than their precursors.

2.5.4. Ambient Concentrations and Exposure to Diesel Exhaust

Because of changes in engine technology and DPM emissions over time, ambient concentrations reported from studies before 1990 are compared here to those reported after 1990. There are no studies in which direct comparisons can be made because of different analytical and modeling tools used to assess DPM ambient levels.

DPM concentrations reported from CMB and dispersion modeling studies in the 1980s suggest that in urban and suburban areas (Phoenix, AZ, and Southern California), annual average DPM concentrations ranged from 2 to 13 $\mu g/m^3$, with possible maximum daily values in Phoenix of 22 $\mu g/m^3$. In these studies, the average contribution of DPM in urban areas to total ambient PM ranged from 7% in Pasadena, CA, to 36% in Los Angeles.

In the 1990 timeframe, annual or seasonal average DPM concentrations reported in CMB studies and from EC measurements for urban and suburban areas range from 1.2 to 4.5 $\mu g/m^3$. The contribution of DPM to ambient PM at these sites averaged 10%-15% on a seasonal or annual basis, with contributions up to 38% on individual days (Brighton, CO). Dispersion modeling on individual days in Southern California in the 1990s predicts DPM concentrations ranging from 1.9 to 4.4 $\mu g/m^3$ (8%-12% of ambient PM). On individual days at a major bus stop in New York City, DPM concentrations were reported to reach 46.7 $\mu g/m^3$ and averaged 53% of ambient PM, highlighting the important influence of diesel bus traffic in an urban street canyon.

In nonurban and rural areas in the 1980s, DPM concentrations reported range from 1.4 to 5 $\mu g/m^3$ and on average comprised 5%-12% of the ambient aerosol. In the 1990s, nonurban air basins in California were reported to have DPM concentrations ranging from 0.2-2.6 $\mu g/m^3$.

Although estimates from emissions models suggest that DPM emissions from on-road sources decreased during the 1990s, the atmospheric data available do not provide a clear indication of trends in DPM concentrations but are likely to be more a reflection of the choice in sampling sites, source apportionment methods, and modeling techniques. In general, from the limited number of studies available it appears that DPM concentrations averaged over at least a season in the 1990s typically ranged from 1-4 $\mu g/m^3$. These data can be used in model-monitor comparisons and to provide an indication of long-term average exposures in some urban areas. Additional work is needed to assess ambient DPM and DE concentrations in several urban environments, to assess microenvironments, and to evaluate the relative impact of nonroad and on-road sources on concentrations.

A comprehensive exposure assessment cannot currently be conducted because of the lack of data. Information regarding DPM in occupational environments suggests that exposure ranges up to approximately 1,280 $\mu g/m^3$ for miners, with lower exposure measured for railroad workers (39-191 $\mu g/m^3$), firefighters (4-748 $\mu g/m^3$), public transit personnel who work with diesel equipment (7-98 $\mu g/m^3$), mechanics and dockworkers (5-65 $\mu g/m^3$), truck drivers (2-7 $\mu g/m^3$), and bus drivers (1-3 $\mu g/m^3$). Work area concentrations at fixed sites are often higher than measured exposures, especially for mining operations or other enclosed spaces. For several occupations involving DE exposure, an increased risk of lung cancer has been reported by epidemiologic studies (discussed in Chapter 7). An estimate of the 70-year lifetime environmental exposure equivalent to these occupational exposures provides one means of comparing the potential overlap between occupational exposures and exposures modeled for the general public. The estimated 70-year lifetime exposures equivalent to those for the occupational groups discussed above range from 0.4-2 $\mu g/m^3$ on the low end to 2-269 $\mu g/m^3$ on the high end.

The EPA has performed a national-scale exposure assessment for DPM from on-road sources. Current national exposure modeling using the HAPEM-MS3 model suggests that in 1996, annual average DPM exposure from on-road DE sources in urban areas was 0.8 $\mu g/m^3$, whereas in rural areas, exposures were 0.4 $\mu g/m^3$. Among 10 urban areas in which DPM exposures were modeled, 1996 annual average exposure from on-road DE sources ranged from 0.6 $\mu g/m^3$ to 1.2 $\mu g/m^3$. Outdoor workers and children who spent a large amount of time outdoors were estimated to have elevated DPM exposures in 1990, ranging up to 4.0 $\mu g/m^3$ from on-road sources only. Based on the national inventory, nonroad emission sources could contribute at least twofold more DPM than that emitted by on-road sources. Results of the draft National-Scale Assessment for 1996 indicate that national average exposure to DPM, including nonroad sources, is 1.4 $\mu g/m^3$, with 0.9 $\mu g/m^3$ of that average attributed to emissions from nonroad sources.

Low-end exposures for many of the occupational groups overlap 1990 and 1996 exposures from on-road sources modeled for the general population (0.8 $\mu g/m^3$) and for the more highly exposed groups. This potential overlap, or small difference between occupational and ambient exposures, presents a concern that health effects observed in occupational groups may also be evidenced in the general population. The potential magnitude of this risk is discussed in Chapter 8.

In different exposure environments, the types of diesel vehicles, their mode of operation, maintenance, atmospheric transformation, and many additional factors influence the chemical nature and quantity of DPM to which people are exposed. The potential health consequences of both short- and long-term exposures to DE are discussed in the following chapters of this document.

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3. DOSIMETRY OF DIESEL PARTICULATE MATTER

3.1. INTRODUCTION

Animals and humans receive different internal doses when breathing the same external concentrations of airborne materials such as diesel particulate matter (DPM) (Brain and Mensah, 1983; Schlesinger, 1985). The dose received in different species differs from the aspects of the total amount deposited within the respiratory tract, the relative distribution of the dose to specific regions in the respiratory tract, and the residence time of these materials within the respiratory tract, i.e., clearance. Using an external concentration breathed by laboratory animals as a basis for any guidance for human exposure to DPM would then be an inadequate approximation of the total and regional dose that humans may receive.

The reason for the existence of this chapter and for consideration about interspecies dosimetry is the lack of human health effect data on DPM and the concomitant need to be able to evaluate existing animal data from the aspect of an equivalent human dose. The objective of this chapter is to evaluate and address this issue of interspecies dosimetric differences through:

- A general overview of what is known about how particles like DPM are deposited, transported to, and cleared from the respiratory tract. Information on both laboratory animals (mainly rodents) and humans will be considered and interspecies similarities and differences highlighted.
- An overview of what is known about the bioavailability of the organic compounds adsorbed onto DPM from information in humans, animals, and in vitro studies, and from model predictions.
- An evaluation of the suitability of available dosimetric models and procedures for DPM to estimate interspecies extrapolations whereby an exposure scenario, conditions, and outcome in laboratory animals are adjusted to an equivalent outcome in humans via calculation of an internal dose.

The focus in this chapter will be on the particulate fraction of diesel emissions, i.e, DPM. Although diesel engine exhaust consists of a complex mixture of typical combustion gases, vapors, low-molecular-weight hydrocarbons, and particles, it is the particle phase that is considered to be of major health concern. The major constituents of diesel engine exhaust (DE) and their atmospheric reaction products are described in Chapter 2.

As will be deduced in Chapter 5, pulmonary toxicity and carcinogenicity are the major focal points of diesel toxicity and of DPM deposition. Therefore, dosimetric considerations are limited to the lung although DPM deposition would occur throughout the respiratory tract, from

the nares to the alveoli. Aspects of respiratory tract dosimetry to be considered in this chapter include the characteristics of DPM, deposition of DPM throughout the respiratory tract, the conducting airways and alveolar regions, normal DPM clearance mechanisms and rates of clearance in both these regions, clearance rates during lung overload (in rats), elution of organics from DPM, transport of DPM to extra-alveolar sites, and the interrelationships of these factors.

The overall goal in this chapter follows from the objective—to judge the feasibility and suitability of procedures allowing for derivation of an internal dose estimate of DPM for humans, i.e., of a human equivalent concentration to exposure concentrations and conditions used in animal studies. This goal is of significance especially in the quantitative dose-response analysis of DPM effects in laboratory animals proposed in Chapter 6.

3.2. CHARACTERISTICS OF INHALED DIESEL PARTICULATE MATTER

The formation, transport, and characteristics of DPM are among the subjects considered in detail in Chapter 2. DPM consists of aggregates of spherical carbonaceous particles (typically about 0.2 μm mass median aerodynamic diameter [MMAD] or, more appropriately, mass median thermodynamic diameter [MMTD]) to which significant amounts of higher-molecular-weight organic compounds are adsorbed. DPM has an extremely large surface area that allows for the adsorption of organic compounds (see Chapter 2, Section 2.2.2). The organic carbon portion of DPM can range from at least 19% to 43% from highway diesel engines; no data are available to characterize the organic content of DPM from nonroad engines. The toxicologically relevant organic chemicals include high-molecular-weight hydrocarbons such as the polycyclic aromatic hydrocarbons (PAHs) and their derivatives (Chapter 2, Section 2.2.8).

3.3. REGIONAL DEPOSITION OF INHALED DIESEL PARTICULATE MATTER

This section discusses the major factors controlling the disposition of inhaled particles. Note that disposition is defined as encompassing the processes of deposition, absorption, distribution, metabolism, and elimination. The regional deposition of particulate matter in the respiratory tract is dependent on the interaction of a number of factors, including respiratory tract anatomy (airway dimensions and branching configurations), ventilatory characteristics (breathing mode and rate, ventilatory volumes and capacities), physical processes (diffusion, sedimentation, impaction, and interception), and the physicochemical characteristics (particle size, shape, density, and electrostatic attraction) of the inhaled particles. Regional deposition of particulate material is usually expressed as deposition fraction of the total particles or mass inhaled and may be represented by the ratio of the particles or mass deposited in a specific region to the number or mass of particles inspired. The factors affecting deposition in these various regions and their importance in understanding the fate of inhaled DPM are discussed in the following sections.

It is beyond the scope of this document to present a comprehensive account of the complexities of respiratory mechanics, physiology, and toxicology, and only a brief review will be presented here. The reader is referred to publications that provide a more in-depth treatment of these topics (Weibel, 1963; Brain and Mensah, 1983; Raabe et al., 1988; Stöber et al., 1993; U.S. EPA, 1996).

The respiratory tract in both humans and experimental mammals can be divided into three general regions on the basis of structure, size, and function: the extrathoracic (ET), the tracheobronchial (TB), and the alveolar (A). In humans, inhalation can occur through the nose or mouth or both (oronasal breathing). Animal models used in respiratory toxicology studies, particularly the rat, however, are obligate nose breathers.

3.3.1. Deposition Mechanisms

This section provides an overview of the basic mechanisms by which inhaled particles deposit within the respiratory tract. Details concerning the aerosol physics that explain both how and why particle deposition occurs as well as data on total human respiratory tract deposition are presented in detail in the earlier PM Criteria Document (U.S. EPA, 1996) and will only be briefly summarized here. For more extensive discussions of deposition processes, refer to reviews by Morrow (1966), Raabe (1982), U.S. EPA (1982), Phalen and Oldham (1983), Lippmann and Schlesinger (1984), Raabe et al. (1988), and Stöber et al. (1993).

As pictorially represented in Figure 3-1, particles may deposit by five major mechanisms (inertial impaction, gravitational settling, Brownian diffusion, electrostatic attraction, and interception). The relative contribution of each deposition mechanism to the fraction of inhaled particles deposited varies for each region of the respiratory tract.

It is important to appreciate that these processes are not necessarily independent but may, in some instances, interact with one another such that total deposition in the respiratory tract may be less than the calculated probabilities for deposition by the individual processes (Raabe, 1982). Depending on the particle size and mass, varying degrees of deposition may occur in the ET (or nasopharyngeal), TB, and A regions of the respiratory tract.

Upon inhalation of particulate matter such as that found in DE, particle deposition will occur throughout the respiratory tract. Because of high airflow velocities and abrupt directional changes in the ET and TB regions, inertial impaction is a primary deposition mechanism, especially for particles ≥ 2.5 µm d_{ae} (aerodynamic equivalent diameter). Although inertial impaction is a prominent process for deposition of larger particles in the tracheobronchial region, it is of considerably less significance as a determinant of regional deposition patterns for

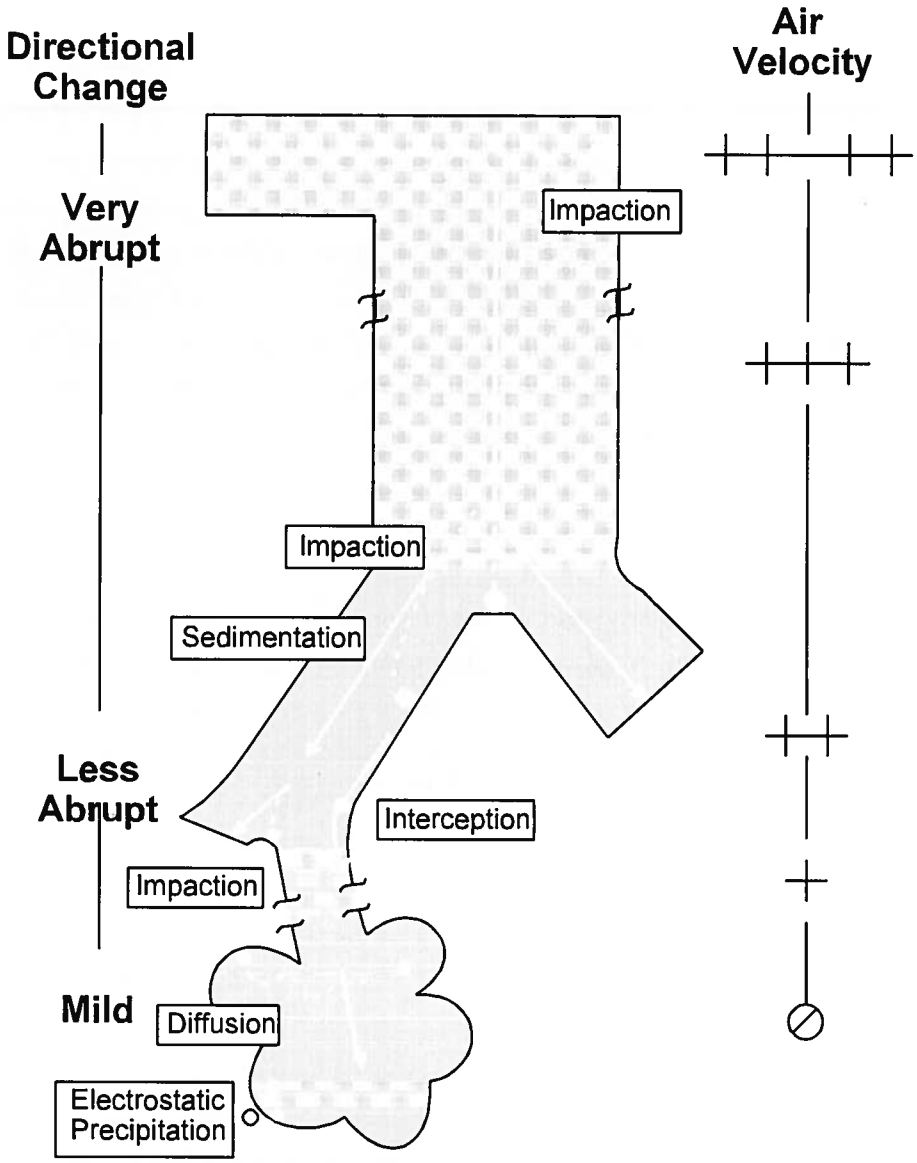

Figure 3-1. Schematic representation of major mechanisms, including diffusion, involved in particle deposition. Airflow is signified by the arrows and particle trajectories by the dashed line.

DPM, which have a $d_{ae} \leq 0.2$ μm and may be considered a rather polydisperse distribution with sigma g values of 2.4 and greater.

All aerosol particles are continuously influenced by gravity, but particles with a $d_{ae} > 0.5$ μm are affected to the greatest extent. A spherical compact particle will acquire a terminal settling velocity when a balance is achieved between the acceleration of gravity acting on the particle and the viscous resistance of the air; it is this velocity that brings the particle into contact with airway surfaces. Both sedimentation and inertial impaction cause the deposition of many particles within the same size range. These deposition processes act together in the ET and TB regions, with inertial impaction dominating in the upper airways and sedimentation becoming increasingly dominant in the lower conducting airways, especially for the largest particles that can penetrate into the smaller bronchial airways.

As particle diameters become <1 μm, the particles are increasingly subjected to diffusive deposition because of random bombardment by air molecules, which results in contact with airway surfaces. A d_{ae} of 0.5 μm is often considered a boundary between diffusion and aerodynamic (sedimentation and impaction) mechanisms of deposition. Thus, instead of having a d_{ae}, diffusive particles of different shapes can be related to the diffusivity of a thermodynamic equivalent size based on spherical particles (Heyder et al., 1986). Diffusive deposition of particles is favored in the A region of the respiratory tract as particles of this size are likely to penetrate past the ET and TB regions.

Electrostatic precipitation is deposition related to particle charge. The electrical charge on some particles may result in an enhanced deposition over what would be expected from size alone. This is due to image charges induced on the surface of the airway by these particles, or to space-charge effects whereby repulsion of particles containing like charges results in increased migration toward the airway wall. The effect of charge on deposition is inversely proportional to particle size and airflow rate. A recent study employing hollow airway casts of the human tracheobronchial tree that assessed deposition of ultrafine (0.02 μm) and fine (0.125 μm) particles found that deposition of singly charged particles was 5-6 times that of particles having no charge, and 2-3 times that of particles at Boltzmann equilibrium (Cohen et al., 1998). This suggests that within the TB region of humans, electrostatic precipitation may be a significant deposition mechanism for ultrafine and some fine particles, the latter of which are inclusive of DPM. Thus, although electrostatic precipitation is generally a minor contributor to overall particle deposition, it may be important for DPM.

Interception is deposition by physical contact with airway surfaces and is most important for fiber deposition (U.S. EPA, 1996).

Figure 3-2 shows the regional (ET, TB, A) deposition in the human respiratory tract as influenced by particle size. Keeping in mind that DPM is a polydisperse distribution with 0.2 μm

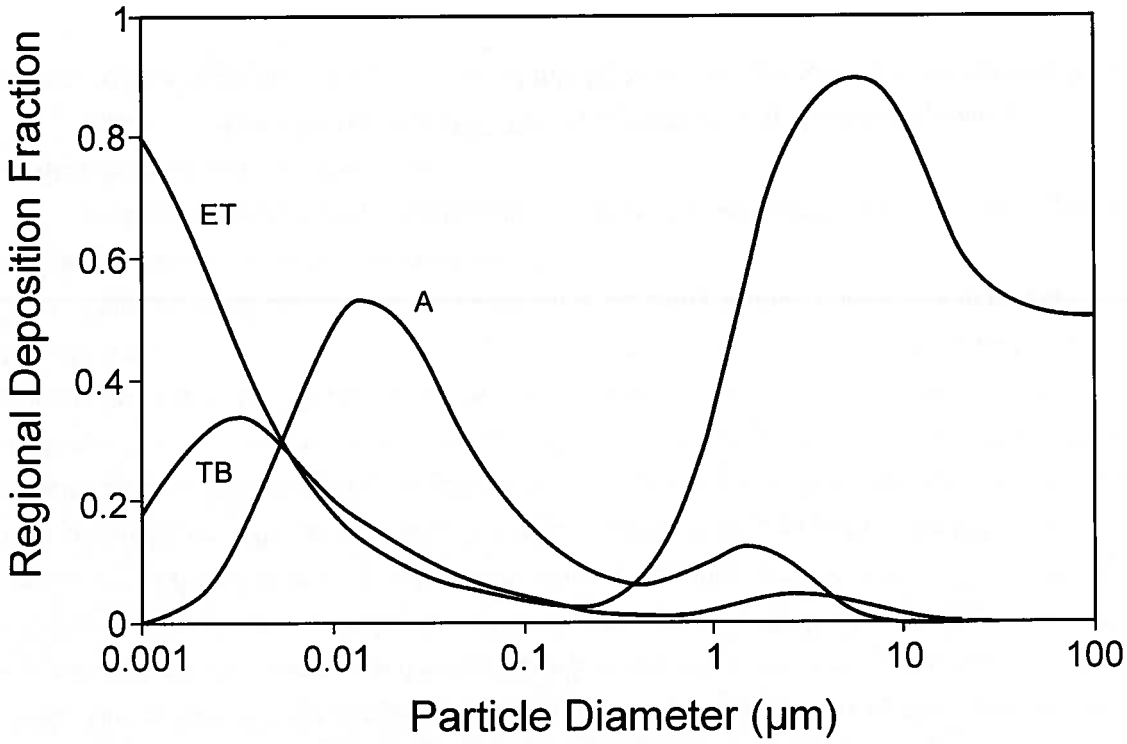

Figure 3-2. Generalized regional deposition fractions of various sized particles in the human respiratory tract. (Adapted from the International Commission on Radiological Protection (ICRP) Publication 66 (1994) model. For unit density, spherical particles inhaled through the nose by an adult male with a tidal volume of 1250 mL, respiratory frequency of 20 min^{-1}, and functional residual capacity (FRC) of 3300 mL.) ET, extrathoracic; TB, tracheobronchial; A, alveolar.

being only the median diameter, it can be seen that principal fraction particles sized from < 0.2 down to around 0.002 μm would, as predicted based on their size and the expected mechanism of diffusion, deposit in the alveolar region. Particles below this size range (and above around 4 μm) tend to deposit in the ET region. Specific modeling results for deposition of DPM particles inclusive of their distribution (i.e., σ_g) are presented in Section 3.6.

3.3.1.1. *Biological Factors Modifying Deposition*

The available experimental deposition data in humans are commonly derived using healthy adult Caucasian males. Various factors can act to alter deposition patterns from those obtained in this group. The effects of different biological factors, including gender, age, and respiratory tract disease, on particle deposition have been reviewed previously (U.S. EPA, 1996, Section 10.4.1.6). In general, there appears to be an inverse relationship between airway resistance and total deposition.

Differences in patterns of deposition between humans and animals have been summarized (U.S. EPA, 1996; Schlesinger, 1985) and show clearly that when exposed to the same aerosol or gas, humans and animals receive doses that may differ in both total and regional (i.e., ET, TB, or A) deposition from a number of variables including particle size, especially for larger sized particles, i.e. $d_{ae} \geq 1$ μm. Such interspecies differences are important because the adverse toxic effect is likely more related to the quantitative pattern of deposition within the respiratory tract than to the exposure concentration; this pattern determines not only the initial respiratory tract tissue dose but also the specific pathways by which the inhaled material is cleared and redistributed (Schlesinger, 1985). Such differences in initial deposition must be considered when relating biological responses obtained in laboratory animal studies to effects in humans.

The deposition patterns of inhaled diesel particles in the respiratory tract of humans and mammalian species has been reviewed (Health Effects Institute, 1995). Schlesinger (1985) showed that physiological differences in the breathing mode for humans (nasal or oronasal breathers) and laboratory rats (obligatory nose breathers), combined with different airway geometries, resulted in significant differences in lower respiratory tract deposition patterns for larger sized particles (>1 μm d_{ae}) in that a much lower fraction of inhaled larger particles is deposited in the alveolar region of the rat compared with humans. However, alveolar deposition of the much smaller DPM (around 0.2 μm d_{ae}) was not affected as much by the differences among species, as was demonstrated in model calculations by Xu and Yu (1987). These investigators modeled the deposition efficiency of inhaled DPM in rats, hamsters, and humans on the basis of calculations of the models of Schum and Yeh (1980) and Weibel (1963). These simulations (Figure 3-3) indicate relative deposition patterns in the lower respiratory tract (trachea = generation 1; alveoli = generation 23) and are similar among hamsters, rats, and humans. Variations in alveolar deposition of DPM over one breathing cycle in these different species were predicted to be within 30% of one another (Xu and Yu, 1987). Xu and Yu (1987) note that this similarity is concordant with the premise that deposition of the submicron diesel particles is dominated by diffusion rather than sedimentation or impaction. Although these data assumed nose-breathing by humans, the results would not be very different for mouth-breathing because of the low filtering capacity of the nose for particles in the 0.1 to 0.5 μm range (see Figure 3-2).

The preceding discussion addresses deposition patterns and deposition efficiencies of DPM in the respiratory tract of various species including humans. The alveolar region was focused upon primarily because, as shown in Chapter 5, this region is where adverse effects from long-term DPM exposure are typically observed. For dosimetric calculations and modeling, however, it would be of much greater importance to consider the actual deposited dose. Table 3-1 presents the analysis of Xu and Yu (1987) on prediction of the deposited doses of DPM

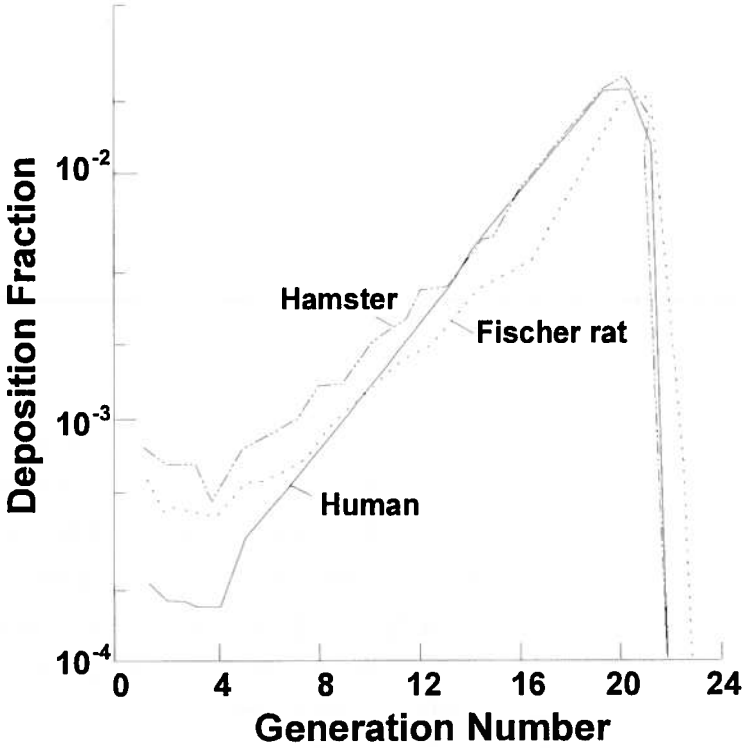

Figure 3-3. Modeled deposition distribution patterns of inhaled DE particles in the airways of different species. Generation 1-18 are TB; >18 are A.

inhaled in 1 min in the lungs of humans, rats, and hamsters on three different bases: the total lung volume (M), the surface area of all lung airways (M_1), or the surface area of the epithelium of the alveolar region only (M_2). According to this analysis, the deposited dose is lower in humans than in the two rodent species regardless of how the deposited dose is expressed. These results are most certainly due predominately to the greater respiratory exchange rate in rodents and smaller size of the rodent lung. Table 3-1 also indicates that the differences (between humans to animals) are less on a surface area basis (≈3-fold) than on a lung volume basis (≈14-fold). This is due to larger alveolar diameters and concomitant lower surface area per unit of lung volume in humans. Such differences in the deposited dose in relevant target areas such as the alveolar region are important and have to be considered when extrapolating the results from DPM exposure studies in animals to humans. As will be discussed elsewhere in this document, procedures for dose extrapolation from animals to humans includes considering the process of clearance, with clearance measurements being in relation to surface area rather than to volume. Thus predicted doses of particulates would be based on surface areas, such as M_1 andM_2 in Table 3-1, rather than on volume, M.

Table 3-1. Predicted doses of inhaled DPM per minute based on total lung volume (M), total airway surface area (M_1), or surface area in alveolar region (M_2)

Species	M (10^{-3} μg/min/cm^3)	M_1 (10^{-6} μg/min/cm^2)	M_2 (10^{-6} μg/min/cm^2)
Hamster	3.548	3.088	2.382
Fischer rat	3.434	3.463	2.608
Human	0.249	1.237	0.775

$$M = \frac{\text{mass DPM deposited in lung per minute}}{\text{total lung volume}}$$

$$M_1 = \frac{\text{mass DPM deposited in lung per minute}}{\text{total airway surface area}}$$

$$M_2 = \frac{\text{mass DPM deposited on the unciliated airways per minute}}{\text{surface area of the unciliated airways}}$$

Based on the following conditions: (1) mass median aerodynamic diameter (MMAD) = 0.2 μm; geometric standard deviation (σ_g) = 1.9; packing density (ϕ) = 0.3; and particle mass density (ρ) = 1.5 g/cm^2; (2) particle concentration = 1 mg/m^3; and (3) nose-breathing. For humans, total lung volume = 3200 cm^2, total airway surface area = 633,000 cm^2, surface area of the unciliated airways = 627,000 cm^2. Corresponding values for Fisher rats are 418cm^2, 412cm^2, and 409cm^2; for hamsters, 282cm^2, 262cm^2, and 261cm^2. Tidal volumes (in cm^2) and respiratory frequency (per min) used for humans were 500 and 14; for Fisher rats, 1.6 and 98; for hamsters, 67 and 1.0.

Source: Xu and Yu, 1987.

Particle deposition will initiate particle redistribution processes (e.g., clearance mechanisms, phagocytosis) that transfer the particles to various subcompartments, including the alveolar macrophage pool, pulmonary interstitium, and lymph nodes. Over time, therefore, only small amounts of the original particle intake would be associated with the alveolar surface areas.

3.3.2. Particle Clearance and Translocation Mechanisms

This section provides an overview of the mechanisms and pathways by which particles are cleared from the respiratory tract. The mechanisms of particle clearance as well as clearance routes from the various regions of the respiratory tract have been considered in the PM Criteria Document (U.S. EPA, 1996) and reviewed by Schlesinger et al. (1997).

Particles that deposit upon airway surfaces may be cleared from the respiratory tract completely, or be translocated to other sites within this system, by various regionally distinct processes. These clearance mechanisms can be categorized as either absorptive (i.e., dissolution) or nonabsorptive (i.e., transport of intact particles) and may occur simultaneously or with

temporal variations. Particle solubility in terms of clearance refers to solubility within the respiratory tract fluids and cells. Thus, a poorly soluble particle is one whose rate of clearance by dissolution is insignificant compared to its rate of clearance as an intact particle (as is the case with DPM). The same clearance mechanisms act on different particles to different degrees, with their ultimate fate being a function of deposition site, physicochemical properties (including any toxicity), and sometimes deposited mass or number concentration. However, the duration of clearance for poorly soluble particles such as DPM as it exists between species, months for rats vs. years or even decades for humans, can make dissolution of DPM a significant contributor for humans (Kreyling, 1992).

Figure 3-4 outlines many of the known and suspected clearance pathways for poorly soluble particles, such as DPM, that deposit in the alveolar region. Included are the representations of the translocation pathways from the alveolar epithelium through the insterstitium and on through the lymph nodes; this latter path will be referred to frequently later in this chapter.

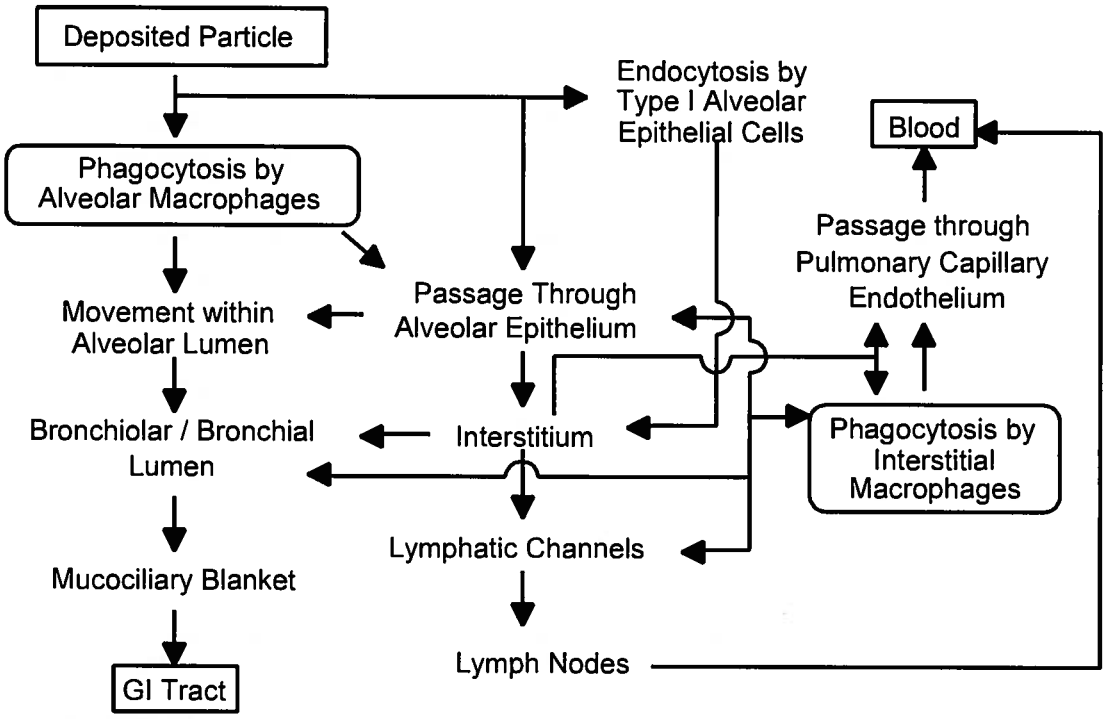

Figure 3-4. Diagram of known and suspected clearance pathways for poorly soluble particles depositing in the alveolar region. (Modified from Schlesinger, 1995).

3.3.2.1. *Extrathoracic Region*

The clearance of poorly soluble particles deposited in the nasal passages occurs via mucociliary transport, and the general flow of mucus is backwards, i.e., towards the nasopharynx. Mucus flow in the most anterior portion of the nasal passages is forward, clearing deposited particles to the vestibular region where removal is by sneezing, wiping, or blowing.

Soluble material deposited on the nasal epithelium is accessible to underlying cells via diffusion through the mucus. Dissolved substances may be subsequently translocated into the bloodstream. The nasal passages have a rich vasculature, and uptake into the blood from this region may occur rapidly.

Clearance of poorly soluble particles deposited in the oral passages is by expectoration or by swallowing into the gastrointestinal tract.

3.3.2.2. *Tracheobronchial Region*

The dynamic relationship between deposition and clearance is responsible for determining lung burden at any point in time. Clearance of poorly soluble particles from the TB region is mediated primarily by mucociliary transport, a more rapid process than those operating in alveolar regions. Mucociliary transport (often referred to as the mucociliary escalator) is accomplished by the rhythmic beating of cilia that line the respiratory tract from the trachea through the terminal bronchioles. This movement propels the mucous layer containing deposited particles (or particles within alveolar macrophages [AMs]) toward the larynx. Clearance rate by this system is determined primarily by the flow velocity of the mucus, which is greater in the proximal airways and decreases distally. These rates also exhibit interspecies and individual variability. Considerable species-dependent variability in tracheobronchial clearance has been reported, with dogs generally having faster clearance rates than guinea pigs, rats, or rabbits (Felicetti et al., 1981). The half-time ($t_{1/2}$) values for tracheobronchial clearance of relatively insoluble particles are usually on the order of hours, as compared to alveolar clearance, which is on the order of hundreds of days in humans and dogs. The clearance of particulate matter from the tracheobronchial region is generally recognized as being biphasic or multiphasic (Raabe, 1982). Some studies have shown that particles are cleared from large, intermediate, and small airways with $t_{1/2}$ of 0.5, 2.5, and 5 h, respectively. However, reports have indicated that clearance from airways is biphasic and that the long-term component for humans may take much longer for a significant fraction of particles deposited in this region, and may not be complete within 24 h as generally believed (Stahlhofen et al., 1990; ICRP, 1994).

Although most of the particulate matter will be cleared from the tracheobronchial region towards the larynx and ultimately swallowed, the contribution of this fraction relative to carcinogenic potential is unclear. With the exception of conditions of impaired bronchial

clearance, the desorption $t_{1/2}$ for particle-associated organics is generally longer than the tracheobronchial clearance times, thereby making uncertain the importance of this fraction relative to toxicity in the respiratory tract (Pepelko, 1987). However, Gerde et al. (1991a) showed that for low-dose exposures, particle-associated PAHs were released rapidly at the site of deposition indicating that they would be available for involvement in postulated carcinogenic processes. The relationship between the early clearance of poorly soluble particles of 4 µm aerodynamic diameter from the tracheobronchial regions and their longer-term clearance from the alveolar region is illustrated in Figure 3-5, clearly showing the rapid depuration from the TB region compared with the A region. This relationship, although demonstrated with 4 µm particles, is probably relevant and applicable to DPM-sized particles (i.e., 0.2 µm) as clearance mechanisms are believed not to be particularly particle-sized dependent (Morrow et al., 1967a,b; Snipes et al., 1983).

Cuddihy and Yeh (1986) reviewed respiratory tract clearance of particles inhaled by humans. Depending on the type of particle (ferric oxide, Teflon discs, or albumin microspheres), the technique employed, and the anatomic region (midtrachea, trachea, or main bronchi), particle

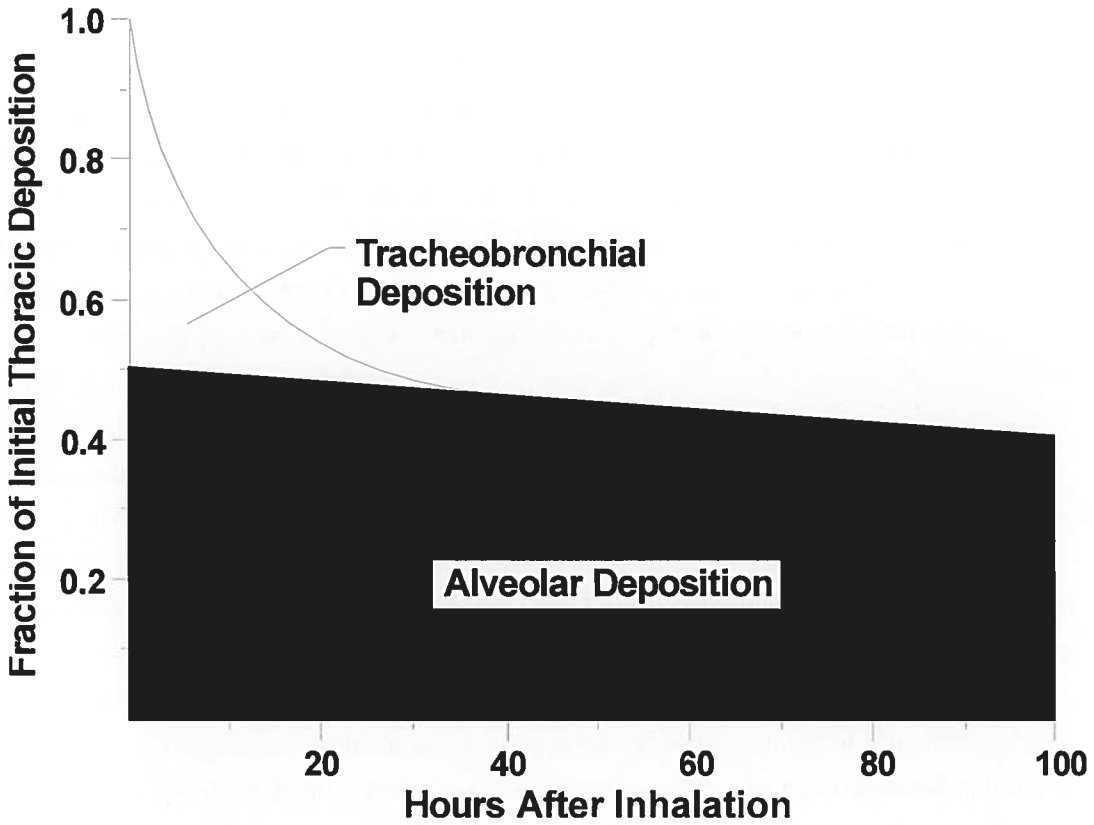

Figure 3-5. Modeled clearance of poorly soluble 4-µm particles deposited in tracheobronchial and alveolar regions in humans.

velocity (moved by mucociliary transport) ranged from 2.4 to 21.5 mm/min. The highest velocities were recorded for midtracheal transport, and the lowest were for main bronchi.

Cuddihy and Yeh (1986) described salient points to be considered when estimating particle clearance velocities from tracheobronchial regions: these include respiratory tract airway dimensions, calculated inhaled particle deposition fractions for individual airways, and thoracic (A + TB) clearance measurements. Predicted clearance velocities for the trachea and main bronchi were found to be similar to those experimentally determined for inhaled radiolabeled particles, but not those for intratracheally instilled particles. The velocities observed for inhalation studies were generally lower than those of instillation studies. Figure 3-6 illustrates a comparison of the short-term clearance of inhaled particles by human subjects and the model predictions for this clearance. However, tracheobronchial clearance via the mucociliary escalator is of limited importance for long-term clearance.

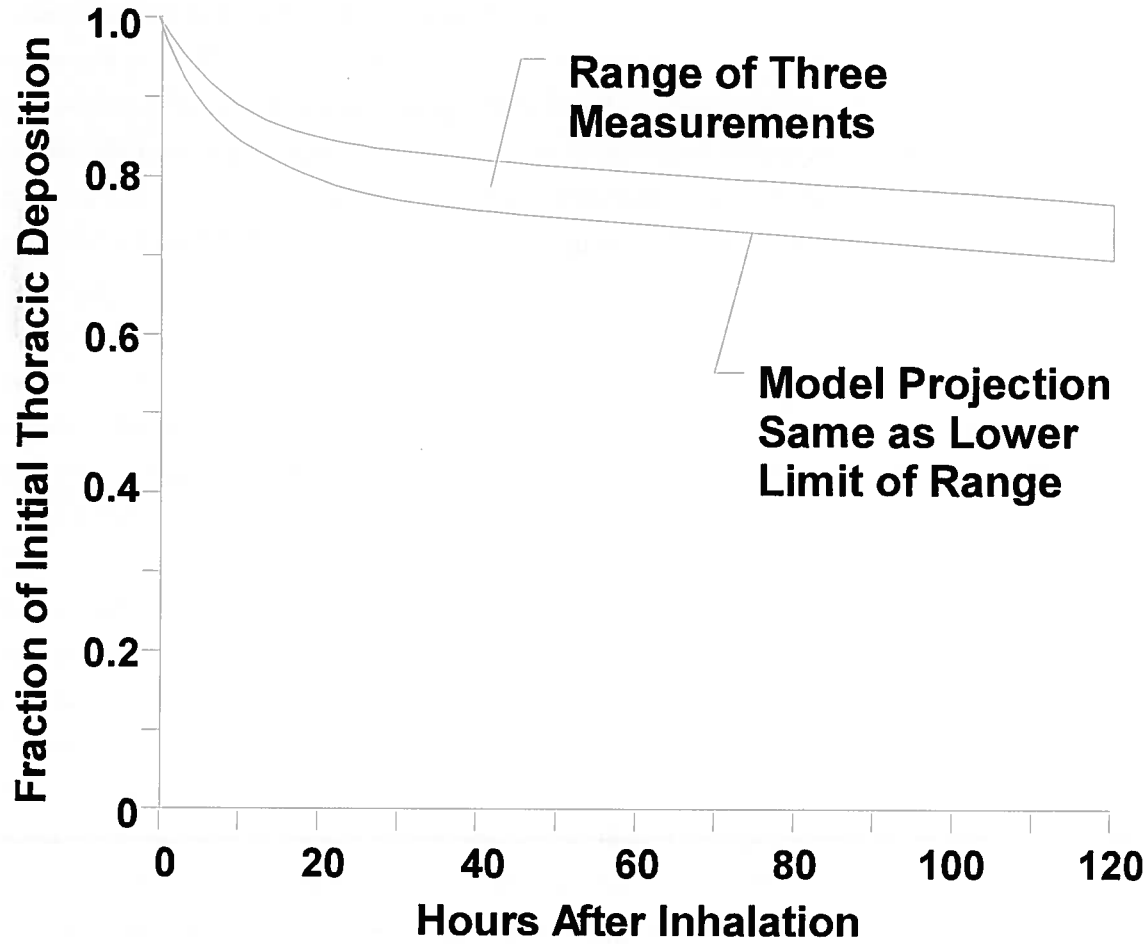

Figure 3-6. Short-term thoracic clearance of inhaled particles as determined by model prediction and experimental measurement.

Source: Cuddihy and Yeh, 1986 (from Stahlhofen et al., 1980).

Exposure of F344 rats to whole exhaust containing DPM at concentrations of 0.35, 3.5, or 7.1 mg/m^3 for up to 24 mo did not significantly alter tracheal mucociliary clearance as assessed by clearance of ^{99m}Tc-macroaggregated albumin instilled into the trachea (Wolff et al., 1987). The authors stated that measuring retention would yield estimates of clearance efficiency comparable to measuring the velocity for transport of the markers in the trachea. The results of this study were in agreement with similar findings of unaltered tracheal mucociliary clearance in rats exposed to DPM (0.21, 1.0, or 4.4 mg/m^3) for up to 4 mo (Wolff and Gray, 1980). However, the 1980 study by Wolff and Gray, as well as an earlier study by Battigelli et al. (1966), showed that acute exposure to high concentrations of DE soot (1.0 and 4.4 mg/m^3 in the study by Wolff and Gray [1980] and 8 to 17 mg/m^3 in the study by Battigelli et al. [1966]) produced transient reductions in tracheal mucociliary clearance. Battigelli et al. (1966) also noted that the compromised tracheal clearance was not observed following cessation of exhaust exposure.

That tracheal clearance does not appear to be significantly impaired or is impaired only transiently following exposure to high concentrations of DPM is consistent with the absence of pathological effects in the tracheobronchial region of the respiratory tract in experimental animals exposed to DPM. The apparent retention of a fraction of the deposited dose in the airways could be cause for some concern regarding possible effects in this region, especially in light of the results from simulation studies by Gerde et al. (1991b) suggesting that release of PAHs from particles may occur within minutes and therefore at the site of initial deposition. However, the absence of effects in the TB areas in long-term DPM studies and experimental evidence that particle-associated PAHs are released at the site of particle deposition together suggest that these PAHs and other organics may be of lesser importance in tumorigenic responses of rats than originally suspected. On the other hand, the data of Nikula et al. (1997a,b) could be interpreted to suggest that a larger fraction of particles are translocated to the interstitium of the respiratory tract in primates that are heavily exposed (and therefore presumably in humans) than in rats that are heavily exposed, including the interstitium of the respiratory bronchioles, an anatomical site absent in rats (Section 3.6). Moreover, eluted PAHs in the TB region are retained longer than those in the alveoli (Gerde et al., 1999), allowing time for activation. Also, the results of Kreyling (1992) indicate that appreciable dissolution of even poorly soluble particles may occur as a consequence of long absolute duration of clearance, such as years or decades, in humans. Thus PAHs may have a role in human response to DE that cannot be evaluated with the rat model.

Also, impairment of mucociliary clearance function as a result of exposure to occupational or environmental respiratory tract toxicants or to cigarette smoke may significantly enhance the retention of particles in the TB region. For example, Vastag et al. (1986) demonstrated that not only smokers with clinical symptoms of bronchitis but also symptom-free

smokers have significantly reduced mucociliary clearance rates. Although impaired tracheobronchial clearance could conceivably have an impact on the effects of deposited DPM in the conducting airways, it does not appear to be relevant to the epigenetic mechanism likely responsible for DE-induced rat pulmonary tumors as the tumors observed in these studies were all or nearly all of A vice TB origin.

Poorly soluble particles such as DPM that are deposited within the TB region are cleared predominantly by mucociliary transport towards the oropharynx, followed by swallowing. Poorly soluble particles may also be cleared by traversing the epithelium by endocytotic processes, and enter the peribronchial region. Clearance may occur following phagocytosis by airway macrophages, located on or beneath the mucous lining throughout the bronchial tree, or via macrophages that enter the airway lumen from the bronchial or bronchiolar mucosa (Robertson, 1980).

3.3.2.3. *A Region*

A number of investigators have reported on the alveolar clearance kinetics of human subjects. Bohning et al. (1980) examined alveolar clearance in eight humans who had inhaled <0.4 mg of ^{85}Sr-labeled polystyrene particles (3.6 ± 1.6 μm diam.). A double-exponential model best described the clearance of the particles and provided $t_{1/2}$ values of 29 ± 19 days and 298 ± 114 days for short-term and long-term phases, respectively. It was noted that of the particles deposited in the alveolar region, 75% ± 13% were cleared via the long-term phase. Alveolar retention $t_{1/2}$ values of 330 and 420 days were reported for humans who had inhaled aluminosilicate particles of MMAD 1.9 and 6.1 μm (Bailey et al., 1982). In a comprehensive study Bailey et al. (1985) followed the long-term retention of inhaled particles in a human respiratory tract. The retention of 1 and 4 μm fused aluminosilicate particles labeled with strontium-85 and yttrium-88, respectively, was followed in male volunteers for about 533 days. Approximately 7% of the initial lung deposit of 1 μm particles and 40% of the 4 μm particles were associated with a rapid clearance phase corresponding to the calculated tracheobronchial deposits. Retention of the remaining material followed a two-component exponential function, with phases having half-times of the order of tens of days and several hundred days, respectively.

Quantitative data on clearance rates in humans having large lung burdens of particulate matter are lacking. Bohning et al. (1982) and Cohen et al. (1979), however, did provide evidence for slower clearance in smokers, and Freedman and Robinson (1988) reported slower clearance rates in coal miners who had mild pneumoconiosis with presumably high lung burdens of coal dust. Although information on particle burden and particle overload relationships in humans is much more limited than in experimental animal models, inhibition of clearance does seem to occur. Stöber et al. (1967) estimated a clearance $t_{1/2}$ of 4.9 years in coal miners with nil or slight

silicosis, based on postmortem lung burdens. The lung burdens and estimated exposure histories ranged from 2 to 50 mg/g of lung or more, well above the value at which clearance impairment is observed in the rat. Furthermore, impaired clearance resulting from smoking or exposure to other respiratory toxicants may increase the possibility of an enhanced particle accumulation effect resulting from exposure to other particle sources such as DPM.

Normal alveolar clearance rates in laboratory animals exposed to DPM have been reported by a number of investigators (Table 3-2). Because the rat is, historically, the species for which experimentally induced lung cancer data are available and for which most clearance data exist, it is the species most often used for assessing human risk, and reviews of alveolar clearance studies have been generally limited to this species.

Chan et al. (1981) subjected 24 male F344 rats to nose-only inhalation of diluted DE generated from a diesel engine (6 mg/m^3) labeled with ^{131}Ba or ^{14}C for 40 to 45 min and assessed total lung deposition, retention, and elimination. Based on radiolabel inventory, the deposition efficiency in the respiratory tract was 15% to 17%. Measurement of ^{131}Ba label in the feces during the first 4 days following exposure indicated that 40% of the deposited DPM was eliminated via mucociliary clearance. Clearance of the particles from the lower respiratory tract followed a two-phase elimination process consisting of a rapid ($t_{1/2}$ of 1 day) elimination by mucociliary transport and a slower ($t_{1/2}$ of 62 days) macrophage-mediated alveolar clearance. This study provided data for normal alveolar clearance rates of DPM not affected by prolonged exposure or particle overloading.

Several studies have investigated the effects of exposure concentration on the alveolar clearance of DPM by laboratory animals. Wolff et al. (1986, 1987) provided clearance data ($t_{1/2}$) and lung burden values for F344 rats exposed to DE for 7 h/day, 5 days/week for 24 mo. Exposure concentrations of 0.35, 3.5, and 7.1 mg of DPM/m^3 were employed in this whole body-inhalation exposure experiment. Intermediate (hours-days) clearance of $^{67}Ga_2O_3$ particles (30 min, nose-only inhalation) was assessed after 6, 12, 18, and 24 mo of exposure at all of the DPM concentrations. A two-component function described the clearance of the administered radiolabel:

$$F_{(t)} = A\exp(-0.693\ t/\tau_1) + B\exp(-0.693\ t/\tau_2), \qquad (3\text{-}1)$$

where $F_{(t)}$ was the percentage retained throughout the respiratory tract, A and B were the magnitudes of the two components (component A included nasal, lung, and gastrointestinal clearance, while component B represented intermediate lung clearance) and τ_1 and τ_2 were the

Table 3-2. Alveolar clearance in laboratory animals exposed to DPM in whole exhaust

Species/sex	Exposure technique	Exposure duration	Particles mg/m^3	Observed effects	Reference
Rats, F-344, M	Nose only; Radiolabeled DPM	40-45 min	6	Four days after exposure, 40% of DPM eliminated by mucociliary clearance. Clearance from lower RT was in 2 phases. Rapid mucociliary ($t_{1/2}$ = 1 day); slower macrophage-mediated ($t_{1/2}$ = 62 days).	Chan et al. (1981)
Rats, F-344	Whole body; assessed effect on clearance of $^{67}Ga_2O_3$ particles	7 h/day 5 days/week 24 mo	0.35 3.5 7.1	τ_1 significantly higher with exposure to 7.1 mg/m^3 for 24 mo; τ_2 significantly longer after exposure to 7.1 mg/m^3 for 6 mo and to 3.5 mg/m^3 for 18 mo.	Wolff et al. (1986, 1987)
Rats	Whole body	19 h/day 5 days/week 2.5 years	4	Estimated alveolar deposition = 60 mg; particle burden caused lung overload. Estimated 6-15 mg particle-bound organics deposited.	Heinrich et al. (1986)
Rats, F-344, MF	Whole body	7 h/day 5 days/week 18 mo	0.15 0.94 4.1	Long-term clearance was 87 ± 28 and 99 ± 8 days for 0.15 and 0.94 mg/m^3 groups, respectively; $t_{1/2}$ = 165 days for 4.1 mg/m^3 group.	Griffis et al. (1983)
Rats, F-344;	Nose-only; Radiolabeled ^{14}C	45 min 140 min	7 2	Rats demonstrated 3 phases of clearance with $t_{1/2}$ = 1, 6, and 80 days, representing tracheobronchial, respiratory bronchioles, and alveolar clearance, respectively. Guinea pigs demonstrated negligible alveolar clearance from day 10 to 432.	Lee et al. (1983)
Guinea pigs, Hartley		45 min	7		
Rats, F-344		20 h/day 7 days/week 7-112 days	0.25 6	Monitored rats for a year. Proposed two clearance models. Clearance depends on initial particle burden; $t_{1/2}$ increases with higher exposure. Increases in $t_{1/2}$ indicate increasing impairment of AM mobility and transition into overload condition.	Chan et al. (1984)

RT = respiratory tract.
AM = alveolar macrophage.
τ_1 = clearance from primary, ciliated airways.
τ_2 = clearance from nonciliated passages.

half-times for the *A* and *B* components, respectively. The early clearance half-times (τ_1), were similar for rats in all exposure groups at all time points except in the high-exposure (7.1 mg/m^3) group following 24 mo of exposure, which was faster than the controls. Significantly longer *B* component retention half-times, representing intermediate clearance probably from nonciliated structures such as alveolar ducts and alveoli, were noted after as little as 6 mo exposure to DPM at 7.1 mg/m^3 and 18 mo exposure to 3.5 mg/m^3.

Nose-only exposures to ^{134}Cs fused aluminosilicate particles (FAP) were used to assess long-term (weeks-months) clearance. Following 24-mo exposure to DPM, long-term clearance of ^{134}Cs-FAP was significantly ($p<0.01$) altered in the 3.5 (cumulative exposure [C × T] of 11,760 mg·h/m^3) and 7.1 mg/m^3, C × T = 23,520 mg·h/m^3) exposure groups ($t_{1/2}$ of 264 and 240 days, respectively) relative to the 0.35 mg/m^3 and control groups ($t_{1/2}$ of 81 and 79 days, respectively). Long-term clearance represents the slow component of particle removal from the alveoli. The decreased clearance correlated with the greater particle burden in the lungs of the 3.5 and 7.1 mg/m^3 exposure groups. Based on these findings, the cumulative exposure of > 11,760 mg·h/m^3 (or 3.5 mg/m^3 for a lifetime exposure) represented a particle overload condition resulting in compromised alveolar clearance mechanisms; the clearance rate at the lowest concentration (0.35 mg/m^3; cumulative exposure of 118 mg·h/m^3) was not different from control rates (Figure 3-7).

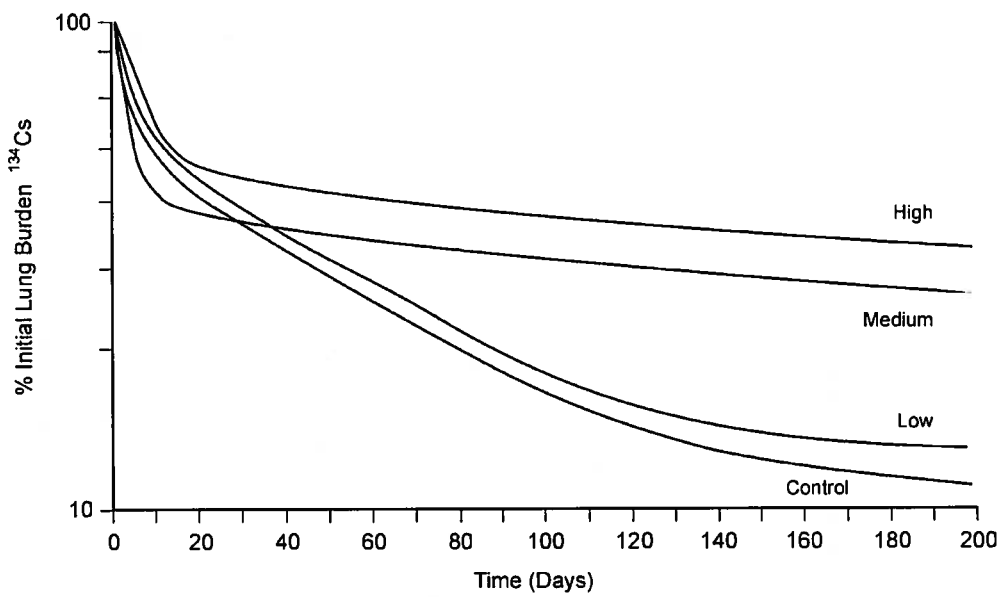

Figure 3-7. Clearance from lungs of rats of ^{134}Cs-FAP fused aluminosilicate tracer particles inhaled after 24 months of DE exposure at concentrations of 0 (control), 0.35 (low), 3.5 (medium), and 7.1 (high) mg DPM/m^3.

Heinrich et al. (1986) exposed rats 19 h/day, 5 days/week for 2.5 years to DPM at a particle concentration of about 4 mg/m^3, equal to a "C × T" of 53,200 mg·h/m^3. The deposition in the alveolar region was estimated to equal 60 mg. The lung particle burden was apparently sufficient to result in a "particle overload" condition (Section 3.4). With respect to the organic matter adsorbed onto the particles, the authors estimated that over the 2.5-year period, 6-15 mg of particle-bound organic matter had been deposited and was potentially available for biological effects. This estimation was based on the analysis of the DE used in the experiments, values for rat ventilatory functions, and estimates of deposition and clearance.

Accumulated burden of DPM in the lungs following an 18-mo, 7 h/day, 5 days/week exposure to whole DE was reported by Griffis et al. (1983). Male and female F344 rats exposed to 0.15, 0.94, or 4.1 mg DPM/m^3 were sacrificed at 1 day and 1, 5, 15, 33, and 52 weeks after exposure, and DPM was extracted from lung tissue dissolved in tetramethylammonium hydroxide. Following centrifugation and washing of the supernatant, DPM content of the tissue was quantitated using spectrophotometric techniques. The analytical procedure was verified by comparing results to recovery studies using known amounts of DPM with lungs of unexposed rats. Lung burdens were 0.035, 0.220, and 1.890 mg/g lung tissue, respectively, in rats exposed to diluted whole exhaust at 0.15, 0.94, and 4.1 mg DPM/m^3. Long-term retention for the 0.15 and 0.94 mg/m^3 groups had estimated half-times of 87 ± 28 and 99 ± 8 days, respectively. The retention $t_{1/2}$ for the 4.1-mg/m^3 exposure group was 165 ± 8 days, which was significantly (p<0.0001) greater than those of the lower exposure groups. The 18-mo exposures to 0.15 or 0.96 mg/m^3 levels of DPM [C × T] equivalent of 378 and 2,368 mg·h/m^3, respectively) did not affect clearance rates, whereas the exposure to the 4.1 mg/m^3 concentration C × T = 10,332 mg·h/m^3) resulted in impaired clearance.

Lee et al. (1983) described the clearance of DPM (7 mg/m^3 for 45 min or 2 mg/m^3 for 140 min) by F344 rats (24 per group) and Hartley guinea pigs exposed by nose-only inhalation to diluted whole exhaust with no apparent particle overload in the lungs as being in three distinct phases. The exposure protocols provided comparable total doses based on a ^{14}C radiolabel. $^{14}CO_2$ resulting from combustion of ^{14}C-labeled diesel fuel was removed by a diffusion scrubber to avoid erroneous assessment of ^{14}C intake by the animals. Retention of the radiolabeled particles was determined up to 335 days after exposure and resulted in a three-phase clearance with retention $t_{1/2}$ values of 1, 6, and 80 days. The three clearance phases are taken to represent removal of tracheobronchial deposits by the mucociliary escalator, removal of particles deposited in the respiratory bronchioles, and alveolar clearance, respectively. Species variability in clearance of DPM was also demonstrated because the Hartley guinea pigs exhibited negligible alveolar clearance from day 10 to day 432 following a 45-min exposure to a DPM concentration

of 7 mg/m^3. Initial deposition efficiency (20% ± 2%) and short-term clearance were, however, similar to those for rats.

Lung clearance in male F344 rats preexposed to diluted whole DE containing DPM at 0.25 or 6 mg/m^3 20 h/day, 7 days/week for periods lasting from 7 to 112 days was studied by Chan et al. (1984). Following this preexposure protocol, rats were subjected to 45-min nose-only exposure to ^{14}C-DE, and alveolar clearance of radiolabel was monitored for up to 1 year. Two models were proposed: a normal biphasic clearance model and a modified lung retention model that included a slow-clearing residual component to account for sequestered aggregates of macrophages. The first model described a first-order clearance for two compartments: $R(t) = Ae^{-u1t} + Be^{-u2t}$. This yielded clearance $t_{1/2}$ values of 166 and 562 days for rats preexposed to 6.0 mg/m^3 for 7 and 62 days, respectively. These values were significantly ($p<0.05$) greater than the retention $t_{1/2}$ of 77 ± 17 days for control rats. The same retention values for rats of the 0.25 mg/m^3 groups were 90 ± 14 and 92 ± 15 days, respectively, for 52- and 112-day exposures and were not significantly different from controls. The two-compartment model represents overall clearance of the tracer particles, even if some of the particles were sequestered in particle-laden macrophages with substantially slower clearance rates. For the second model, which excluded transport of the residual fractions in sequestered macrophage aggregates, slower clearance was observed in the group with a lung burden of 6.5 mg (exposed to 6.0 mg/m^3 for 62 days), and no clearance was observed in the 11.8 mg group (exposed to 6.0 mg/m^3 for 112 days). Clearance was shown to be dependent on the initial burden of particles, and therefore the clearance $t_{1/2}$ would increase in higher exposure scenarios. This study emphasizes the importance of particle overloading of the lung and the ramifications on clearance of particles; the significant increases in half-times indicate an increasing impairment of the alveolar macrophage mobility and subsequent transition into an overload condition as is discussed further in Section 3.4.

Long-term alveolar clearance rates of particles in various laboratory animals and humans have been reviewed by Pepelko (1987). Although retention $t_{1/2}$ varies both among and within species and is also dependent on the physicochemical properties of the inhaled particles, the retention $t_{1/2}$ for humans is much longer (>8 mo) than the average retention $t_{1/2}$ of 60 days for rats.

Clearance from the A region occurs via a number of mechanisms and pathways, but the relative importance of each is not always certain and may vary between species. Particle removal by macrophages comprises the main nonabsorptive clearance process in this region. Alveolar macrophages reside on the epithelium, where they phagocytize and transport deposited material, which they contact by random motion or via directed migration under the influence of local chemotactic factors (Warheit et al., 1988).

Particle-laden macrophages may be cleared from the A region along a number of pathways (U.S. EPA, 1996). Uningested particles or macrophages in the interstitium may

traverse the alveolar-capillary endothelium, directly entering the blood (Raabe, 1982; Holt, 1981); endocytosis by endothelial cells followed by exocytosis into the vessel lumen seems, however, to be restricted to particles <0.1 μm diameter, and may increase with increasing lung burden (Lee et al., 1985; Oberdörster, 1988). Once in the systemic circulation, transmigrated macrophages, as well as uningested particles, can travel to extrapulmonary organs.

Alveolar macrophages constitute an important first-line cellular defense mechanism against inhaled particles that deposit in the alveolar region of the lung. It is well established that a host of diverse materials, including DPM, are phagocytized by AMs shortly after deposition (White and Garg, 1981; Lehnert and Morrow, 1985) and that such cell-contained particles are generally rapidly sequestered from both the extracellular fluid lining in the alveolar region and the potentially sensitive alveolar epithelial cells. In addition to this role in compartmentalizing particles from other lung constituents, AMs are prominently involved in mediating the clearance of relatively insoluble particles from the air spaces (Lehnert and Morrow, 1985). Although the details of the actual process have not been delineated, AMs with their particle burdens gain access and become coupled to the mucociliary escalator and are subsequently transported from the lung via the conducting airways. Although circumstantial, numerous lines of evidence indicate that such AM-mediated particle clearance is the predominant mechanism by which relatively insoluble particles are removed from the alveolar region of the lungs (Gibb and Morrow, 1962; Ferin, 1982; Harmsen et al., 1985; Lehnert and Morrow, 1985; Powdrill et al., 1989).

The removal characteristics for particles deposited in the alveolar region of the lung have been descriptively represented by numerous investigators as a multicompartment or multicomponent process in which each component follows simple first-order kinetics (Snipes and Clem, 1981; Snipes et al., 1988; Lee et al., 1983). Although the various compartments can be described mathematically, the actual physiological mechanisms determining these differing clearance rates have not been well characterized.

Lehnert et al. (1988, 1989) performed studies using laboratory rats to examine particle-AM relationships over the course of alveolar clearance of low to high lung burdens of noncytotoxic microspheres (2.13 μm diam.) to obtain information on potential AM-related mechanisms that form the underlying bases for kinetic patterns of alveolar clearance as a function of particle lung burdens. The intratracheally instilled lung burdens varied from 1.6×10^7 particles (about 85 μg) for the low lung burden to 2.0×10^8 particles (about 1.06 mg) for the mid-dose and 6.8×10^8 particles (about 3.6 mg) for the highest lung burden. The lungs were lavaged at various times postexposure and the numbers of spheres in each macrophage counted. Although such experiments provide information regarding the response of the lung to particulate matter, intratracheal instillation is not likely to result in the same depositional characteristics as

inhalation of particles. Therefore, it is unlikely that the response of alveolar macrophages to these different depositional characteristics will be quantitatively similar.

The $t_{1/2}$ values of both the early and later components of clearance were virtually identical following deposition of the low and medium lung burdens. For the highest lung burden, significant prolongations were found in both the early, more rapid, as well as the slower component of alveolar clearance. The percentages of the particle burden associated with the earlier and later components, however, were similar to those of the lesser lung burdens. On the basis of the data, the authors concluded that translocation of AMs from alveolar spaces by way of the conducting airways is fundamentally influenced by the particle burden of the cells so translocated. In the case of particle overload that occurred at the highest lung burden, the translocation of AMs with the heaviest cellular burdens of particles (i.e., greater than about 100 microspheres per AM) was definitely compromised.

On the other hand, analysis of the disappearance of AMs with various numbers of particles indicates that the particles may not exclusively reflect the translocation of AMs from the lung. The observations are also consistent with a gradual redistribution of retained particles among the AMs in the lung concurrent with the removal of particle-containing AMs via the conducting airways. Experimental support suggestive of potential processes for such particle redistribution comes from a variety of investigations involving AMs and other endocytic cells (Heppleston and Young, 1973; Evans et al., 1986; Aronson, 1963; Sandusky et al., 1977; Heppleston, 1961; Riley and Dean, 1978).

3.3.3. Translocations of Particles to Extra-Alveolar Macrophage Compartment Sites

Although the phagocytosis of particles by cells free within the lung and the mucociliary clearance of the cells with their particulate matter burdens represent the most prominent mechanisms that govern the fate of particles deposited in the alveolar region, other mechanisms exist that can affect both the retention characteristics of relatively insoluble particles in the lung and the lung clearance pathways for the particles. One mechanism is endocytosis of particles by alveolar lining (Type I) cells (Sorokin and Brain, 1975; Adamson and Bowden, 1978, 1981) that normally provide >90% of the cell surface of the alveoli in the lungs of a variety of mammalian species (Crapo et al., 1983). This process may be related to the size of the particles that deposit in the lungs and the numbers of particles that are deposited. Adamson and Bowden (1981) found that with increasing loads of carbon particles (0.03 μm diam.) instilled in the lungs of mice, more free particles were observed in the alveoli within a few days; it should be noted, however, that this phenomenon was demonstrated with very high doses given as a bolus such that the mechanism and relevance of this phenomenon at lower concentrations may be different or even unrelated to what may happen at much lower concentrations. The relative abundance of particles

endocytosed by Type I cells also increased with increasing lung burdens of the particles, but instillation of large particles (1.0 μm) rarely resulted in their undergoing endocytosis. A 4 mg burden of 0.1 μm diameter latex particles is equivalent to 8×10^{12} particles, whereas a 4 mg burden of 1.0 μm particles is composed of 8×10^{9} particles. Regardless, DPM with volume median diameters between 0.05 and 0.3 μm (Frey and Corn, 1967; Kittleson et al., 1978) would be expected to be within the size range for engulfment by Type I cells should suitable encounters occur. Indeed, it has been demonstrated that DPM is endocytosed by Type I cells in vivo (White and Garg, 1981).

Unfortunately, information on the kinetics of particle engulfment (endocytosis) by Type I cells relative to that by AMs is scanty. Even when relatively low burdens of particulate matter are deposited in the lungs, some fraction of the particles usually appears in the regional lymph nodes (Ferin and Feldstein, 1978; Lehnert, 1989). As will be discussed, endocytosis of particles by Type I cells is an initial, early step in the passage of particles to the lymph nodes. Assuming particle phagocytosis is not sufficiently rapid or perfectly efficient, increasing numbers of particles would be expected to gain entry into the Type I epithelial cell compartment during chronic aerosol exposures. Additionally, if particles are released on a continual basis by AMs that initially sequestered them after lung deposition, some fraction of the "free" particles so released could also undergo passage from the alveolar space into Type I cells.

The endocytosis of particles by Type I cells represents only the initial stage of a process that can lead to the accumulation of particles in the lung's interstitial compartment and the subsequent translocation of particles to the regional lymph nodes. As suggested by the results of Adamson and Bowden (1981), a vesicular transport mechanism in the Type I cell can transfer particles administered at high concentrations by instillation from the air surface of the alveolar epithelium into the lung's interstitium, where particles may be phagocytized by interstitial macrophages or remain in a "free" state for a poorly defined period that may be dependent on the physicochemical characteristics of the particle. The lung's interstitial compartment accordingly represents an anatomical site for the retention of particles in the lung, although the kinetics on movement into and out of this site remain obscure for both humans and test species. Whether or not AMs, and perhaps polymorphonuclear neutrophils (PMNs) that have gained access to the alveolar space compartment and phagocytize particles there, also contribute to the particle translocation process into the lung's interstitium also remains a controversial issue.

Translocation of particulate matter to the various interstitial spaces within the lung is a prominent phenomenon occurring at least at high (occupational) exposures that has been examined extensively for both DPM and coal dust in a species comparison between rats and primates (Nikula et al., 1997a,b). Detailed pulmonary morphometry conducted on F344 rats and cynomolgus monkeys that had been exposed for 24 months to occupational levels of DPM (1.95

mg/m^3; see Lewis et al., 1989) showed major differences in the pulmonary sites of particulate deposition. In rats, about 73% of DPM was present in the alveolar ducts/alveoli and 27% in interstitial compartments; for monkeys the corresponding figures were markedly different at 43% and 57%. The corresponding pulmonary histopathology confirmed that both species were affected, although rats are more sensitive, as incidence and severity scores for alveolar effects ranged from 15 of 15 with severity scores from 1-4 (minimal to moderate), whereas for monkeys the corresponding values were only 4 of 15 at a range of 0-2 (not observed to minimal). Similarly, both species exhibited histopathology at the interstitial sites of deposition but with effects in monkeys being slightly more severe (1 of 15 graded as slight, 14 of 15 graded as minimal) than those in rats (14 of 15 graded as slight, 1 of 15 graded as minimal). The basis for this interspecies difference may be due to any number of clear contrasts that exist between rat and primate lungs, including anatomical (primates and humans have respiratory bronchioles whereas rats do not), kinetic (primates and human clearance processes allow more residence time of particles in the lung than do those in rats or rats may have faster interstitial to lymph node clearance rates than do humans and primates), or morphological (primates and humans have more interstitial tissue, more and thicker pleura, and wider interstitial spaces than do rats). Aspects of the study itself that may obscure its interpretation include the relative lifespan the exposure represented between the tested species (lifetime for rat vs. about 10% lifetime of primate), that there was only the single time point at which the relative burdens were determined, and that rat lymph node burdens were not included in the analysis. The analysis of Kuempel (2000) using human occupational data clearly showed that models require an interstitialization process to provide adequate fits to the empirical human (miners') lung deposition data discussed in that study. Hypotheses about possible mechanisms for the interstitialization process are scant, although Harmsen et al. (1985) provided some evidence in dogs that migration of AMs may contribute to the passage of particles to the interstitial compartment and also may be involved in the subsequent translocation of particles to draining lymph nodes. Translocation to the extrapulmonary regional lymph nodes apparently can involve the passage of free particles as well as particle-containing cells via lymphatic channels in the lungs (Harmsen et al., 1985; Ferin and Feldstein, 1978; Lee et al., 1985). Further, it has been noted that particles accumulate both more rapidly and more abundantly in lymph nodes that receive lymphatic drainage from the lung (Ferin and Feldstein, 1978; Lee et al., 1985). It should be stressed that further investigation is required to confirm the character and even existence of the interstitialization process in the lungs of humans with exposures to particles at lower environmental concentrations, or to submicrometer particles such as DPM, or to examine the kinetics and time course of the interstitialization process.

3.3.3.1. *Clearance Kinetics*

The clearance kinetics of PM have been reviewed in the PM CD (U.S. EPA, 1996) and by Schlesinger et al. (1997), the results of which indicate that clearance kinetics may be profoundly influenced by several factors. The influence of time, for example, is definitively showed by the work of Bailey et al. (1985; discussed above), who showed that the rate of clearance from the pulmonary region to the GI tract decreased nearly fourfold from initial values to those noted at 200 days and beyond after particle inhalation.

3.3.3.2. *Interspecies Patterns of Clearance*

The inability to study the retention of certain materials in humans for direct risk assessment requires the use of laboratory animals. Adequate toxicological assessment necessitates that interspecies comparisons consider aspects of dosimetry including knowledge of clearance rates and routes. The basic mechanisms and overall patterns of clearance from the respiratory tract are similar in humans and most other mammals. Regional clearance rates, however, can show substantial variation between species, even for similar particles deposited under comparable exposure conditions (U.S. EPA, 1996; Schlesinger et al., 1997; Snipes et al., 1989).

In general, there are species-dependent rate constants for various clearance pathways. Differences in regional and total clearance rates between some species are a reflection of differences in mechanical clearance processes. For consideration in assessing particle dosimetry, the end result of interspecies differences in clearance is that the retained doses in the lower respiratory tract can differ between species, which may result in differences in response to similar particulate exposures.

3.3.3.3. *Clearance Modifying Factors and Susceptible Populations*

A number of host and environmental factors may modify clearance kinetics and may consequently make individuals exhibiting or afflicted with these factors particularly susceptible to the effects resulting from exposure to DPM. These include age, gender, physical activity, respiratory tract disease, and inhalation of irritants (U.S. EPA, 1996, Section 10.4.2.5). Respiratory tract clearance appears to be prolonged in a number of pathophysiological conditions in humans, including chronic sinusitis, chronic bronchitis, asthma, chronic obstructive lung disease, and various acute respiratory infections.

3.3.3.4. *Respiratory Tract Disease*

Earlier studies reviewed in the PM CD (U.S. EPA, 1996) noted that various respiratory tract diseases are associated with alterations in overall clearance and clearance rates. Prolonged

nasal mucociliary clearance in humans is associated with chronic sinusitis or rhinitis, and cystic fibrosis. Bronchial mucus transport may be impaired in people with bronchial carcinoma, chronic bronchitis, asthma, and various acute infections. In certain of these cases, coughing may enhance mucus clearance, but it generally is effective only if excess secretions are present.

The rates of A region particle clearance are reduced in humans with chronic obstructive lung disease and in laboratory animals with viral infections, whereas the viability and functional activity of macrophages are impaired in human asthmatics and in animals with viral-induced lung infections (U.S. EPA, 1996). However, any modification of functional properties of macrophages appears to be injury specific, reflecting the nature and anatomic pattern of disease.

3.4. PARTICLE "OVERLOAD"

3.4.1. Introduction

Some experimental studies using laboratory rodents employed high exposure concentrations of relatively nontoxic, poorly soluble particles. These particle loads interfered with normal clearance mechanisms, producing clearance rates different from those that would occur at lower exposure levels. Prolonged exposure to high particle concentrations is associated with what is termed particle overload. This is defined as the overwhelming of macrophage-mediated clearance by the deposition of particles at a rate exceeding the capacity of that clearance pathway. Aspects and occurrence of this phenomenon have already been alluded to in earlier portions of this chapter on alveolar clearance (Section 3.3.2.3). The relevance of this phenomenon for human risk assessment has long been the object of scientific inquiry. A monograph on this matter and many others relevant to DPM has appeared (ILSI, 2000), and the results, opinions, and judgments put forth therein are used extensively in this chapter and in this assessment.

Wolff et al. (1987) used ^{134}Cs-labeled fused aluminosilicate particles to measure alveolar clearance in rats following 24-mo exposure to low, medium, and high concentrations of DE (targeted concentrations of DPM of 0.35, 3.5 and 7.1 mg/m^3). The short-term component of the multicomponent clearance curves was similar for all groups, but long-term clearance was retarded in the medium- and high-exposure groups (Figure 3-7). The half times of the long-term clearance curves were 79, 81, 264, and 240 days, respectively, for the control, low-, medium-, and high-exposure groups. Clearance was overloaded at the high and medium but not at the low exposure level. Lung burdens of DPM were measured after 6, 12, 18, and 24 mo of exposure. The results (Figure 3-8) indicate that the lung burden of deposited particles was appreciably increased or "overloaded" compared with the low level of exposure in the two highest exposures post 6 months. Figure 3-8 also compares these observational results of lung burden with simulated results where no overload would occur (McClellan, 2000). Comparison

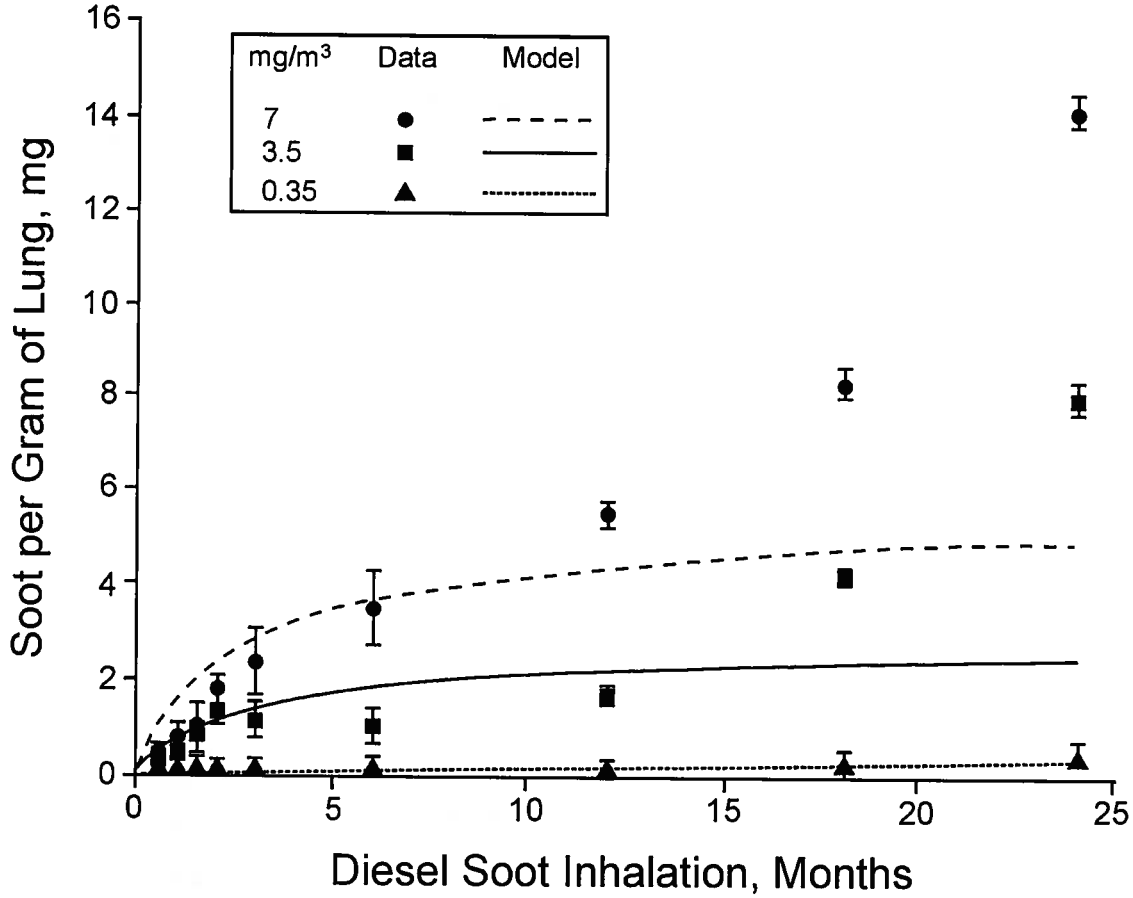

Figure 3-8. Lung burdens (in mg DPM soot/g lung) in rats chronically exposed to DE at 0.35 (low) (●), 3.5 (medium) (▲), and 7.1 (high) mg / m³ (■). The solid figures represent actual data with means and standard errors from animals sacrificed at 6, 12, and 18 months after initiation of exposures. Lines are simulated model results from these same exposure levels, assuming no effect of exposure concentration on deposition or clearance of particles (from Wolff et al., 1987; McClellan, 2000).

of the observed and simulated results clearly shows that the two highest exposure levels resulted in lung burdens that were ever-increasing and not at all concordant with the simulated results, whereas the burdens at the low-exposure level were closely approximated by the simulation. Thus, at the two highest exposure levels, deposition processes were outpacing clearance mechanisms. Results from the low-exposure level indicate that clearance processes were not inhibited, the lung burden remaining the same throughout all time periods examined.

Morrow (1988) has proposed that the condition of particle overloading in the lungs is caused by a loss in the mobility of particle-engorged AMs and that such an impediment is related to the cumulative volumetric load of particles in the AMs. Morrow (1988) has further estimated that the clearance function of an AM may be completely impaired when the particle burden in the AM is of a volumetric size equivalent to about 60% of the normal volume of the AM. Morrow's

hypothesis was the initial basis for the physiology-oriented multicompartmental kinetic (POCK) model derived by Stöber et al. (1989) for estimating alveolar clearance and retention of relatively insoluble, respirable particles in rats.

A revised version of this model refines the characterization of the macrophage pool by including both the mobile and immobilized macrophages (Stöber et al., 1994). Application of the revised version of the model to experimental data suggested that lung overload does not cause a dramatic increase in the total burden of the macrophage pool but results in a great increase in the particle burden of the interstitial space, a compartment that is not available for macrophage-mediated clearance. The revised version of the POCK model is discussed in greater detail in the context of other dosimetry models below.

Oberdörster and co-workers (1992) assessed the alveolar clearance of smaller (3.3 μm diam.) and larger (10.3 μm diam.) polystyrene particles, the latter of which are volumetrically equivalent to about 60% of the average normal volume of a rat AM, after intratracheal instillation into the lungs of rats. Even though both sizes of particles were found to be phagocytized by AMs within a day after deposition, and the smaller particles were cleared at a normal rate, only minimal lung clearance of the larger particles was observed over an approximately 200-day postinstillation period, thus supporting the volumetric AM overload hypothesis.

It has been hypothesized that when the retained lung burden approaches 1 mg particles/g lung tissue, overloading will begin in the rat (Morrow, 1988); at 10 mg particles/g lung tissue macrophage-mediated clearance of particles would effectively cease. Overloading appears to be a nonspecific effect noted in experimental studies, generally in rats, using many different kinds of poorly soluble particles (including TiO_2, volcanic ash, DPM, carbon black, and fly ash) and results in A region clearance slowing or stasis, with an associated inflammation and aggregation of macrophages in the lungs and increased translocation of particles into the interstitium (Muhle et al., 1990a,b; Lehnert, 1990; Morrow, 1994). Following overloading, the subsequent retardation of lung clearance, accumulation of particles, chronic inflammation, and the interaction of inflammatory mediators with cell proliferative processes and DNA may lead to the development of fibrosis, epithelial cell mutations, and fibrosis in rats (Mauderly, 1996). The phenomenon of overload has been discussed in greater detail in the previous PM CD (U.S. EPA, 1996).

3.4.2. Relevance to Humans

The relevance of "lung overload" to humans, and even to species other than laboratory species (rats and mice and hamsters; Muhle et al., 1990a,b), is not clear. Although likely to be of little relevance for most "real world" ambient exposures of humans, this phenomenon is of concern in interpreting some long-term experimental exposure data and perhaps for human

occupational exposure. In addition, relevance to humans is clouded by the fact that macrophage-mediated clearance is slower and perhaps less important in humans than in rats (Morrow, 1994).

Particle overload appears to be an important factor in the pulmonary carcinogenicity observed in rats exposed to DPM. A study by Griffis et al. (1983) demonstrated that exposure (7 h/day, 5 days/week) of rats to diluted whole DE containing DPM at concentrations of 0.15, 0.94, or 4.1 mg/m^3 for 18 mo resulted in lung burdens of 0.035, 0.220, and 1.89 mg/g of lung tissue, respectively. The alveolar clearance of those rats with the highest lung burden (1.89 mg/g of lung) was impaired, as determined by a significantly greater ($p<0.0001$) retention $t_{1/2}$ for DPM. Impaired clearance was reflected in the greater lung burden/exposure concentration ratio at the highest exposure level. Similarly, in the study by Chan et al. (1984), rats exposed for 20 h/day, 7 days/week to diluted whole DE containing DPM (6 mg/m^3) for 112 days had an extraordinarily high lung particle burden of 11.8 mg, with no alveolar particle clearance being detected over 1 year.

Muhle et al. (1990a,b) indicated that overloading of rat lungs occurred when lung particle burdens reached 0.5 to 1.5 mg/g of lung tissue and that clearance mechanisms were totally compromised at lung particle burdens ≥ 10 mg/g for particles with a specific density close to 1, observations that are concordant with those of Morrow (1988).

Pritchard (1989), utilizing data from a number of DE exposure studies, examined alveolar clearance in rats as a function of cumulative exposure. The resulting analysis noted a significant increase in retention $t_{1/2}$ values at exposures above 10 mg/m^3·h/day and also showed that normal lung clearance mechanisms appeared to be compromised as the lung DPM burden approached 0.5 mg/g of lung.

Animal studies have revealed that impairment of alveolar clearance can occur following chronic exposure to DPM (Griffis et al., 1983; Wolff et al., 1987; Vostal et al., 1982; Lee et al., 1983) or a variety of other diverse poorly soluble particles of low toxicity (Lee et al., 1986, 1988; Ferin and Feldstein, 1978; Muhle et al., 1990). Because high lung burdens of relatively insoluble, biochemically inert particles result in diminution of normal lung clearance kinetics or in what is now called particle overloading, this effect appears to be more related to the mass and/or volume of particles in the lung than to the nature of the particles per se. Particle overload relates only to poorly soluble particles of low toxicity. It must be noted, however, that some types of particles may be cytotoxic and impair clearance at lower lung burdens (e.g., crystalline silica may impair clearance at much lower lung burdens than DPM). Regardless, as pointed out by Morrow (1988), particle overloading in the lung modifies the dosimetry for particles in the lung and thereby can alter toxicologic responses.

Although quantitative data are limited regarding lung overload associated with impaired alveolar clearance in humans, impairment of clearance mechanisms appears to occur, and at a lung burden generally in the range reported to impair clearance in rats, i.e., approximately 1 mg/g lung tissue. Stöber et al. (1967), in their study of coal miners, reported lung particle burdens of 2 to 50 mg/g lung tissue, for which estimated clearance $t_{1/2}$ values were very long (4.9 years). Freedman and Robinson (1988) also reported slower alveolar clearance rates in coal miners, some of whom had a mild degree of pneumoconiosis. It must be noted, however, as has been reported even in some studies with rats exposed lifetime to overload conditions (50 mg/m^3 TiO_2; Lee et al., 1986) that no lung cancer was reported among those miners with apparent particle overload.

Consideration of the above information further clarifies the human relevance of noncancer effects that may be elicited from overload-type conditions in rats studies. Under conditions that would be most likely to elicit overload conditions in humans, such as the excessive dust burdens in the lungs of miners, cancer is not observed although noncancer responses such as fibrosis and macrophage responses are documented (Freedman and Robinson, 1988; Haschek and Witschi, 1991; Oberdörster, 1994). In deliberation on the matter of whether the rat lung nonneoplastic responses to poorly soluble particles (such as DPM) are predictive of a similar hazard in humans, an expert panel (ILSI, 2000) opined that such responses would indeed be a useful predictor for similar responses in humans.

3.4.3. Potential Mechanisms for an AM Sequestration Compartment for Particles During Particle Overload

Several factors may be involved in the particle-load-dependent retardations in the rate of particle removal from the lung and the corresponding functional appearance of an abnormally slow clearing or particle sequestration compartment. As previously mentioned, one potential site for particle sequestration is the containment of particles in the Type I cells. Information on the retention kinetics for particles in the Type I cells is not currently available. Also, no morphometric analyses have been performed to date to estimate what fraction of a retained lung burden may be contained in the Type I cell population of the lung during lung overloading.

Another anatomical region in the lung that may be a slow clearing site is the interstitial compartment (Kuempel, 2000). Little is known about the kinetics of removal of free particles or particle-containing macrophages from the interstitial spaces, or what fraction of a retained burden of particles is contained in the lung's interstitium during particle overload. The gradual accumulation of particles in the regional lymph nodes and the appearance of particles and cells with associated particles in lymphatic channels and in the peribronchial and perivascular

lymphoid tissue (Lee et al., 1985; White and Garg, 1981) suggest that the mobilization of particles from interstitial sites via local lymphatics is a continual process.

Indeed, it is clear from histologic observations of the lungs of rodents chronically exposed to DPM that Type I cells, the interstitium, the lymphatic channels, and pulmonary lymphoid tissues could collectively comprise subcompartments of a more generalized slow clearing compartment.

Although these sites must be considered potential contributors to the increased retention of particles during particle overload, a disturbance in particle-associated AM-mediated clearance is undoubtedly the predominant cause, inasmuch as, at least in rodents, the AMs are the primary reservoirs of deposited particles. The factors responsible for a failure of AMs to translocate from the alveolar space compartment in lungs with high particulate matter burdens remain uncertain, although a hypothesis concerning the process involving volumetric AM burden has been offered (Morrow, 1988).

Other processes also may be involved in preventing particle-laden AMs from leaving the alveolar compartment under conditions of particle overload in the lung. Clusters or aggregates of particle-laden AMs in the alveoli are typically found in the lungs of laboratory animals that have received large lung burdens of a variety of types of particles (Lee et al., 1985), including DPM (White and Garg, 1981; McClellan et al., 1982). The aggregation of AMs may explain, in part, the reduced clearance of particle-laden AM during particle overload. The definitive mechanism(s) responsible for this clustering of AMs has not been elucidated to date. Whatever the underlying mechanism(s) for the AM aggregation response, it is noteworthy that AMs lavaged from the lungs of DE-exposed animals continue to demonstrate a propensity to aggregate (Strom, 1984). This observation could result either from the surface characteristics of AMs being fundamentally altered or from macrophage activation by phagocytized particles that then release chemotactic factors (Bellmann et al., 1990) in a manner that promotes their adherence to one another in the alveolar region. AM aggregation may not simply be directly caused by their abundant accumulation as a result of immobilization by large particle loads. Furthermore, even though overloaded macrophages may redistribute particle burden to other AMs, clearance may remain inhibited (Lehnert, 1988). This may, in part, be because attractants from the overloaded AMs cause aggregation of those that are not carrying a particle burden.

3.5. BIOAVAILABILITY OF ORGANIC CONSTITUENTS PRESENT ON DIESEL EXHAUST PARTICLES

Because it has been shown that DPM extract is not only mutagenic but also contains known carcinogens, the organic fraction was originally considered to be the primary source of carcinogenicity in animal studies. Since then, evidence has been presented that carbon black,

lacking an organic component, is capable of inducing lung cancer at exposure concentrations sufficient to induce lung particle overload. This suggested that the relatively insoluble carbon core of the particle may be of greater importance for the pathogenic and carcinogenic processes observed in the rat inhalation studies conducted at high exposure concentrations. (See Chapter 7 for a discussion of this issue.) However, lung cancer reported in epidemiologic studies was associated with diesel exposure levels far below those inducing particle overload in lifetime studies in rats. It is therefore suggested that compounds in the organic fraction of DPM may have some role in the etiology of human lung cancers. This leads to an interest in characterizing the bioavailability of organics.

The bioavailability of toxic organic compounds adsorbed to DPM can be influenced by a variety of factors. Although the agent may be active while present on the particle, most particles are taken up by AMs, a cell type not generally considered to be a target site. In order to reach the target site, elution from the particle surface is necessary followed by diffusion and uptake by the target cell. Metabolism to an active form by either the phagocytes or the target cells is also required for activity of many of the compounds present.

This section describes only the various manner and mechanisms by which organics adsorbed onto DPM may become bioavailable. In vivo and in vitro results involving various biological extraction media as well as modeled scenarios of bioavailability are presented. Actual estimates of the amount of organics from DPM to which respiratory tract tissues may be exposed are discussed and presented in Section 3.6.2.7.

3.5.1. In Vivo Studies

3.5.1.1. *Laboratory Investigations*

Several studies reported on the retention of particle-adsorbed organics following administration to various rodent species. In studies reported by Sun et al. (1982, 1984) and Bond et al. (1986), labeled organics were deposited on DPM following heating to vaporize away the organics originally present. Sun et al. (1982) compared the disposition of either pure or diesel particle-adsorbed benzo[*a*]pyrene (B[*a*]P) following nose-only inhalation by F344 rats. About 50% of particle-adsorbed B[*a*]P was cleared with a half-time of 1 h, predominantly by mucociliary clearance. The long-term retention of particle-adsorbed ^{3}H-B[*a*]P at 18 days was approximately 230-fold greater than that for pure ^{3}H-B[*a*]P (Sun et al., 1982). At the end of exposure, about 15% of the ^{3}H label was found in blood, liver, and kidney. Similar results were reported in a companion study by Bond et al. (1986), and by Sun et al. (1984) with another PAH, 1-nitropyrene, except the retention half-time was 36 days.

Ball and King (1985) studied the disposition and metabolism of intratracheally instilled ^{14}C-labeled 1-NP (>99.9% purity) coated onto DPM. About 50% of the ^{14}C was excreted within

the first 24 h; 20% to 30% of this appeared in the urine, and 40% to 60% was excreted in the feces. Traces of radiolabel were detected in the trachea and esophagus. Five percent to 12% of the radiolabel in the lung co-purified with the protein fraction, indicating some protein binding. The corresponding DNA fraction contained no ^{14}C above background levels.

Bevan and Ruggio (1991) assessed the bioavailability of B[*a*]P adsorbed to DPM from a 5.7-L Oldsmobile diesel engine. In this study, exhaust particles containing 1.03 μg B[*a*]P/g particles were supplemented with exogenous ^{3}H-B[*a*]P to provide 2.62 μg B[*a*]P/g of exhaust particles. In vitro analysis indicated that the supplemented B[*a*]P eluted from the particles at the same rate as the original B[*a*]P. Twenty-four hours after intratracheal instillation in Sprague-Dawley rats, 68.5% of the radiolabel remained in the lungs. This is approximately a 3.5-fold greater proportion than that reported by Sun et al. (1984), possibly because smaller amounts of B[*a*]P adsorbed on the particles resulted in stronger binding or possibly because of differences between inhalation exposure and intratracheal exposure. At 3 days following administration, more than 50% of the radioactivity remained in the lungs, nearly 30% had been excreted into the feces, and the remainder was distributed throughout the body. Experiments using rats with cannulated bile ducts showed that approximately 10% of the administered radioactivity appeared in the bile over a 10-h period and that less than 5% of the radioactivity entered the feces via mucociliary transport. Results of these studies showed that when organics are adsorbed to DPM the retention of organics in the lungs is increased considerably. Because retention time is very short following exposure to pure compounds not bound to particles, it can be concluded that the increased retention time is primarily the result of continued binding to DPM. The detection of labeled compounds in blood, systemic organs, urine, and bile as well as the trachea, however, provides evidence that at least some of the organics are eluted from the particles following deposition in the lungs and would not be available as a carcinogenic dose to the lung. As discussed above, the results of Gerde (1999a,b) indicate that most of the organics eluted from particles deposited in the alveolar region, especially PAHs, are predicted to rapidly enter the bloodstream and thus not to contribute to potential induction of lung cancer.

3.5.1.2. *Studies in Occupationally Exposed Humans*

DNA adducts in the lungs of experimental animals exposed to DE have been measured in a number of animal experiments (World Health Organization, 1996). Such studies, however, provide limited information regarding bioavailability of organics, as positive results may well have been related to factors associated with lung particle overload, a circumstance reported by Bond et al. (1990), who found carbon black, a substance virtually devoid of organics, to induce DNA adducts in rats at lung overload doses. These authors showed that levels of DNA adducts present in pulmonary type II cells from the lungs of rats (n=15) exposed to equivalent conditions

of either carbon black or DE (each at 6.2 mg/m^3) were nearly the same and 4- to 5-fold more than air-exposed controls. This similarity was noted despite a difference of nearly three orders of magnitude in solvent-extractable organic content between DE (30%) and carbon black (0.04%). None of the DE or carbon black adducts comigrated with B[*a*]P diol epoxide.

On the other hand, DNA adduct formation and/or mutations in blood cells following exposure to DPM, especially at levels insufficient to induce lung overload, can be presumed to be the result of organics diffusing into the blood. Hemminki et al. (1994) reported increased levels of DNA adducts in lymphocytes of bus maintenance and truck terminal workers. Österholm et al. (1995) studied mutations at the hprt-locus of T-lymphocytes in bus maintenance workers. Although they were unable to identify clear-cut exposure-related differences in types of mutations, adduct formation was significantly increased in the exposed workers. Nielsen et al. (1996) reported significantly increased levels of lymphocyte DNA adducts, hydroxyvaline adducts in hemoglobin, and 1-hydroxypyrene in urine of garage workers exposed to DE.

3.5.2. In Vitro Studies

3.5.2.1. *Extraction of Diesel Particle-Associated Organics by Biological Fluids*

In vitro extraction of mutagenic organics by biological fluids can be estimated by measurement of mutagenic activity in the particular fluid. Using this approach, Brooks et al. (1981) reported extraction efficiencies of only 3% to 10% that of dichloromethane following DPM incubation in lavage fluid, serum, saline, albumin, or dipalmitoyl lecithin. Moreover, extraction efficiency did not increase with incubation time up to 120 h. Similar findings were reported by King et al. (1981), who also reported that lung lavage fluid and lung cytosol fluid extracts of DPM were not mutagenic. Serum extracts of DPM did exhibit some mutagenic activity, but considerably less than that of organic solvent extracts. Furthermore, the mutagenic activity of the solvent extract was significantly reduced when combined with serum or lung cytosol fluid, suggesting protein binding or biotransformation of the mutagenic components. Siak et al. (1980) assessed the mutagenicity of material extracted from DPM by bovine serum albumin in solution, simulated lung surfactant, fetal calf serum (FCS), and physiological saline. Only FCS was found to extract some mutagenic activity from the DPM. Keane et al. (1991), however, reported positive effects for mutagenicity in salmonella and sister chromatid exchange in V79 cells exclusively in the supernatant fraction of DPM dispersed in aqueous mixtures of dipalmitoyl phosphatidyl choline, a major component of pulmonary surfactant, indicating that pulmonary surfactant components can extract active components of DPM and result in bioavailability.

The ability of biological fluids to extract organics in vitro and their effectiveness in vivo remains equivocal because of the character of the particular fluid. For example, extracellular

lung fluid is a complex mixture of constituents that undoubtedly have a broad range of hydrophobicity (George and Hook, 1984; Wright and Clements, 1987), which is fundamentally different from serum in terms of chemical composition (Gurley et al., 1988). Moreover, assessments of the ability of lavage fluids, which actually represent substantially diluted extracellular lung fluid, to extract mutagenic activity from DPM clearly do not reflect the in vivo condition. Finally, except under very high exposure concentrations, few particles escape phagocytosis and possible intracellular extraction. In this respect, Hiura et al. (1999) have shown that whole exhaust containing DPM, but not carbon black or diesel particles devoid of organics, induces apoptosis, apparently through generation of oxygen radicals. This study implicates organic compounds present on DPM. It also indicates the bioavailability of organics for generation of radicals from reaction with particle-associated organics or following elution from DPM.

3.5.2.2. *Extraction of DPM-Associated Organics by Lung Cells and Cellular Components*

A more likely means by which organics may be extracted from DPM and metabolized in the lung is either through particle dissolution or extraction of organics from the particle surface within the phagolysosomes of AMs and other lung cells. This mechanism presupposes that the particles are internalized. Specific details about the physicochemical conditions of the intraphagolysosomal environment, where particle dissolution in AMs presumably occurs in vivo, have not been well characterized. It is known that phagolysosomes constitute an acidic (pH 4 to 5) compartment in macrophages (Nilsen et al., 1988; Ohkuma and Poole, 1978). The relatively low pH in the phagolysosomes has been associated with the dissolution of some types of inorganic particles (some metals) by macrophages (Marafante et al., 1987; Lundborg et al., 1984), but few studies provide quantitative information concerning how organics from DPM may be extracted in the phagolysosomes (Bond et al., 1983). Whatever the mechanism, assuming elution occurs, the end result is a prolonged exposure of the respiratory epithelium to DPM organics, which include low concentrations of carcinogenic agents such as PAH.

Early studies by King et al. (1981) found that when pulmonary alveolar macrophages were incubated with DPM, amounts of organic compounds and mutagenic activity decreased measurably from the amount originally associated with the particles, suggesting that organics were removed from the phagocytized particles. Leung et al. (1988) studied the ability of rat lung and liver microsomes to facilitate transfer and metabolism of B[*a*]P from diesel particles. ^{14}C-B[*a*]P coated diesel particles, previously extracted to remove the original organics, were incubated directly with liver or lung microsomes. About 3% of the particle-adsorbed B[*a*]P was transferred to the lung microsomes within 2 h. Of this amount about 1.5% was metabolized, for a total of about 0.05% of the B[*a*]P originally adsorbed to the DPM. Although transformation is

slow, the long retention of particles, including DPM, in humans may cause the fraction eluted and metabolized to be considerably higher than this figure.

In analyzing phagolysosomal dissolution of various ions from particles in the lungs of Syrian golden hamsters, however, Godleski et al. (1988) demonstrated that solubilization did not necessarily result in clearance of the ions (and therefore general bioavailability) in that binding of the solubilized components to cellular and extracellular structures occurred. It is reasonable to assume that phagocytized DPM particles may be subject to similar processes and that these processes would be important in determining the rate of bioavailability of the particle-bound constituents of DPM.

Alveolar macrophages or macrophage cell lines that were exposed to high concentrations of DPM in vitro were observed to undergo apoptosis, which was attributed to the generation of reactive oxygen radicals (ROR) (Hiura et al. 1999). Further experimentation showed that DPM with the organic constituents extracted was no longer able to induce apoptosis or generate ROR. The organic extracts alone, however, were able to induce apoptosis as well as the formation of stress-activated protein kinases that play definitive roles in cellular apoptotic pathways. The injurious effects of nonextracted DPM or of DPM extracts were observed to be reversible by the antioxidant radical scavenger N-acetyl cysteine. These data suggest strongly that, at least at high concentrations of DPM, the organic constituents contained on DPM play a central role in cellular toxicity and that this toxicity may be attributable to the generation of ROR.

3.5.3. Modeling Studies

Gerde et al. (1991a,b) described a model simulating the effect of particle aggregation and PAH content on the rate of PAH release in the lung. According to this model, particle aggregation will occur with high exposure concentrations, resulting in a slow release of PAHs and prolonged exposure to surrounding tissues. However, large aggregates of particles are unlikely to form at doses typical of human exposures. Inhaled particles, at low concentrations, are more likely to deposit and react with surrounding lung medium without interference from other particles. The model predicts that under low-dose exposure conditions, more typical in humans, particle-associated organics will be released more rapidly from the particles because they are not aggregated. Output from this model suggests strongly that sustained exposure of target tissues to PAHs will result from repeated exposures, not from increased retention due to association of PAHs with carrier particles. This distinction is important because at low doses PAH exposure and lung tumor formation would be predicted to occur at sites of deposition rather than retention, as occurs with high doses.

The site of release of PAHs influences effective dose to the lungs because, as noted previously, at least some free organic compounds deposited in the lungs are rapidly absorbed into

the bloodstream. Gerde et al. (1991b) predicted PAHs would be retained in the alveoli less than 1 min, whereas they may be retained in the conducting airways for hours. These predictions were based on an average diffusion distance to capillaries of only about 0.5 μm in the alveoli, as compared to possibly greater than 50 μm in the conducting airways such as the bronchi. An experimental study by Gerde et al. (1999) provided support for this prediction. Beagle dogs were exposed to ^{3}H-B[*a*]P adsorbed on the carbonaceous core of DPM at a concentration of 15 μg B[*a*]P/gm particles. A rapidly eluting fraction from DPM deposited in the alveoli was adsorbed into the bloodstream and metabolized in the liver, whereas the rapidly eluting fraction from DPM deposited in the conducting airways was to a large extent retained and metabolized in situ in the airway epithelium. Thus, organics eluting from DPM depositing in the conducting airways (i.e., the TB region) would have a basis for a longer residence time in the tissues (and for consequent biological activity) than would organics eluting from DPM depositing in the pulmonary parenchyma. And, given the same overall deposited dose of DPM to the total pulmonary system, a deposited dose with a higher proportion in the TB region would incur a higher probability of tissue interactions with any eluted organics. This may be the case when comparing regional doses of DPM to humans as compared to rats for two reasons. First, one deposition model (Freijer et al., 1999) projects that for air concentrations of DPM at either 0.1 or 1.0 mg/m^3, a higher proportion of the total DPM dose to the pulmonary system would be deposited in the TB area for humans at 31% (TB/Total; 0.098 / 0.318) than for rats at only 16% (0.04 / 0.205). Second, comparative morphometry data of DPM from chronically exposed rats and primates showed higher levels of DPM adjacent to conducting airways in primates (i.e., the interstitium of the respiratory bronchioles) than were present in parallel regions in the rat (interstitium of the alveolar ducts) (Nikula et al., 1997a,b). The focal nature of this deposition could give rise to localized high concentrations of any organics eluted.

3.5.4. Summary and Bioavailability

At present, the available data are insufficient to accurately model the effective dose of organics in the respiratory tract of humans or animals exposed to DPM. As mentioned above, though, the following Section (3.6.2.7) does present estimates of the actual amount of organics, including carcinogenic PAH such as B[*a*]P, that are deposited in the lung and could become bioavailable.

Overall, the results of studies presented in Section 3.6 provide evidence that at least some of the organic matter adsorbed to DPM deposited in the respiratory tract is eluted. The percentage taken up and metabolized to an active form by target cells is, however, uncertain. Organics eluted from particles deposited in alveoli are likely to rapidly enter the bloodstream via translocation across endothelial cells, where they may undergo metabolism by enzymes such as

cytochromes P-450 that are capable of producing reactive species. Organics eluted from particles deposited in the conducting airways (the bronchioles, bronchi, and trachea) may also undergo metabolism in other cell types such as the Clara cells with constituent or inducible cytochrome P-450 species. Risk of harmful effects for particles deposited in the conducting airways is predicted to be greater because solubilized organic compounds will be retained in the thicker tissue longer, allowing for metabolism by epithelial cells lining the airways. Furthermore, since some deposition in conducting airways occurs primarily at bifurcations, localized higher concentrations may occur.

3.6. MODELING THE DEPOSITION AND CLEARANCE OF PARTICLES IN THE RESPIRATORY TRACT

3.6.1. Introduction

The biological effects of inhaled particles are a function of their disposition, i.e., their deposition and clearance. This, in turn, depends on their patterns of deposition (i.e., the sites within which particles initially come into contact with airway epithelial surfaces and the amount removed from the inhaled air at these sites) and clearance (i.e., the rates and routes by which deposited materials are removed from the respiratory tract). Removal of deposited materials involves the competing processes of macrophage-mediated clearance and dissolution-absorption. Over the years, mathematical models for predicting deposition, clearance and, ultimately, retention of particles in the respiratory tract have been developed. Such models help interpret experimental data and can be used to make predictions of deposition for cases where data are not available. A review of various mathematical particle deposition models was given by Morrow and Yu (1993) and in U.S. EPA (1996).

Currently available data for long-term inhalation exposures to poorly soluble particles (e.g., TiO_2, carbon black, and DPM) show that pulmonary retention and clearance of these particles are not adequately described by simple first-order kinetics and a single compartment representing the alveolar macrophage particle burden. Several investigators have developed models for deposition, transport, and clearance of poorly soluble particulate matter in the lungs. All of these models identify various compartments and associated transport rates, but empirically derived data are not available to substantiate many of the assumptions made in these models.

3.6.2. Dosimetry Models for DPM

3.6.2.1. *Introduction*

The extrapolation of toxicological results from laboratory animals to humans, the goal of this chapter, requires the use of dosimetry models for both species that include, first, the deposition of DPM in various regions of the respiratory tract, and second, the transport and

clearance of the particles, including adsorbed constituents, from their deposited sites. Therefore the ideal model structure would incorporate both deposition and clearance in animals and humans.

Deposition of particles in the respiratory tract, as described above, can be by impaction, sedimentation, interception, and diffusion, with the contribution from each mechanism a function of particle size, lung structure, and size and breathing parameters. Because of the size of diesel particles, under normal breathing conditions most of this deposition takes place by diffusion, and the fraction of the inhaled mass that is deposited in the thoracic region (i.e., TB plus A regions) is substantially similar for rats and humans.

Among deposition models that include aspects of lung structure and breathing dynamics, the most widely used have been typical-path or single-path models (Yu, 1978; Yu and Diu, 1983). The single-path models are based on an idealized symmetric geometry of the lung, assuming regular dichotomous branching of the airways and alveolar ducts (Weibel, 1963). They lead to modeling the deposition in an average regional sense for a given lung depth. Although the lower airways of the lung may be reasonably characterized by such a symmetric representation, there are major asymmetries in the upper airways of the tracheobronchial tree that in turn lead to different apportionment of airflow and particulate burden to the different lung lobes. The rat lung structure is highly asymmetric because of its monopodial nature, leading to significant errors in a single-path description. This is rectified in the multiple-path model of the lung, which incorporates asymmetry and heterogeneity in lung branching structure and calculates deposition at the individual airway level. This model has been developed for the rat lung (Anjilvel and Asgharian, 1995; Freijer et al., 1999) and, in a limited fashion because of insufficient morphometric data, for the human lung (Subramaniam et al., 1998; Yeh and Schum, 1980). Such models are particularly relevant for fine and ultrafine particles such as occur in DPM. However, models for clearance have not yet been implemented in conjunction with the use of the multiple-path model.

Clearance of particles in the respiratory tract takes place (1) by mechanical processes: mucociliary transport in the ciliated conducting airways and macrophage phagocytosis and migration in the nonciliated airways, and (2) by dissolution. The removal of material such as the carbonaceous core of DPM is largely by mechanical clearance, whereas the clearance of the organics adsorbed onto the carbon core is principally by dissolution.

Several models currently exist that integrate both deposition and clearance, some specific for humans and others specific for laboratory animals. They differ significantly in the level of physiological detail that is captured in the model and in the uncertainties associated with the values of the parameters used. All of these models identify various compartments and associated transport rates, but empirically derived data are not available to validate many of the assumptions

made in the models. A review of the principal human and animal deposition/clearance models, including candidate models for use in animal-to-human extrapolation in this assessment, are considered below.

3.6.2.2. *Human Models*

The International Commission on Radiological Protection (ICRP) recommends specific mathematical dosimetry models as a means to calculate the mass deposition and retention by different parts of the human respiratory tract and, if needed, tissues beyond the respiratory tract. The latest ICRP-recommended model, ICRP66 (1994), considers the human respiratory tract as four general anatomical regions: the ET region, which is divided into two subregions; the TB region, which is also subdivided into two regions; and the gas-exchange tissues, which are further defined as the alveolar-interstitial (AI) region but are exactly comparable to the pulmonary or A region. The fourth region is the lymph nodes. The deposition component of the model for the ET, TB, and A regions is semi-empirical based on equations derived from fitting experimental deposition data. The dimensional model used for the TB and A regions was adopted from several sources (Weibel, 1963; Yeh and Schum, 1980; and Phalen et al., 1985); the physical aspects of the individual airway generations for these regions were all averaged after each source was adjusted to a standard functional residual capacity. The equations for estimating deposition in these areas was empirical, obtained from fitting data obtained from partial human lung casts or from theoretical calculation for these regions. Deposition in the four regions is given as a function of particle size with two different types of particle size parameters: activity median thermodynamic diameter (AMTD) for deposition of particles ranging in size from 0.0005 to 1.0 μm and the activity median aerodynamic diameter (AMAD) for deposition of particles from 0.1 to 100μm. Reference values of regional deposition are provided and guidance is given for extrapolating to specific individuals and populations under different levels of activity. This model also includes consideration of particle inhalability, a measure of the degree to which particles can enter the respiratory tract and be available for deposition. After deposition occurs in a given region, two different intrinsic clearance processes act competitively on the deposited particles: particle transport, including mucociliary clearance from the respiratory tract and physical clearance of particles to the regional lymph nodes; and absorption, including movement of material to blood and both dissolution-absorption and transport of ultrafine particles. Rates of particle clearance derived from studies with human subjects are assumed to be the same for all types of particles. The ICRP model provides average concentration or average number values on a regional basis, i.e., mass or number deposited or retained in the ET, TB, or A regions. Additionally, while the ICRP66 model was developed primarily for use with airborne radioactive

particles and gases in humans, its use for describing the dosimetry of inhaled mass of nonradioactive substances in humans is also appropriate.

The National Council on Radiation Protection (NCRP) has issued a human respiratory tract dosimetry model that was developed concurrently with the ICRP model (NCRP, 1997; Phalen et al.,1991). It addresses (1) inhalability of particles, (2) new subregions of the respiratory tract, (3) dissolution-absorption as an important aspect of the model, and (4) body size (and age). The proposed NCRP model defines the respiratory tract in terms of a naso-oro-pharyngo-laryngeal (NOPL) region, a TB region, a pulmonary (P) region, and the lung-associated lymph nodes (LN). Like the ICRP model, the deposition component of the model for the ET region is semi-empirical, based on equations derived from fitting experimental deposition data. The dimensional model used for the TB and A regions was that of Yeh and Schum (1980). The data from this model were used to estimate physical processes along a typical lung path (vice multiple-path; see MPPDep model description below) on a generation-by-generation basis. The rates of dissolution-absorption of particles and their constituents are derived from clearance data from humans and laboratory animals. The effect of body growth on particle deposition is also considered in the model, although particle clearance rates are assumed to be independent of age. The NCRP model currently available considers deposition only within these regions of the respiratory tract. As with the ICRP model, the NCRP model can be used for evaluating inhalation exposures to all types of particles. Comparison of regional deposition patterns estimated by the ICRP66 and the current NCRP models have been reported (Yeh et al., 1996). One principal difference between the models is the enhanced deposition of ultrafines in the tracheobronchial region predicted by the NCRP model compared with the ICRP model. This effect of enhanced deposition is claimed to be due to the entrance configuration of an airway bifurcation.

The model of Freijer et al. (1999) is a multiple-path particle deposition model (MPPDep) for the human respiratory tract that differs fundamentally from the above two models as described in the Introduction. Calculations from the model may be based on either single-path or multiple-path methods for tracking air flow and calculating aerosol deposition in the lung. The single-path method calculates deposition for a typical path, whereas the multiple-path method is capable of incorporating the asymmetry in lung structure and providing lobar-specific and airway-specific information. Two options are provided for idealizing the geometry of the human lung; one uses a symmetric geometry for the whole lung and the second option captures the asymmetry in the lobar structure, but treats the geometry within each lung lobe in a symmetric fashion. Both models are constructed using morphometric data compiled by Yeh and Schum (1980). Within each airway, deposition is calculated using theoretically derived efficiencies for deposition by diffusion (most relevant to DPM), sedimentation, and impaction within the airway

or airway bifurcation. Filtration of particulate aerosols by the head is determined using empirical efficiency functions. The model calculates deposition of monodisperse and polydisperse aerosols in the respiratory tract of both humans (and rats) for particles ranging from ultrafine (0.01 microns) to coarse (20 microns) sizes. Various breathing patterns may be simulated: endotratracheal, nasal, oral, and combined nasal and oral (oronasal). The exposure scenario may be constant or variable. For the variable scenario, the user may specify different breathing patterns either on an hourly basis during the day or activity patterns for variable time durations. Adjustment for inhalability of the particle is also included as an option. The software in this model provides results for the deposition fraction and mass deposited in the various regions of the respiratory tract in graphical and text formats.

The combined model of Yu et al. (1991) has a human component that will be discussed below.

3.6.2.3. *Animal Models*

Strom et al. (1988) developed a multicompartmental model for particle retention that partitioned the alveolar region into two compartments on the basis of the physiology of clearance. The alveolar region has a separate compartment for sequestered macrophages, corresponding to phagocytic macrophages that are heavily laden with particles and clustered, and consequently have significantly lowered mobility. The model has the following compartments: (1) tracheobronchial tree, (2) free particulate on the alveolar surface, (3) mobile phagocytic alveolar macrophages, (4) sequestered particle-laden alveolar macrophages, (5) regional lymph nodes, and (6) gastrointestinal tract. The model is based on mass-dependent clearance (the rate coefficients reflect this relationship), which dictates sequestration of particles and their eventual transfer to the lymph nodes. The transport rates between various compartments were obtained by fitting the calculated results to lung and lymph node burden experimental data for both exposure and postexposure periods. Because the number of fitted parameters was large, the model is not likely to provide unique solutions that would simulate experimental data from various sources and for different exposure scenarios. For the same reason, it is not readily possible to use this model for extrapolating to humans.

Stöber and co-workers have worked extensively in developing models for estimating retention and clearance of relatively insoluble respirable particles (as DPM) in the lung. Their most recent work (1994), a revised version of the POCK model, is a rigorous attempt to incorporate most of the physiologically known aspects of alveolar clearance and retention of inhaled relatively insoluble particles. Their multicompartmental kinetics model has five subcompartments. The transfer of particles between any of the compartments within the alveolar region is macrophage mediated. There are two compartments that receive particles cleared from

the alveolar regions: the TB tract and the lymphatic system. The macrophage pool includes both mobile and particle-laden immobilized macrophages. The model assumes a constant maximum volume capacity of the macrophages for particle uptake and a material-dependent critical macrophage load that results in total loss of macrophage mobility. Sequestration of those macrophages heavily loaded with a particle burden close to a volume load capacity is treated in a sophisticated manner by approximating the particle load distribution in the macrophages. The macrophage pool is compartmentalized in terms of numbers of macrophages that are subject to discrete particle load intervals. Upon macrophage death, the phagocytized particle is released back to the alveolar surface; thus phagocytic particle collection competes to some extent with this release back to the alveolar surface. This recycled particle load is also divided into particle clusters of size intervals defining a cluster size distribution on the alveolar surface. The model yields a time-dependent frequency distribution of loaded macrophages that is sensitive to both exposure and recovery periods in inhalation studies.

The POCK model also emphasizes the importance of interstitial burden in the particle overload phenomenon and indicates that particle overload (Section 3.4) is a function of a massive increase in particle burden of the interstitial space rather than total burden of the macrophage pool. The relevance of the increased particle burden in the interstitial space lies with the fact that this compartmental burden is not available for macrophage-mediated clearance and, therefore, persists even after cessation of exposure.

Although the POCK model is the most sophisticated in the physiological complexity it introduces, it suffers from a major disadvantage. Experimental retention studies provide data only on total alveolar and lymph node mass burdens of the particles as a function of time. The relative fraction of the deposition between the alveolar subcompartments in the Stöber model therefore cannot be obtained experimentally; the model thus uses a large number of parameters that are simultaneously fit to experimental data. Although the model predictions are tenable, experimental data are not currently available to substantiate the proposed compartmental burdens or the transfer rates associated with these compartments. Thus, overparameterization in the model leads to the possibility that the model may not provide a unique solution that may be used for a variety of exposure scenarios, and for the same reason, cannot be used for extrapolation to humans. Stöber et al. have not developed an equivalent model for humans; therefore the use of their model in our risk assessment for diesel is not attempted.

3.6.2.4. *Combined Models (for interspecies extrapolation)*

Currently available data for long-term inhalation exposures to poorly soluble particles (e.g., TiO_2, carbon black, and DPM) show that pulmonary retention and clearance of these particles are not adequately described by simple first-order kinetics and a single compartment

representing the alveolar macrophage particle burden. A two-compartment lung model that could be applied to both humans and animals was developed by Smith (1985) and includes alveolar and interstitial compartments. For uptake and clearance of particles by alveolar surface macrophages and interstitial encapsulation of particles (i.e., quartz dust), available experimental data show that the rate-controlling functions followed Michaelis-Menton type kinetics, whereas other processes affecting particle transfer are assumed to be linear. The model was used in an attempt to estimate interstitial dust and fibrosis levels among a group of 171 silicon carbide workers; the levels were then compared with evidence of fibrosis from chest radiographs. A significant correlation was found between estimated fibrosis and profusion of opacities on the radiographs. This model provides as many as seven different rate constants derived by various estimations and under various conditions from both animal and human sources. The model was intended for estimation of generalized dust described only as respirable without any other regard to sizing for establishing the various particle-related rate constants. As most of the described functions could not be validated with experimental data, the applicability of this model, especially for particulates in the size range of DPM, was unclear.

Yu et al. (1991; also reported as Yu and Yoon, 1990) have developed a three-compartment lung model that consists of tracheobronchial (T), alveolar (A), and lymph node (L) compartments (Appendix A, Figure A-1) and, in addition, considered filtration by a nasopharyngeal or head (H) compartment. The tracheobronchial compartment is important for short-term considerations, whereas long-term clearance takes place via the alveolar compartment. In contrast to the Stöber and Strom approaches, the macrophage compartment in the Yu model contains all of the phagocytized particles; that is, there is no separate (and hypothetical) sequestered macrophage subcompartment. Absorption by the blood (B) and gastrointestinal (G) compartments was also considered. Although the treatment of alveolar clearance is physiologically less sophisticated than that of the Stöber et al. model, the Yu model provides a more comprehensive treatment of clearance by including systemic compartments and the head, and including the clearance of the organic components of DPM in addition to the relatively insoluble carbon core.

In order to progress beyond the classical human ICRP66 retention model, Yu has addressed the impairment of long-term clearance (the overload effect) by using a set of variable transport rates for clearance from the alveolar region as a function of the mass of DPM in the alveolar compartment. A functional relationship for this was derived mathematically (Yu et al., 1989) based upon Morrow's hypothesis for the macrophage overload effect discussed earlier in the section on pulmonary overload. The extent of the impairment depends on the initial particle burden, with greater particulate concentration leading to slower clearance.

Within this model, DPM is treated as being composed of three material components: a relatively insoluble carbonaceous core, slowly cleared organics (10% particle mass), and fast-cleared organics (10% particle mass). Such a partitioning of organics was based on observations that the retention of particle-associated organics in lungs shows a biphasic decay curve (Sun et al., 1984; Bond et al., 1986). For any compartment, each of these components has a different transport rate. The total alveolar clearance rate of each material component is the sum of clearance rates of that material from the alveolar to the tracheobronchial, lymph, and blood compartments. In the Strom and Stöber models discussed above, the clearance kinetics of DPM were assumed to be entirely dictated by those of the relatively insoluble carbonaceous core. For those organic compounds that become dissociated from the carbon core, clearance rates are likely to be very different, and some of these compounds may be metabolized in the pulmonary tissue or be absorbed by blood.

The transport rates for the three components were derived from experimental data for rats using several approximations. The transport rates for the carbonaceous core and the two organic components were derived by fitting to data from separate experiments. Lung and lymph node burdens from the experiment of Strom et al. (1988) were used to determine the transport rate of the carbonaceous core. The Yu model incorporates the impairment of clearance by including a mass dependency in the transport rate. This mass dependency is easily extracted because the animals in the experiment were sacrificed over varying periods following the end of exposure.

It was assumed that the transport rates from the alveolar and lymph compartments to the blood were equal and independent of the particulate mass in the alveolar region. The clearance rates of particle-associated organics for rats were derived from the retention data of Sun et al. (1984) for B[a]P and the data of Bond et al. (1986) for nitropyrene adsorbed on diesel particles.

In their model Yu et al. (1991) make two important assumptions to carry out the extrapolation in consideration of inadequate human data. First, the transport rates of organics in the DPM do not change across species. This is based upon lung clearance data of inhaled lipophilic compounds (Schanker et al., 1986), where the clearance was seen to be dependent on the lipid/water partition coefficient. In contrast, the transport rate of the carbonaceous core is considered to be significantly species dependent (Bailey et al., 1982). DPM clearance rate is determined by two terms in the model (see Equation A-82 in Appendix A). The first, corresponding to macrophage-mediated clearance, is a function of the lung burden and is assumed to vary significantly across species. The second term, a constant, corresponding to clearance by dissolution, is assumed to be species independent. The mass-dependent term for humans is assumed to vary in the same proportion as in rats under the same unit surface particulate dose. The extrapolation is then achieved by using the data of Bailey et al. (1982) for the low lung burden limit of the clearance rate. This value of 0.0017/day was lower (i.e., slower)

than the rat value by a factor of 7.6. This is elaborated further in Appendix A. Other transport rates that have lung burden dependence are extrapolated in the same manner.

It should be noted that the Bailey et al. (1982) experiment in humans used fused monodisperse aluminosilicate particles of 1.9 and 6.1 μm aerodynamic diameters. Yu and co-workers have used the longer of the half-times observed in this experiment to obtain an alveolar human clearance rate (λ), of 0.00169/day. In using such data for DPM 0.2 μm in diameter, they have assumed the clearance of relatively insoluble particles to be independent of size over the range in diameter from 6.1 down to 0.2 μm. This assumption is consistent with observations and views currently in the literature indicating that clearance mechanisms are not particularly particle-size dependent (Morrow et al., 1967a,b; Snipes et al., 1983). That the linear dimensions of an alveolar macrophage, considered to be the principal means of clearance in the A region, are significantly larger, roughly 10 μm (Yu et al., 1996), and could therefore accommodate engulfment of a range of particle sizes also makes this assumption reasonable. Snipes (1979), however, has reported in rats a λ (converted here from half-time values) of 0.0022/day for 1 and 2 μm particles but a higher value of 0.0039/day for 0.4 μm particles indicating that clearance rates may indeed depend on size. In the absence of reliable data for 0.2 μm particles, the slower clearance rate pertaining to this larger particle size, i.e., 0.00169/day, is being used. Such a choice may underestimate the actual DPM clearance rate in humans. The resulting model output (i.e., lung DPM burden) from this slower rate would predict more DPM in the alveolar space than may actually be present at any given time. Therefore, use of this slower λ may be considered to be more protective of human health. Long-term clearance rates for particle sizes more comparable to DPM are available, e.g., iron oxide and polystyrene spheres (Waite and Ramsden, 1971; Jammet et al., 1978), but these data show a large range in the values obtained for half-lives or are based upon a very small number of trials, and therefore compare unfavorably with the quality of data from the Bailey experiment.

The deposition fractions of particulate matter in the pulmonary and tracheobronchial regions of the human lung remain relatively unchanged over the particle size range between 0.2 and 1.0 μm, on the basis of analysis done with the ICRP model (ICRP66, 1994). As the clearance of relatively insoluble particles is also likely to remain the same over this range, the dosimetry results in this report for the carbonaceous core component of DPM could also be extended to other particles in this size range within the $PM_{2.5}$. For respirable particles with diameters larger than this range, e.g., between 1.0 and 3.5 μm, the extent of the fraction deposited in the pulmonary region is unclear. Results from the ICRP66 (1994) model predict little change in human deposition for this diameter range, whereas the earlier model of Yu and Diu (1983) predicts a significant increase as reported in ICRP66 (1994). It is therefore unclear if either model would be applicable for particles in this larger-sized range without changing the value for

the deposition fractions. As will be presented and discussed below, regional deposition fractions of DPM-sized particles from the MPPDep, the ICRP66 (1994) and draft NCRP models compare favorably with the human alveolar deposition in humans specific for DPM, which has been estimated with the Yu model to be 7% to 13% (Yu and Xu, 1986).

Although there was good agreement between experimental and modeled results, this agreement follows a circular logic (as adequately pointed out by Yu and Yoon [1990]) because the same experimental data that figured into the derivation of transport rates were used in the model. Nevertheless, even though this agreement is not a validation, it provides an important consistency check on the model. Further experimental data and policy definitions on what constitutes validation would be necessary for a more formal validation.

The model showed that at low lung burdens, alveolar clearance is dominated by mucociliary transport to the tracheobronchial region, and at high lung burdens, clearance is dominated by transport to the lymphatic system. The head and tracheobronchial compartments showed quick clearance of DPM by mucociliary transport and dissolution. Lung burdens of both the carbonaceous core and organics were found to be greater in humans than in rats for similar periods of exposure.

The Yu and Yoon (1990) version of the model provides a parametric study of the dosimetry model, examining variation over a range of exposure concentrations, breathing scenarios, and ventilation parameters; particle mass median aerodynamic diameters; and geometric standard deviations of the aerosol size distribution. It examines how lung burden varies with age for exposure over a lifespan, provides dosimetry extrapolations to children, and examines changes in lung burden with lung volume. The results showed that children would exhibit more diminished alveolar clearance of DPM at high lung burden than adults when exposed to equal concentrations of DPM. These features make the model easy to use in risk assessment studies. The reader is referred to Appendix A for further details on the model and for analyses of the sensitivity of the model to change in parameter values.

The Yu model presents some uncertainties in addition to those discussed earlier in the context of particle size dependence of clearance rate. The reports of Yu and Yoon (1990) as well as Yu et al. (1991) underwent extensive peer review; we list below the most important among the model uncertainties discussed by the review panel. The experimental data used by the Yu model for adsorbed organics used passively adsorbed radiolabeled compounds as surrogates for combustion-derived organics. These compounds may adhere differently to the carbon core than do those formed during combustion. Yu has estimated that slowly cleared organics represent 10% of the total particle mass; the actual figure could be substantially less; the reviewers estimate that the amount of tightly bound organics is probably only 0.1% to 0.25% of the particle mass.

The model was based upon the experimental data of Strom et al. (1988), where Fischer-344 rats were exposed to DPM at a concentration of 6.0 mg/m^3 for 20 h/day and 7 days/week for periods ranging from 3 to 84 days. Such exposures lead to particle overload effects in rats, whereas human exposure patterns are usually to much lower levels at which overload will not occur. Parameters obtained by fitting to data under the conditions of the experimental scenario for rats may not be optimal for the human exposure and concentration of interest.

The extrapolation of retained dose from rats to humans assumed that the macrophage-mediated mechanical clearance of the DPM varies with the specific particulate dose to the alveolar surface in the same proportion in humans and in rats, whereas clearance rates by dissolution were assumed to be invariant across species. These assumptions have not been validated.

It should also be noted that the Yu et al. (1991) model does not possess a formal interstitial compartment although the lymph nodes, which would be the repository of particles from the interstitium, are represented. The work of Nikula et al. (1997a,b) and of Kuempel (2000) provide compelling information on the significance of an extensive interstitilization process in primates and in humans. Kuempel (2000) developed a lung dosimetry model to describe the kinetics of particle clearance and retention in coal miners' lungs. Models with overloading of lung clearance, as observed in rodent studies, were found to be inadequate to describe the end-of-life lung dust burdens in those miners. The model that provided the best fit to the human data included a sequestration process representing the transfer of particles to the interstitium. These findings are consistent with a study showing reduced lung clearance of particles in retired coal miners (Freedman and Robinson, 1988) and with studies showing increased retention of particles in the lung interstitium of humans and nonhuman primates compared to rodents exposed to coal dust and/or DE (Nikula et al., 1997a,b). These findings are also consistent with the established observation that humans and primates clear particles slowly from the alveolar interstitium compared with rates in rodent species such as rats and mice (Hsieh and Yu, 1998). Because several aspects of the Yu model have not been validated on human data and because it does not include a formal interstitial compartment, it is acknowledged that this model may therefore have some uncertainty concerning the lung burdens in humans exposed to occupational levels of dust. However, it is also not known whether the model based on coal miner data (Kuempel, 2000) would also describe the clearance and retention processes in the lungs of humans with exposures to particles at lower environmental concentrations, or to submicrometer particles such as DE particulate. Further investigation of these issues is needed.

3.6.2.5. *Use of the Yu et al. (1991) Model for Interspecies Extrapolation*

In addressing the objectives of this chapter, i.e., consideration of what is known and applicable to DPM concerning particle disposition and the bioavailability of adsorbed organics on DPM, it is apparent that the database is considerable for both the processes involved in particle dosimetry and for DPM. This information makes the goal of predicting a human internal dose from animal data through a model utilizing this database both feasible and appropriate.

In their charge to EPA through "Science and Judgment in Risk Assessment" (NRC, 1995), the National Research Council opines that EPA should have principles for judging when and how to depart from default options. The extensive data presented in this chapter their scientific validity, and the limitations of the current default procedures provide a basis for departing from the default options currently identified by the Agency for extrapolating from animals to humans. The default option of assuming external concentrations of DPM in animal studies as being representative of a human concentration (and an equivalent internal dose) is clearly not adequate given the differences in the basic processes of deposition and clearance between animals and humans documented by these data. Use of an alternate default option, the Agency's dosimetric adjustment procedures for inhaled particles in animal-to-human scenarios (described in U.S. EPA, 1994), is also inadequate as only deposition is predicted and then only down to an MMAD of 0.5 μm, whereas the MMAD of DPM is typically 0.2 μm or smaller. Models have been described in this section that consider both deposition and retention specifically for DPM in both laboratory animals and in humans. These points provide justification for moving away from default options and utilizing the best scientific information available (i.e., that integrated into deposition/clearance models) in performing the animal-to-human extrapolation.

Evaluation of the various models discussed in this chapter should be considered from the aspect of both the rat and the human. For rats it is fairly clear that the rat portion of the model of Yu et al. (1991) is the most appropriate because it is based on data, especially extensive information on lung burdens, from actual DPM exposures. The model provides for both deposition and integrated clearance for DPM as well as for two classes of adsorbed organics. The transport rates in the Yu model are derived directly from experiments with DPM exposed rats.

For humans, however, several models are available and discussed above, none of which is based on DPM-specific data. Deposition, but not clearance, modules are available for all models, and Table 3-3 is an attempt to compare deposition projections of the various models to the extent possible for particles in the range of characteristics of size, distribution, and density of DPM. Intake parameters such as breathing rates and minute volumes were also matched among the various models. As alluded to above and shown in Table 3-3, DPM deposition is predicted to

Table 3-3. Model comparison for deposition of DPM under equivalent conditions

Compartment	Yu[a]	ICRP66[b]	MPPDep1.11[c]	NCRP[d]
A (model designation)	13% (A)	14.1% (AI)	16.6% (P)	17.3% (P)
ET (model designation)	8% (H)	6% ($ET_1 + ET_2$)	8.7% (H)	6.6% (NOPL)
TB (model designation)	8% (TB)	4% (BB + bb)	7.2% (TB)	6.2% (TB)
Total	29%	24.1%	32.5%	30.1%

[a]Yu and Xu, 1987 (estimated from Figures 1 and 3).
[b]Jarvis et al., 1996.
[c] Freijer et al., 1999 (The Yeh-Schum 5-lobe and URT volume of 50 mL options were used.)
[d]NCRP, 1997.
Note: Particle characteristics were set at 0.2 MMAD, 2.4 sigma g, 1.5 shape factor (equivalent to 0.3 packing factor), density 1.5 and a concentration of 5 $\mu g/m^3$. Lung parameters were set at 15 breaths per minute, a tidal volume of 0.926 L/hr, and a functional residual capacity (FRC) of 3300 mL.

occur in all regions of the respiratory tract but, because diffusion would be the most likely mechanism of deposition, is most prominent in the alveolar region. When run under equivalent conditions, all models show that higher deposition in the alveolar region is higher, generally by a factor of about 2, than the other regions of the respiratory tract. The percentages projected by the different models to be deposited in the alveolar regions were all similar to one another with a range of only 13% for the Yu model to 17.3 % for the NCRP model. The total deposition of DPM-like particles predicted by the models was also very similar at around 30%. Only the ICRP model differed appreciably from the others in total deposition by a factor of about 1.3 less at 22.9%. Due to its verity and completeness in representation of the lung, the MPPDep model could be considered the most theoretically advanced of these deposition models and, presumably, the most accurate. It can be seen that, at least at the concentration tested, the Yu results and those of the MPPDep model could be judged very similar if not the same in the ET and TB regions, albeit with the MPPDep predicting slightly more deposition in the A region. Based on this limited analysis, total and regional DPM deposition in the human respiratory tract predicted by the Yu model appear similar to other available human models.

Further model comparison may be undertaken for those human models that have clearance as well as deposition modules available; from Table 3-3, these include the Yu et al. (1991) and ICRP66 models. Therefore, the human lung burden outputs of these two models were compared under equivalent physiological parameters, particle characteristics, and duration (70 years) and concentrations of exposure (Figure 3-9).

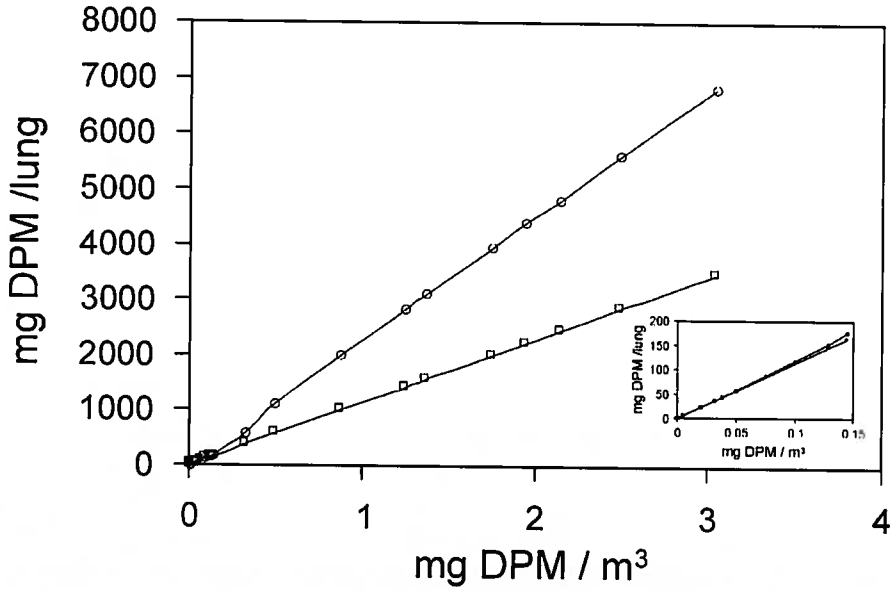

Figure 3-9. Modeled estimates of lung burden in humans after a simulated lifetime exposure to DPM using the Yu et al. (1991;[o]) and ICRP66 (□) models. Simulations include both deposition and clearance. Simulations were run for 70 years using a respiratory frequency of 15 min^{-1} and a tidal volume of 0.926 L/breath for a total daily air intake of 20 m^3/day for the various concentrations shown. Particle characteristics in the ICRP66 model, including MMAD, σ_g, density, and packing/shape factor were all matched to those used in the Yu model.

At DPM concentrations up to about 0.2 mg/m^3, the outputs (lung burden) from these two models are essentially identical (see insert) indicating little if any difference between them in this concentration range. This observation is consonant with the minor differences noted in deposition (Table 3-3).

Above 0.2 mg/m^3 DPM, both models continue to demonstrate a monotonic increase in lung burden with increasing concentration. However, the output of the Yu et al. (1991) model begins to diverge markedly from the burdens predicted by the ICRP model such that the Yu model predicts a greater burden for a given concentration of DPM than does the ICRP66 model. This situation would be predicted based on the assumption in the human portion of the Yu model of a concentration-dependent macrophage inhibition and particle overload occurring in humans; such an inhibition would result in impaired clearance processes, thereby allowing for a greater accumulation of material in the lung with increasing concentrations of DPM. This assumption is not made in the ICRP model, and materials are therefore not predicted to accumulate in the lung to the extent predicted by the Yu model.

Based on this limited analysis of models and the predictions from them for both deposition and clearance of DPM in humans, the model of Yu et al. (1991) can be seen to perform similarly to other available state-of-the-art models. The Yu model(s) are chosen for further analysis for the purposes of this document primarily because the animal portion of the model is based on DPM-specific data and the human components of the model have both deposition and clearance capacities that do not appear different from other available human respiratory tract models.

3.6.2.6. *Model Variability*

As demonstrated in Table 3-3 and Figure 3-9, there appears to be little variability among state-of-the-art models available for predicting disposition (both for deposition and for clearance integrated with deposition) of low levels of DPM (i.e., up to about 200 $\mu g/m^3$) in the respiratory tracts of humans.

Intersubject variability and its relationship to model output, however, is acknowledged in the ICRP model for deposition efficiencies (ICRP, 1994). This variability, recognized as substantial by ICRP, is addressed through use of scaling constants derived from estimates of the upper and lower confidence bounds for regional deposition efficiencies, with the scaling constants representing the variability in the population. It should be noted that the same philosophy is inherent in dose-response methodologies such as the RfC, where variability in the population is accommodated by a 10-fold uncertainty factor rather than by scaling constants. Inspection of data in ICRP66 (e.g., Figures D-4 through D-7 in the ICRP reference) on nasal and extrathoracic deposition in adult males shows that these upper and lower boundaries on output due to intersubject variability are considerably less than 10-fold different from one another. Thus, dividing model outputs by a factor of 10 such as is done in RfC derivation may well be inclusive of not only intersubject variability but also of any model-to-model variability as they exist currently.

3.6.2.7. *Model Comparison — Estimations of Deposition of Adsorbed Organics*

The data presented in Table 3-3 may be viewed as single-breath estimates of DPM deposition patterns in the various regions of the human lung under the breathing patterns and conditions described in the table for the different models considered in this report. From these data it is possible to estimate the total mass of DPM deposited in the pulmonary region under a given set of conditions. Furthermore, if the fraction of organics present on DPM and their ability to be desorbed or eluted from the DPM are assumed also to be the same, then these deposition data could be used to estimate the dose of organics to pulmonary tissues. Such a comparison would not only yield an estimate of the amount of organics but also lend a further comparison

between the different human models. This exercise was performed for humans breathing 5 μg DPM/m^3 continuously, and the results are presented in Table 3-4 below.

Table 3-4. Comparative model estimates of DPM deposition in human lungs from exposure to 5 μg/m^3 continuously for one year

	A	B	C	D
Human deposition model	Alveolar Dep[a]	μg DPM deposited/year[b]	μg organics deposited/year[c]	μg carcinogenic PAH deposited/year[d]
Yu et al. (1991)	13%	4745	598	1.82
ICRP66	14.1%	5147	649	1.98
MPPDep	16.6%	6059	763	2.33
NCRP	17.3%	6315	796	2.43

[a]Alveolar deposition fractions predicted for DPM (Yu et al., 1991) and for particles with DPM characteristics (from Table 3-3). No clearance is included in this calculation.

[b]A total air intake of 20 m^3/day is assumed. These numbers were obtained by factoring 20 m^3 × 5 μg DPM/m^3 × Alveolar deposition % (column A) × 365 days/year.

[c]In three samples of DPM extract, DPM-associated organics were noted as being 11.1%, 14.7%, and 12.1% wt. organics/wt. DPM (Tong and Karasek, 1984) with the average being 12.6%; column B is factored by this average to generate column C.

[d]Those seven PAHs identified as being carcinogenic either to humans or to animals (U.S. EPA, 1993) were summed from the data of Tong and Karasek (1984), where they are reported as a concentration in extract from DPM-associated organics. In three different samples, the content of these 7 PAHs was noted as 4739, 2054, and 2360 ng/mg of organic extract, with the average being 3051 ng/mg (3.051 μg/mg) organic extract. This average value was factored with Column C (in mg) to generate column D.

Note: Estimates from different human deposition models of the total amount of DPM-associated organics deposited in the pulmonary regions in humans breathing DPM at 5 μg/m^3 continuously for 1 year.

As may be expected, the relatively minor differences (17.3 % / 13% = 1.3) in the deposition of DPM among the different human models leads to similarly minor differences in projections of dose of carcinogenic PAHs to the lung at a relatively low concentration of 5 μg/m^3 DPM. Somewhat unexpected is the small absolute quantity of carcinogenic PAH that may be delivered to the lung tissues under the conditions of exposure to DPM in this exercise. It should be noted that exercises similar to this have been carried out by others, e.g., Valberg and Watson (1999). However, the possibility that high concentrations of DPM may result in localized areas of deposition (such as the conducting airways), the fact that human exposures may be

considerably greater than those presupposed in the exercise (e.g., 5 μg/m^3), the nature of the assays (i.e., in vitro in Chapter 4 vs. actual inhalation exposures), and the findings that DNA adducts may result from other known noncarcinogens such as carbon black (Bond et al., 1990) make the interpretation of such exercises problematic and their meaning unclear.

3.7. SUMMARY AND DISCUSSION

The most consistent historical measure of exposure for DE is DPM in units of μg or mg particles/m^3, with the underlying assumption that all components of diesel emissions (e.g., organics in the form of volatilized liquids or gases) are present in proportion to the DPM mass. DPM is used as the basic dosimeter for effects from various scenarios such as chronic and acute exposures as well as for different endpoints such as irritation, fibrosis, or even cancer. There is, however, little evidence currently available to prove or refute DPM as being the most appropriate dosimeter.

DPM dose to the tissue is related to the extent of the deposition and clearance of DPM. DPM may deposit throughout the respiratory tract via sedimentation or diffusion, with the latter being prevalent in the alveolar region. Particles that deposit upon airway surfaces may be cleared from the respiratory tract completely or may be translocated to other sites by regionally distinct processes that can be categorized as either absorptive (i.e., dissolution) or nonabsorptive (i.e., transport of intact particles via mucociliary transport). Other mechanisms that can affect retention of DPM include endocytosis by alveolar lining cells and interstitialization, which lead to the accumulation of DPM in the interstitial compartment of the lung and subsequent translocation of DPM to lymph nodes; interstitialization of poorly soluble particles may be prominent in primates and humans compared with rodents, although different rates for this path could also explain observed results. For poorly soluble particles such as DPM, species-dependent rate constants exist for the various clearance pathways that can be modified by factors such as respiratory tract disease.

In rats, prolonged exposure to high concentrations of particles will result in particle overload, a condition that is defined as the overwhelming of macrophage-mediated clearance by the deposition of particles at a rate exceeding the capacity of that clearance pathway. This condition seems to begin to occur in rats when the pulmonary dust burden exceeds about 1 mg particles/g lung tissue. On the other hand, there is no clear evidence for particle overload in humans. Macrophage-mediated clearance is slower in humans than in rats, and kinetics relating to interstitialization of poorly soluble particulate matter may have a greater consequence in humans than in rats.

The degree of bioavailability of the organic fraction of DPM is still somewhat uncertain. However, reports of DNA alterations in occupationally exposed workers, as well as results of

animal studies using radiolabeled organics deposited on DPM, indicate that at least a fraction of the organics present are eluted prior to particle clearance. Carcinogenic organics eluted in regions where diffusion may be a relatively long process, such as in the conducting airways vs the alveolar region, may remain in the lung long enough to be metabolized to an active form or to interact directly with vital cellular components. The current information suggests that DPM-associated organics could be involved in a carcinogenic process, although the quantitative data are far from adequate to make any firm conclusions.

Use of laboratory animal data in an assessment meant to be applied to humans obligates some form of interspecies extrapolation. Review and evaluation of the considerable, specific database in humans and animals on disposition of DPM, its adsorbed organics, and other poorly soluble particles led to the judgment that default options available for interspecies dosimetry adjustment could be set aside for more scientifically valid, DPM-specific processes. Refinement of this process led to the evaluation of several applicable dosimetry models that in turn led to the identification and choice of the Yu et al. (1991) model to conduct interspecies extrapolation. This model has a three-compartment lung consisting of tracheobronchial, alveolar, and lymph node compartments. It treats DPM as being composed of the insoluble carbonaceous core, slowly cleared organics, and fast-cleared organics, and considers in an integrative manner the simultaneous processes of both deposition and clearance through empirical data derived from both laboratory animals and humans. Also, the model has some limited consideration of model variability in its outputs describing dose to the lung. Major assumptions made in this model include that transport rates of organics in DPM do not change across species and that the transport rate of the carbonaceous core is species dependent, with the clearance rate varying with the dose to the alveolar surface in the same proportion in humans as in rats. Limitations of the model include the lack of definitive information on variability and, quite possibly, the lack of a formal interstitial compartment that may be of consequence in humans. The basis of this model is to derive an internal dose from an external DPM concentration by utilizing species-specific physiological and pharmacokinetic parameters and, as such, is considered to have addressed the pharmacokinetic aspects of interspecies dosimetry. This aspect of the model addresses some of the critical data needs for the quantitative analysis of noncancer effects from DPM, the subject of Chapter 6.

As parallels have been drawn between DPM and $PM_{2.5}$ in other chapters, it is perhaps appropriate to compare them also from the aspect of dosimetry. Obvious comparisons include the nature of the particle distribution, defined artificially for $PM_{2.5}$ as compared with the thorough characterization of DPM for both MMAD (which, at around 0.2 μm, is typically more than an order of magnitude less than the $PM_{2.5}$ cutoff and which, more properly, should be termed a mass median thermodynamic diameter, an MMTD) and geometric standard deviation. It is clear that a

larger portion of $PM_{2.5}$ particles than DPM would be above the aerodynamic equivalent diameter (d_{ae}) of 0.5 μm, which is often considered as a boundary between diffusion and aerodynamic mechanisms of deposition. This would imply that a somewhat larger portion of DPM may pass on to the lower respiratory tract than would $PM_{2.5}$. Alveolar deposition in humans specific for DPM has been estimated with the Yu model to be 7%-13% (Yu and Xu, 1986), a figure that is consistent with deposition predictions of other human models (see Table 3-3). This fractional deposition may be compared to one calculated for $PM_{2.5}$ and reported in U.S. EPA (1996a); assuming a MMAD of 2.25 μm and a geometric standard deviation of 2.4, a fractional alveolar deposition of 10.2% was reported. This value is within the range and quite comparable to that obtained by Yu and Xu (1986), indicating that little difference may exist in alveolar deposition between DPM and $PM_{2.5}$, at least for this assumed geometric standard deviation.

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4. MUTAGENICITY

The application of mutagenicity data to the question of the potential carcinogenicity of diesel emissions is based on the premise that genetic alterations are found in all cancers and that several of the chemicals found in diesel emissions possess mutagenic activity in a variety of genetic assays. These genetic alterations can be produced by gene mutations, deletions, translocations, aneuploidy, or amplification of genes; hence no single genotoxicity assay should be expected to predict rodent carcinogenicity. Additionally, because of the inherent biological differences of measured endpoints, both within genotoxicity assays and between genotoxicity assays and cancer bioassays, a direct extrapolation should not be expected (see Brusick [1987] for a more detailed discussion). Indeed, most genotoxicity data are generated with in vitro assays that frequently employ concentrations of test agent that may be orders of magnitude greater than encountered in environmental situations. With diesel emissions or other mixtures, additional complications arise because of the complexity of the material being tested.

Since 1978, more than 100 publications have appeared in which genotoxicity assays were used with diesel emissions, the volatile and particulate fractions (including extracts), or individual chemicals found in diesel emissions. The Huisingh et al. (1978) report not only identified mutagenic activity in salmonella in several fractions of diesel particular mater (DPM) extracts, but also indicated that the mutagenic activity, especially quantitatively, was affected by the extraction solvent as well as method and length of storage. Much of the ensuing research employed bioassays (most commonly salmonella TA98 without S9) to evaluate (1) extraction procedures, (2) fuel modifications, (3) bioavailability of chemicals from DPM, and (4) exhaust filters or other modifications and other variables associated with diesel emissions. The interest in the contribution of mutagens to carcinogenicity was high in the early 1980s and the lack of long- term rodent carcinogenicity information on diesel emissions led to the use of semiquantitative mutagenicity (and in vitro cell transformation) data from diesel emissions and epidemiology based cancer potency estimations to derive a comparative potency estimate for diesel emissions first published by Albert et al. (1983) and more fully discussed in Appendix C of this report.

As indicated in Chapter 2, the number of chemicals in diesel emissions is very large. Many of these have been determined to exhibit mutagenic activity in a variety of assay systems (see Table II. in Claxton, 1983). Although a detailed discussion of those data is beyond the scope of this document, some of the mutagenically active compounds found in the gas phase are ethylene, benzene, 1,3-butadiene, acrolein and several PAHs (see Table 2-21). Of the particle-associated chemicals, several PAHs and nitro-PAHs have been the focus of mutagenic investigations both in bacteria and in mammalian cell systems (see Table 2-22). Several review

articles, some containing more detailed descriptions of the available studies, are available (Claxton, 1983; Pepelko and Peirano, 1983; International Agency for Research on Cancer, 1989; Shirnamé-Moré, 1995). Discussions of genotoxicity in the proceedings of several symposia on the health effects of diesel emissions (U.S. EPA, 1980; Lewtas, 1982; Ishinishi et al., 1986) are also available.

4.1. GENE MUTATIONS

Huisingh et al. (1978) demonstrated that dichloromethane extracts from DPM were mutagenic in strains TA1537, TA1538, TA98, and TA100 of *S. typhimurium*, both with and without rat liver S9 activation. This report contained data from several fractions as well as DPM from different vehicles and fuels. Similar results with diesel extracts from various engines and fuels have been reported by a number of investigators using the salmonella frameshift-sensitive strains TA1537, TA1538, and TA98 (Siak et al., 1981; Claxton, 1981; Dukovich et al., 1981; Brooks et al., 1984). Similarly, mutagenic activity was observed in salmonella forward mutation assays measuring 8-azaguanine resistance (Claxton and Kohan, 1981) and in *E. coli* mutation assays (Lewtas, 1983).

One approach to identifying significant mutagens in chemically complex environmental samples such as diesel exhaust or ambient particulate extracts is the combination of short-term bioassays with chemical fractionation (Scheutzle and Lewtas, 1986). The analysis is most frequently carried out by sequential extraction with increasingly polar or binary solvents. Fractionation by silica-column chromatography separates compounds by polarity or into acidic, basic, and neutral fractions. The resulting fractions are too complex to characterize by chemical methods, but the bioassay analysis can be used to determine fractions for further analysis. In most applications of this concept, salmonella strain TA98 without the addition of S9 has been used as the indicator for mutagenic activity. Generally, a variety of nitrated polynuclear aromatic compounds have been found that account for a substantial portion of the mutagenicity (Liberti et al., 1984; Schuetzle and Frazer, 1986; Schuetzle and Perez, 1983). However, not all bacterial mutagenicity has been identified in this way, and the identity of the remaining mutagenic compounds remains unknown. The nitrated aromatics thus far identified in diesel engine exhaust (DE) were the subject of review in the IARC monograph on DE (International Agency for Research on Cancer, 1989). In addition to the simple qualitative identification of mutagenic chemicals, several investigators have used numerical data to express mutagenic activity as activity per distance driven or mass of fuel consumed. These types of calculations have been the basis for estimates that the nitroarenes (both mono- and dinitropyrenes) contribute a significant amount of the total mutagenic activity of the whole extract (Nishioka et al., 1982; Salmeen et al., 1982; Nakagawa et al., 1983). In a 1983 review, Claxton discussed a number of

factors that affected the mutagenic response in salmonella assays. Citing the data from the Huisingh et al. (1978) study, the author noted that the mutagenic response could vary by a factor of 100 using different fuels in a single diesel engine. More recently, Crebelli et al. (1995) used salmonella to examine the effects of different fuel components. They reported that although mutagenicity was highly dependent on aromatic content, especially di- or triaromatics, there was no clear effect of sulfur content of the fuel. Later, Sjögren et al. (1996) using multivariate statistical methods with ten diesel fuels concluded that the most influential chemical factors in salmonella mutagenicity were sulfur contents, certain PAHs (1-nitropyrene) and naphthenes.

Matsushita et al. (1986) tested particle-free DE gas and a number of benzene nitro-derivatives and polycyclic aromatic hydrocarbons (PAHs) (many of which have been identified as components of DE gas). The particle-free exhaust gas was positive in both TA100 and TA98, but only without S9 activation. Of the 94 nitrobenzene derivatives tested, 61 were mutagenic, and the majority showed greatest activity in TA100 without S9. Twenty-eight of 50 PAHs tested were mutagenic, all required the addition of S9 for detection, and most appeared to show a stronger response in TA100. When 1,6-dinitropyrene was mixed with various PAHs or an extract of heavy-duty (HD) DE, the mutagenic activity in TA98 was greatly reduced when S9 was absent but was increased significantly when S9 was present. These latter results suggested that caution should be used in estimating mutagenicity (or other toxic effects) of complex mixtures from the specific activity of individual components.

Mitchell et al. (1981) reported mutagenic activity of DPM extracts of diesel emissions in the mouse lymphoma L5178Y mutation assay. Positive results were seen both with and without S9 activation in extracts from several different vehicles, with mutagenic activity only slightly lower in the presence of S9. These findings have been confirmed in a number of other mammalian cell systems using several different genetic markers. Casto et al. (1981), Chescheir et al. (1981), Li and Royer (1982), and Brooks et al. (1984) all reported positive responses at the HPRT locus in Chinese hamster ovary (CHO) cells. Morimoto et al. (1986) used the APRT and Oua^r loci in CHO cells; Curren et al. (1981) used Oua^r in BALB/c 3T3 cells. In all of these studies, mutagenic activity was observed without S9 activation. Liber et al. (1981) used the thymidine kinase (TK) locus in the TK6 human lymphoblast cell line and observed induced mutagenesis only in the presence of rat liver S9 when testing a methylene chloride extract of DE. Barfknecht et al. (1982) also used the TK6 assay to identify some of the chemicals responsible for this activation-dependent mutagenicity. They suggested that fluoranthene, 1-methylphenanthrene, and 9-methylphenanthrene could account for over 40% of the observed activity.

Morimoto et al. (1986) injected DPM extracts (250 to 4,000 mg/kg) into pregnant Syrian hamsters and measured mutations at the APRT locus in embryo cells cultivated 11 days after i.p.

injection. Although neutral fractions from both light-duty (LD) and HD particle extracts resulted in increased mutation frequency at 2,000 and 4,000 mg/kg, the response at 1,000 mg/kg was not different from controls. Also, because the authors did not present data on toxicity or cloning efficiency, the value of the apparent positive findings at extremely high concentrations is uncertain at best. Belisario et al. (1984) applied the Ames test to urine from Sprague-Dawley rats exposed to single applications of DPM administered by gastric intubation, i.p. injection, or s.c. gelatin capsules. In all cases, dose-related increases were seen in TA98 (without and with S9) from urine concentrates taken 24 h after particle administration. Urine from Swiss mice exposed by inhalation to filtered exhaust (particle concentration 6 to 7 mg/m^3) for 7 weeks (Pereira et al., 1981a) or Fischer 344 rats exposed to DPM at a concentration of 1.9 mg/m^3 for 3 months to 2 years (Ong et al., 1985) was negative in salmonella strains.

Schuler and Niemeier (1981) exposed drosophila males in a stainless steel chamber connected to the 3 m^3 chamber used for the chronic animal studies at EPA (see Hinners et al., 1980 for details). Flies were exposed for 8 h and mated to untreated females 2 days later. Although the frequency of sex-linked recessive lethals from treated males was not different from that of controls, the limited sample size precluded detecting less than a threefold increase over controls. The authors noted that, because there were no signs of toxicity, the flies might tolerate exposures to higher concentrations for longer time periods.

Driscoll et al. (1996) exposed Fischer 344 male rats to aerosols of carbon black (1.1, 7.1, and 52.8 mg/m^3) or air for 13 weeks (6 hr/day, 5 days/week) and measured *hprt* mutations in alveolar type II cells in animals immediately after exposure and at 12 and 32 weeks after the end of exposure. Both of the two higher concentrations resulted in significant increases in mutant frequency. Whereas the mutant frequency from the 7.1 mg/m^3 group returned to control levels by 12 weeks, the mutant frequency of the high-exposure group was still higher than controls even after 32 weeks. Carbon black particles have very little adsorbed PAHs, hence a direct chemically induced mechanism is highly unlikely. Induction of *hprt* mutations were also observed in rat alveolar epithelial cells after intratracheal instillation with carbon black, α-quartz, and titanium dioxide (Driscoll et al., 1997). All three types of particles elicited an inflammatory response as shown by significant increases of neutrophils in bronchoalveolar lavage (BAL) fluid. Culturing the BAL from exposed rats with a rat lung epithelial cell line also resulted in elevation of *hprt* mutational response. This response was effectively eliminated when catalase was included in the incubation mixture, providing evidence for cell-derived oxidative damage. Recently, Sato et al. (2000) exposed male Big Blue transgenic F344 rats to diluted DE (1 and 6 mg/m^3 suspended particle concentration) for 4 weeks. Mutant frequency in lung DNA was significantly elevated (4.8x control) at 6 mg/m^3 but not at 1 mg/m^3. Lung DNA adduct levels measured by ^{32}P-postlabeling and 8-hydroxydeoxyguanosine measured by HPLC

were elevated at both particle concentrations, but to a lesser extent than mutant frequencies. Sequence analysis of mutants indicated that some, but not all, of the mutations could be explained by an oxidative damage mechanism.

Specific-locus mutations were not induced in (C3H × 101)F_1 male mice exposed to DE 8 h/day, 7 days/week for either 5 or 10 weeks (Russell et al., 1980). The exhaust was a 1:18 dilution and the average particle concentration was 6 mg/m^3. After exposure, males were mated to T-stock females and matings continued for the reproductive life of the males. The results were unequivocally negative; no mutants were detected in 10,635 progeny derived from postspermatogonial cells or in 27,917 progeny derived from spermatogonial cells.

Hou et al. (1995) measured DNA adducts and *hprt* mutations in peripheral lymphocytes of 47 bus maintenance workers and 22 control individuals. All were nonsmoking men from garages in the Stockholm area and the exposed group consisted of 16 garage workers, 25 mechanics, and 6 other garage workers. There were no exposure data, but the three groups were considered to be of higher to lower exposure to diesel engine exhaust. Levels of DNA adducts determined by ^{32}P-postlabeling were significantly higher in workers than controls (3.2 versus 2.3 × 10^{-8}), but *hprt* mutant frequencies were not different 8.6 versus 8.4 × 10^{-6}). Although group mean mutant frequencies were not different, both adduct level and mutagenicity were highest among the 16 most exposed and mutant frequency was significantly correlated with adduct level. All individuals were genotyped for glutathione transferase GSTM1 and aromatic amino transferase NAT2 polymorphism. Neither GSTM1 nulls nor NAT2 slow acetylators exhibited effects on either DNA adducts or *hprt* mutant frequencies.

4.2. CHROMOSOME EFFECTS

Mitchell et al. (1981) and Brooks et al. (1984) reported increases in sister chromatid exchanges (SCE) in CHO cells exposed to DPM extracts of emissions from both LD and HD diesel engines. Morimoto et al. (1986) observed increased SCE from both LD and HD DPM extracts in PAH-stimulated human lymphocyte cultures. Tucker et al. (1986) exposed human peripheral lymphocyte cultures from four donors to direct DE for up to 3 h. Exhaust was cooled by pumping through a plastic tube about 20 feet long; airflow was 1.5 L/min. Samples were taken at 16, 48, and 160 min of exposure. Cell cycle delay was observed in all cultures; significantly increased SCE levels were reported for two of the four cultures. Structural chromosome aberrations were induced in CHO cells by DPM extracts from a Nissan diesel engine (Lewtas, 1983) but not by similar extracts from an Oldsmobile diesel engine (Brooks et al., 1984).

DPM dispersed in an aqueous mixture containing dipalmitoyl lecithin (DPL), a component of pulmonary surfactant or extracted with dichloromethane (DCM) induced similar

responses in SCE assays in Chinese hamster V79 cells (Keane et al., 1991), micronucleus tests in V79 and CHO cells (Gu et al., 1992), and unscheduled DNA synthesis (UDS) in V79 cells (Gu et al., 1994). After separating the samples into supernatant and sediment fractions, mutagenic activity was confined to the sediment fraction of the DPL sample and the supernatant of the DCM sample. These findings suggest that the mutagenic activity of DPM inhaled into the lungs could be made bioavailable through solubilization and dispersion of pulmonary surfactants. In a later study in the same laboratory, Liu et al. (1996) found increased micronuclei in V79 cells treated with crystalline quartz and a noncrystalline silica, but response was reduced after pretreatment of the particles with the simulated pulmonary surfactant.

Pereira et al. (1981a) exposed female Swiss mice to DE 8 h/day, 5 days/week for 1, 3, and 7 weeks. The incidence of micronuclei and structural aberrations was similar in bone marrow cells of both control and exposed mice. Increased incidences of micronuclei, but not SCE, were observed in bone marrow cells of male Chinese hamsters after 6 months of exposure to DE (Pereira et al., 1981b).

Guerrero et al. (1981) observed a linear concentration-related increase in SCE in lung cells cultured after intratracheal instillation of DPM at doses up to 20 mg/hamster. However, they did not observe any increase in SCE after 3 months of inhalation exposure to DE particles (6 mg/m^3).

Pereira et al. (1982) measured SCE in embryonic liver cells of Syrian hamsters. Pregnant females were exposed to DE diluted with air 1:9 to contain about 12 mg/m^3 particles from days 5 to 13 of gestation or injected intraperitoneally with diesel particles or particle extracts on gestational day 13 (18 h before sacrifice). Neither the incidence of SCE nor mitotic index was affected by exposure to DE. The injection of DPM extracts but not DPM resulted in a dose-related increase in SCE; however, the toxicity of the DPM was about twofold greater than the DPM extract.

In the only studies with mammalian germ cells, Russell et al. (1980) reported no increase in either dominant lethals or heritable translocations in males of T-stock mice exposed by inhalation to diesel emissions. In the dominant lethal test, T-stock males were exposed for 7.5 weeks and immediately mated to females of different genetic backgrounds (T-stock; [C3H × 101]; [C3H × C57BL/6]; [SEC × C57BL/6]). There were no differences from controls in any of the parameters measured in this assay. For heritable translocation analysis, T-stock males were exposed for 4.5 weeks and mated to (SEC × C57BL/6) females, and the F_1 males were tested for the presence of heritable translocations. Although no translocations were detected among 358 progeny tested, the historical control incidence is less than 1/1,000.

4.3. OTHER GENOTOXIC EFFECTS

Pereira et al. (1981b) exposed male strain A mice to DE emissions for 31 or 39 weeks using the same exposure regimen noted in the previous section. Analyses of caudal sperm for sperm-head abnormalities were conducted independently in three separate laboratories. Although the incidence of sperm abnormalities was not significantly above controls in any of the three laboratories, there were extremely large differences in scoring among the three (control values were 9.2%, 14.9%, and 27.8% in the three laboratories). Conversely, male Chinese hamsters exposed for 6 mo (Pereira et al., 1981c) exhibited almost a threefold increase in sperm-head abnormalities. It is noted that the control incidence in the Chinese hamsters was less than 0.5%. Hence, it is not clear whether the differing responses reflect true species differences or experimental artifacts.

A number of studies measuring DNA adducts in animals exposed to DPM, carbon black or other particles have been reported and are reviewed by Shirnamé-Moré (1995). Although modest increases in DNA adducts have been observed in lung tissue of rats after inhalation of DPM (Wong et al., 1986; Bond et al., 1990), the magnitude of the increases is small in comparison with those induced by chemical carcinogens present in DE (Smith et al., 1993). While Gallagher et al. (1994) found no increases in total DNA adducts in lung tissue of rats exposed to DE, carbon black, or titanium dioxide they did observe an increase in an adduct with migration properties similar to nitrochrysene and nitro-benzo(a)pyrene adducts from diesel but not carbon black or titanium dioxide exposures. The majority of the studies used the ^{32}P-postlabeling assay to detect adducts. Although this method is sensitive, chemical identity of adducts can only be inferred if an adduct spot migrates to the same location as a known prepared adduct.

DNA adducts have also been measured in humans occupationally exposed to DE. Distinct adduct patterns were found among garage workers occupationally exposed to DE when compared to nonexposed controls (Nielsen and Autrup, 1994). Furthermore, the findings were concordant with the adduct patterns observed in groups exposed to low concentrations of PAHs from combustion processes. Hemminki et al. (1994) also reported significantly elevated levels of DNA adducts in lymphocytes from garage workers with known DE exposure compared with unexposed mechanics. Hou et al. (1995) found elevated adduct levels in bus maintenance workers exposed to DE. Although no difference in mutant frequency was observed between the groups, the adduct levels were significantly different (3.2 vs. 2.3×10^{-8}). Nielsen et al. (1996) reported significantly increased levels of three biomarkers (lymphocyte DNA adducts, hydroxyethylvaline adducts in hemoglobin, and 1-hydroxypyrene in urine) in DE-exposed bus garage workers.

The role of oxidative damage in causing mutations has received increasing focus recently. More than 50 different chemicals have been studied in rodents usually measuring the formation of 8-hydroxydeoxyguanosine (8-OH-dG), a highly mutagenic adduct (Loft et al., 1998). Increases in the mutagenic DNA adduct 8-hydroxydeoxyguanosine were found in mouse lung DNA after intratracheal instillation of diesel particles (Nagashima et al., 1995). The response was dose dependent. Mice fed on a high-fat diet showed an increased response whereas the responses were partially reduced when the antioxidant, β-carotene, was included in the diet (Ichinose et al., 1997). Oxidative damage also has been measured in rat lung tissue after intratracheal instillation of quartz (Nehls et al., 1997) and in rat alveolar macrophages after in vitro treatment with silica dust (Zhang et al., 2000). Arimoto et al. (1999) demonstrated that redissolved methanol extracts of DPM also induced the formation of 8-OH-dG adducts in L120 mouse cells. The response was dependent on both DPM concentration and P450 reductase. A detailed discussion of the potential role of oxidative damage in DE carcinogenesis is presented in Chapter 7, Section 7.4.

4.4. SUMMARY AND DISCUSSION

Extensive studies with salmonella have unequivocally demonstrated mutagenic activity in both particulate and gaseous fractions of DE. In most of the studies using salmonella, DPM extracts and individual nitropyrenes exhibited the strongest responses in strain TA98 when no exogenous activation was provided. Gaseous fractions reportedly showed greater response in TA100, whereas benzo[*a*]pyrene and other unsubstituted PAHs are mutagenic only in the presence of S9 fractions. The induction of gene mutations has been reported in several in vitro mammalian cell lines after exposure to extracts of DPM. Note that only the TK6 human cell line did not give a positive response to DPM extracts in the absence of S9 activation. Mutagenic activity was recovered in urine from animals treated with DPM by gastric intubation and i.p. and s.c. implants, but not by inhalation of DPM or diluted diesel exhaust. Dilutions of whole diesel exhaust did not induce sex-linked recessive lethals in drosophila or specific-locus mutations in male mouse germ cells.

Structural chromosome aberrations and SCE in mammalian cells have been induced by particles and extracts. Whole exhaust induced micronuclei but not SCE or structural aberrations in bone marrow of male Chinese hamsters exposed to whole diesel emissions for 6 mo. In a shorter exposure (7 weeks), neither micronuclei nor structural aberrations were increased in bone marrow of female Swiss mice. Likewise, whole DE did not induce dominant lethals or heritable translocations in male mice exposed for 7.5 and 4.5 weeks, respectively.

The application of mutagenicity data to the question of the potential carcinogenicity of diesel emissions is based on the premise that genetic alterations are found in all cancers and that

several of the chemicals found in diesel emissions possess mutagenic activity in a variety of genetic assays. These genetic alterations can be produce by gene mutations, deletions, translocations, aneuploidy, or amplification of genes, hence no single genotoxicity assay should be expected to either qualitatively or quantitatively predict rodent carcinogenicity. With diesel emissions or other mixtures, additional complications arise because of the complexity of the material being tested. Exercises that combined the salmonella mutagenic potency with the total concentration of mutagenic chemicals deposited in the lungs could not account for the observed tumor incidence in exposed rats (Rosenkranz, 1993; Goldstein et al., 1998). However, such calculations ignored the contribution of gaseous phase chemicals which have been estimated to contribute from less than 50% (Rannug et al., 1983) to over 90% (Matsushita et al., 1986) of the total mutagenicity. This wide range is partly reflective of the differences in material tested, semivolatile extracts in the former and whole gaseous emission in the latter. Of greater importance is that these calculations are based on a reverse mutation assay in bacteria with metabolic processes strikingly different from mammals. This is at least partly reflected in the observations that different nitro-PAHs give different responses in bacteria and in CHO cells (Li and Dutcher, 1983) or in human hepatoma-derived cells (Eddy et al., 1986).

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5. NONCANCER HEALTH EFFECTS OF DIESEL EXHAUST

The objective of this chapter is to review and evaluate potential health effects other than cancer associated with inhalation exposure to diesel engine exhaust (DE). Data have been obtained from diverse human, laboratory animal, and in vitro test systems. The human studies comprise both occupational and human experimental exposures, the former consisting of exposure to DE in the occupational environment, and the latter consisting of exposure to diluted DE or diesel particulate matter (DPM) under controlled conditions. The laboratory animal studies consist of both acute and chronic exposures of laboratory animals to DE or DPM. Diverse in vitro test systems composed of human and laboratory animal cells treated with DPM or components of DPM have also been used to investigate the effects of DPM at the cellular and molecular levels. DPM mass (mg/m^3) has been used almost exclusively as a measure of DE exposure in human and experimental studies. The noncancer health effects of DPM have been reviewed previously by the Health Effects Institute (HEI, 1995) and in the Air Quality for Particulate Matter Criteria Document, the PM CD (U.S. EPA, 1996). The noncancer health effects attributable to ambient particulate matter (PM), which is composed in part of DPM, as well as the potential mechanisms underlying these effects have also been previously reviewed in the PM CD (U.S. EPA, 1996) and have been summarized in this document in Chapter 6, Section 6.4.

This chapter begins with descriptions of studies that have shown various health effects occurring as a result of exposure to DE/DPM (Section 5.1). The human studies portion of this section (5.1.1) discusses results from both short-term and long-term studies as well as specialized studies such as those of populations contiguous to major highways (5.1.2). Studies using laboratory animals are ordered into various subsections under Section 5.1.3. Investigations devoted to elucidating the possible modes of action of DE/DPM are covered in Section 5.2; the mode-of-action issue of particle overload in animals is discussed elsewhere in the document (Chapter 3, Section 3.4). Section 5.3 describes evidence for the various interactions of DPM with other conditions such as disease. Other sections address issues such as species-comparative responses to DE/DPM (Section 5.4) and influence of dose rate (Section 5.5). The summary/conclusion of this chapter, relating the totality of this information to possible human effects of DE/DPM, is in Section 5.6.

5.1. HEALTH EFFECTS OF WHOLE DIESEL EXHAUST

5.1.1. Human Studies

5.1.1.1. *Short-Term Exposures*

In a controlled human study, Rudell et al. (1990, 1994) exposed eight healthy subjects in an exposure chamber to diluted exhaust from a diesel engine for 1 h, with intermittent exercise. Dilution of the DE was controlled to provide a median NO_2 level of approximately 1.6 ppm. Median particle number was $4.3 \times 10^6/cm^3$, and median levels of NO and CO were 3.7 and 27 ppm, respectively (particle size and mass concentration were not provided). There were no effects on spirometry or on closing volume using nitrogen washout. Five of eight subjects experienced unpleasant smell, eye irritation, and nasal irritation during exposure. Bronchoalveolar lavage (BAL) was performed 18 hours after exposure and was compared with a control BAL performed 3 weeks prior to exposure; there was no control air exposure. Small but statistically significant reductions were seen in numbers of BAL mast cells, extent of AM phagocytosis of opsonized yeast particles, and lymphocyte CD4/CD8 ratios. A small increase in recovery of polymorphonuclear cells (PMNs) was also observed. These findings suggest that DE may induce mild airway inflammation in the absence of spirometric changes. This study provides an intriguing glimpse of the effect of DE exposure in humans, but only one exposure level was used, the number of subjects was low, and a limited range of endpoints was reported, so the data are inadequate to generalize about the human response.

Rudell et al. (1996) exposed volunteers to DE for 1 h in an exposure chamber. Light work on a bicycle ergometer was performed during exposure. Exposures included either DE or exhaust with particle numbers reduced 46% by a particle trap. The engine used was a new Volvo model 1990, a six-cylinder direct-injection turbocharged diesel with an intercooler, which was run at a steady speed of 900 rpm during the exposures. Comparison of this study with others was difficult because neither exhaust dilution ratios nor particle concentrations were reported. Carbon monoxide concentrations of 27-30 ppm and NO of 2.6-2.7 ppm, however, suggested DPM concentrations may have equaled several mg/m^3. The most prominent symptoms during exposure were irritation of the eyes and nose and an unpleasant smell. Both airway resistance and specific airway resistance increased significantly during the exposures. Despite the 46% reduction in particle numbers by the trap, effects on symptoms and lung function were not significantly attenuated.

Nordenhall et al. (2000) had 15 healthy human subjects (13 males, 2 females) breathe in an exposure chamber diluted DE from an idling diesel engine to give a PM_{10} concentration of 300 $\mu g/m^3$, which was also associated with a median steady-state NO_2 concentration of 1.6 ppm.

Exposures were for 1 h, with each individual serving as their own control by being exposed to filtered air, also for 1 h but at a different time. Sputum production was then induced and sputum examined at 6 and 24 hr postexposure (for both air and DPM) with differential cell counts and soluble protein counts performed. In comparing the same individual's results after exposure to air and after exposure to DE, increases were found in the percentage of sputum neutrophiles (37.7% vs. 26.2%) after 6 hr, along with increases in concentrations of the soluble proteins interleukin-6 (12.0 vs. 6.3 pg/mL) and methylhistamine (0.11 vs. 0.12 ug/L). These differences between air and DPM were not present at 24 hr. Thus, breath exposure to DE produces early induction of an inflammatory response in healthy humans that can be detected using sputum analysis.

Wade and Newman (1993) describe the situation of three railroad workers who developed persistent asthma associated with overexposure to DE from locomotives. The overexposure was a consequence of multiple hours of high levels of diesel exposure from riding in locomotive units trailing immediately behind the lead locomotive. Lines of evidence supporting railroad locomotive DE inducing asthma in these individuals include, (1) all three exhibited clear signs of asthma leading (in two of the three cases) to immediate first-time hospitalization and treatment for asthma, (2) all three developed symptoms within a few hours of the overexposure, and (3) all three experienced exacerbation of symptoms upon reexposure to locomotive DE. Although this report and that of Kahn et al. (1988) described below both provide supporting evidence for DE being able to cause asthma in humans under extreme but uncharacterized conditions, both suffer from the same limitations, including no reliable data on the concentration of diesel emissions and associated gaseous components, the duration of the exposures, or information on others that were exposed under these conditions but who did not develop asthma symptoms.

Kahn et al. (1988) reported the occurrence of 13 cases of acute overexposure to DE among Utah and Colorado coal miners. Twelve miners had symptoms of mucous membrane irritation, headache, and lightheadedness. Eight individuals reported nausea; four reported a sensation of unreality; four reported heartburn; three reported weakness, numbness, and tingling in their extremities; three reported vomiting; two reported chest tightness; and two others reported wheezing. Each miner lost time from work because of these symptoms, which resolved within 24 to 48 h. No air monitoring data were presented; poor work practices were described as the predisposing conditions for overexposure. No follow-up was available for these exposed individuals.

El Batawi and Noweir (1966) reported that among 161 workers from two garages where diesel-powered buses were serviced and repaired, 42% complained of eye irritation, 37% of headaches, 30% of dizziness, 19% of throat irritation, and 11% of cough and phlegm. Ranges of

mean concentrations of DE components in the two diesel bus garages were as follows: 0.4 to 1.4 ppm NO_2, 0.13 to 0.81 ppm SO_2, 0.6 to 44.1 ppm aldehydes, and 1.34 to 4.51 mg/m^3 of DPM; the highest concentrations were obtained close to the exhaust systems of the buses.

Eye irritation was reported by Battigelli (1965) in six subjects after 40 s of chamber exposure to diluted DE containing 4.2 ppm NO_2, 1 ppm SO_2, 55 ppm CO, 3.2 ppm total hydrocarbons, and 1 to 2 ppm total aldehydes; after 3 min and 20 s of exposure to diluted DE containing 2.8 ppm NO_2, 0.5 ppm SO_2, 30 ppm CO, 2.5 ppm total hydrocarbons, and <1 to 2 ppm total aldehydes; and after 6 min of exposure to diluted DE containing 1.3 ppm NO_2, 0.2 ppm SO_2, <20 ppm CO, <2.0 ppm total hydrocarbons, and <1.0 ppm total aldehydes. The concentration of DPM was not reported.

Katz et al. (1960) described the experience of 14 chemists and their assistants monitoring the environment of a train tunnel used by diesel-powered locomotives. Although workers complained on three occasions of minor eye and throat irritation, no correlation was established with concentrations of any particular component of DE.

The role of radicals generated from particulate matter, including DPM, in producing toxicity has been discussed in the literature (Valavanidis et al., 2000), as has the role of antioxidant defenses in protecting against species such as radicals that may arise from acute DE exposure. Blomberg et al. (1998) investigated changes in the antioxidant defense network within the respiratory tract lining fluids of human subjects following DE exposure. Fifteen healthy, nonsmoking, asymptomatic subjects were exposed to filtered air or DE (DPM 300 μg/m^3) for 1 h on two separate occasions at least 3 weeks apart. Nasal lavage fluid and blood samples were collected prior to, immediately after, and 5 ½ h post exposure. Bronchoscopy was performed 6 h after the end of DE exposure. Nasal lavage ascorbic acid concentration increased tenfold during DE exposure, but returned to basal levels 5.5 h postexposure. DE had no significant effects on nasal lavage uric acid or GSH concentrations, and did not affect plasma, bronchial wash, or bronchoalveolar lavage antioxidant concentrations, nor malondialdehyde or protein carbonyl concentrations. The authors concluded that the physiological response to acute DE exposure is an acute increase in the level of the antioxidant ascorbic acid in the nasal cavity.

5.1.1.1.1. ***Diesel exhaust odor.*** The odor of DE is considered by most people to be objectionable; at high intensities, it may produce sufficient physiological and psychological effects to warrant concern for public health. The intensity of the odor of DE is an exponential function of its concentration such that a tenfold change in the concentration will alter the intensity of the odor by one unit. Two human panel rating scales have been used to measure DE odor intensity. In the first (Turk, 1967), combinations of odorous materials were selected to simulate DE odor; a set of 12 mixtures, each having twice the concentration of that of the

previous mixture, is the basis of the diesel odor intensity scale (D-scale). The second method is the TIA (total intensity of aroma) scale based on seven steps, ranging from 0 to 3, with 0 being undetectable, ½ very slight, and 1 slight and increasing in one-half units up to 3, strong (Odor Panel of the CRC-APRAC Program Group on Composition of Diesel Exhaust, 1979; Levins, 1981).

Surveys, utilizing volunteer panelists, have been taken to evaluate the general public's response to the odor of DE. Hare and Springer (1971) and Hare et al. (1974) found that at a D rating of about 2 (TIA = 0.9, slight odor intensity), about 90% of the participants perceived the odor, and almost 60% found it objectionable. At a D rating of 3.2 (TIA = 1.2, slight to moderate odor intensity), about 95% perceived the odor, and 75% objected to it, and, at a D rating of 5 (TIA = 1.8, almost moderate), about 95% objected to it.

Linnell and Scott (1962) reported odor threshold measurement in six subjects and found that the dilution factor needed to reach the threshold ranged from 140 to 475 for this small sample of people. At these dilutions, the concentrations of formaldehyde ranged from 0.012 to 0.088 ppm.

5.1.1.1.2. ***Pulmonary and respiratory effects.*** Battigelli (1965) exposed 13 volunteers to three dilutions of DE obtained from a one-cylinder, four-cycle, 7-hp diesel engine (fuel type unspecified) and found that 15-min to 1-h exposures had no significant effects on pulmonary resistance. Pulmonary resistance was measured by plethysmography utilizing the simultaneous recording of esophageal pressure and airflow determined by electrical differentiation of the volume signal from a spirometer. The concentrations of the constituents in the three diluted exhausts were 1.3, 2.8, and 6.2 ppm NO_2; 0.2, 0.5, and 1 ppm SO_2; <20, 30, and 55 ppm CO; and <1.0, <1 to 2, and 1 to 2 ppm total aldehydes, respectively. DPM concentrations were not reported.

A number of studies have evaluated changes in pulmonary function occurring over a workshift in workers occupationally exposed to DE (specific time period not always reported but assumed to be 8 h). In a study of coal miners, Reger (1979) found that both forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) decreased by 0.05 L in 60 diesel-exposed miners, an amount not substantially different from reductions seen in non-diesel-exposed miners (0.02 and 0.04 L, respectively). Decrements in peak expiratory flow rates were similar between diesel and non-DE-exposed miners. Although the monitoring data were not reported, the authors stated that there was no relationship between the low concentrations of measured respirable dust or NO_2 (personal samplers) when compared with shift changes for any lung function parameter measured for the diesel-exposed miners. In summary, this study (available as an abstract only) states that no evidence was found for additional lung function effect over a shift for miners

exposed to diesel emissions as compared with controls, i.e., nonexposed office workers and coal miners not exposed to diesel emissions.

Ames et al. (1982) compared the pulmonary function of 60 coal miners exposed to DE with that of a control group of 90 coal miners not exposed to DE for evidence of acute respiratory effects associated with exposure to DE. Changes over the workshift in FVC, FEV_1, and forced expiratory flow rate at 50% FVC (FEF_{50}) were the indices for acute respiratory effects. The environmental concentrations of the primary pollutants were 2.0 mg/m^3 respirable dust (<10 μm MMAD), 0.2 ppm NO_2, 12 ppm CO, and 0.3 ppm formaldehyde. The investigators reported a statistically significant decline in FVC and FEV_1 over the workshift in both the diesel-exposed and comparison groups. Current smokers had greater decrements in FVC, FEV_1, and FEF_{50} than did ex-smokers and nonsmokers. There was a marked disparity between the ages and the time spent underground for the two study groups. Diesel-exposed miners were about 15 years younger and had worked underground for 15 fewer years (4.8 versus 20.7 years) than miners not exposed to DE. The significance to the results of these differences between the populations is difficult to ascertain.

Except for the expected differences related to age, 120 underground iron ore miners exposed to DE had no workshift changes in FVC and FEV_1 when compared with 120 matched surface miners (Jörgensen and Svensson, 1970). Both groups had equal numbers (30) of smokers and nonsmokers. The frequency of bronchitis was higher among underground workers, much higher among smokers than nonsmokers, and also higher among older than younger workers. The authors reported that the underground miners had exposures of 0.5 to 1.5 ppm NO_2 and between 3 and 9 mg/m^3 particulate matter, with 20% to 30% of the particles <5 μm MMAD. The majority of the particles were iron ore; quartz was 6% to 7% of the fraction <5 μm MMAD.

Gamble et al. (1979) measured preshift FEV_1 and FVC in 187 salt miners and obtained peak flow forced expiratory flow rates at 25%, 50%, and 75% of FVC (FEF_{25}, FEF_{50}, or FEF_{75}). Postshift pulmonary function values were determined from total lung capacity and flows at preshift percentages of FVC. The miners were exposed to mean NO_2 levels of 1.5 ppm and mean respirable particulate levels of 0.7 mg/m^3. No statistically significant changes were found between changes in pulmonary function and in NO_2 and respirable particles combined. Slopes of the regression of NO_2 and changes in FEV_1, FEF_{25}, FEF_{50}, and FEF_{75} were significantly different from zero. The authors concluded that these small reductions in pulmonary function were attributable to variations in NO_2 within each of the five salt mines that contributed to the cohort.

Gamble et al. (1987a) investigated the acute effects of DE in 232 workers in four diesel bus garages using an acute respiratory questionnaire and before and after workshift spirometry.

The prevalence of burning eyes, headaches, difficult or labored breathing, nausea, and wheeze experienced at work was higher in the diesel bus garage workers than in a comparison population of lead/acid battery workers who had not previously shown a statistically significant association of acute symptoms with acid exposure. Comparisons between the two groups were made without adjustment for age and smoking. There was no detectable association of exposure to NO_2 (0.23 ppm ± 0.24 S.D.) or inhalable (less than 10 μm MMAD) particles (0.24 mg/m^3 ± 0.26 S.D.) and acute reductions in FVC, FEV_1, peak flows, FEF_{50}, and FEF_{75}. Workers who had respiratory symptoms had slightly greater but statistically insignificant reductions in FEV_1 and FEF_{50}.

Ulfvarson et al. (1987) evaluated workshift changes in the pulmonary function of 17 bus garage workers, 25 crew members of two types of car ferries, and 37 workers on roll-on/roll-off ships. The latter group was exposed primarily to DE; the first two groups were exposed to both gasoline and DE. The diesel-only exposures that averaged 8 h consisted of 0.13 to 1.0 mg/m^3 particulate matter, 0.02 to 0.8 mg/m^3 (0.016 to 0.65 ppm) NO, 0.06 to 2.3 mg/m^3 (0.03 to 1.2 ppm) NO_2, 1.1 to 5.1 mg/m^3 (0.96 to 4.45 ppm) CO, and up to 0.5 mg/m^3 (0.4 ppm) formaldehyde. The largest decrement in pulmonary function was observed during a workshift following no exposure to DE for 10 days. Forced vital capacity and FEV_1 were significantly reduced over the workshift (0.44 L and 0.30 L, $p<0.01$ and $p<0.001$, respectively). There was no difference between smokers and nonsmokers. Maximal midexpiratory flow, closing volume expressed as the percentage of expiratory vital capacity, and alveolar plateau gradient (phase 3) were not affected. Similar but less pronounced effects on FVC (−0.16 L) were found in a second, subsequent study of stevedores (n = 24) only following 5 days of no exposure to diesel truck exhaust. Pulmonary function returned to normal after 3 days without occupational exposure to DE. No exposure-related correlation was found between the observed pulmonary effects and concentrations of NO, NO_2, CO, or formaldehyde; however, it was suggested that NO_2 adsorbed onto the DE particles may have contributed to the overall dose of NO_2 to the lungs. In a related study, six workers (job category not defined) were placed in an exposure chamber and exposed to diluted DE containing 0.6 mg/m^3 DPM and 3.9 mg/m^3 (2.1 ppm) NO_2. The exhaust was generated by a 6-cylinder, 2.38-L diesel engine, operated for 3 h and 40 min at constant speed, equivalent to 60 km/h, and at about one-half full engine load. No effect on pulmonary function was observed.

In a hypothesis-generating study, Kilburn (2000) examined neurobehavioral and pulmonary function of a small group of workers exposed to DE either as railroad workers (n=10) over a range of 15 to 50 years or as electricians (n=6) over a range of 0.6 to 1.5 years. Neurobehavioral and visual functions batteries showed nearly all of these individuals to be neurobehaviorally impaired in relation to a referent population in one or more areas, including

reaction time, balance, blink reflex latency, verbal recall, and color vision confusion indices. Pulmonary function tests also showed that 10 of the 16 had airway obstruction and another group of 10 of the 16 had chronic bronchitis, chest pain, tightness, and hyperreactive airways. This work implies that with sufficiently sensitive methods, noncancer effects from DPM/DE exposure may be detectable in sufficiently exposed human populations.

5.1.1.1.3. ***Immunological effects***. Salvi et al. (1999) exposed healthy human subjects to diluted DE (DPM 300 μg/m^3) for 1 h with intermittent exercise. Although there were no changes in pulmonary function, there were significant increases in neutrophils and B lymphocytes as well as histamine and fibronectin in airway lavage fluid. Bronchial biopsies obtained 6 h after DE exposure showed a significant increase in neutrophils, mast cells, and CD4+ and CD8+ T lymphocytes, along with upregulation of the endothelial adhesion molecules ICAM-1 and VCAM-1 and increases in the number of LFA-1+ in the bronchial tissue. Significant increases in neutrophils and platelets were observed in peripheral blood following exposure to DE.

In a follow-up investigation of potential mechanisms underlying the DE-induced airway leukocyte infiltration, Salvi et al. (2000) exposed healthy human volunteers to diluted DE, on two separate occasions for 1 h each, in an exposure chamber. Fiber-optic bronchoscopy was performed 6 h after each exposure to obtain endobronchial biopsies and bronchial wash (BW) cells. These workers observed that DE exposure enhanced gene transcription of IL-8 in the bronchial tissue and BW cells and increased growth-regulated oncogene-a protein expression and IL-8 in the bronchial epithelium; there was also a trend toward an increase in IL-5 mRNA gene transcripts in the bronchial tissue.

In an attempt to evaluate the potential allergenic effects of DPM in humans, Diaz-Sanchez and associates carried out a series of clinical investigations. In the first of these (Diaz-Sanchez et al., 1994), healthy human volunteers were challenged by spraying either saline or 0.30 mg (300 μg) DPM into their nostrils. The authors considered this dose to be equivalent to breathing the outdoor air in Los Angeles for a 24-h period on an average day. Enhanced IgE levels were noted in nasal lavage cells in as little as 24 h, with peak production observed 4 days after DPM challenge. The effects seemed to be somewhat isotype-specific, because in contrast to IgE results, DPM challenge had no effect on the levels of IgG, IgA, IgM, or albumin. The selective enhancement of local IgE production was demonstrated by a dramatic increase in IgE-secreting cells.

Although direct effects of DPM on B-cells have been demonstrated by in vitro studies, it was considered likely that other cells regulating the IgE response may also be affected. Cytokine production was therefore measured in nasal lavage cells from healthy human volunteers challenged with DPM (0 or 0.15 mg in 200 μL saline) sprayed into each nostril (Diaz-

Sanchez et al., 1996). Before challenge with DPM, most subjects' nasal lavage cells had detectable levels of only interferon-γ, IL-2, and IL-13 *m*RNA. After challenge with DPM, the cells produced readily detectable levels of *m*RNA for IL-2, IL-4, IL-5, IL-6, IL-10, IL-13, and interferon-γ. Although the cells in the nasal lavage before and after challenge do not necessarily represent the same ones either in number or type, the broad increase in cytokine production was considered by the authors not to be simply the result of an increase in T cells recovered in the lavage fluid. On the basis of these findings, the authors concluded that the increase in nasal cytokine expression after exposure to DPM can be predicted to contribute to enhanced local IgE production and thus play a role in pollutant-induced airway disease.

The ability of DPM to act as an adjuvant to the ragweed allergen Amb a I was also examined by nasal provocation in ragweed-allergic subjects using 0.3 mg (300 μg) DPM, Amb a I, or both (Diaz-Sanchez et al., 1997). Although allergen and DPM each enhanced ragweed-specific IgE, DPM plus allergen promoted a 16-times greater antigen-specific IgE production. Nasal challenge with DPM also influenced cytokine production. Ragweed challenge resulted in a weak response, DPM challenge caused a strong but nonspecific response, and allergen plus DPM caused a significant increase in the expression of mRNA for TH0 and TH2-type cytokines (IL-4, IL-5, IL-6, IL-10, IL-13), with a pronounced inhibitory effect on IFN-γ gene expression. The author concluded that DPM can enhance B-cell differentiation and, by initiating and elevating IgE production, may be a factor in the increased incidence of allergic airway disease.

In a further extension of these studies, Diaz-Sanchez et al. (1999) examined the potential for DPM to lead to primary sensitization of humans by driving a de novo mucosal IgE response to a neoantigen, keyhole limpet hemocyanin (KLH). Ten atopic subjects were given an initial nasal immunization of KLH followed by two biweekly nasal challenges with KLH. Fifteen different atopic subjects were treated identically, except that DPM was administered 24 h before each KLH exposure. Intranasal administration of KLH alone led to the generation of an anti-KLH IgG and IgA humoral response, which was detected in nasal fluid samples. No anti-KLH IgE was observed in any of these subjects. In contrast, when challenged with KLH preceded by DPM, 9 of the 15 subjects produced anti-KLH-specific IgE. KLH-specific IgG and IgA at levels similar to those seen with KLH alone were also detected. Subjects who received DPM and KLH had significantly increased IL-4, but not IFN-gamma, levels in nasal lavage fluid, whereas these levels were unchanged in subjects receiving KLH alone. These investigators concluded that DPM can function as a mucosal adjuvant to a de novo IgE response and may increase allergic sensitization among atopic individuals.

5.1.1.1.4. ***Human cell culture studies.*** The potential mechanisms by which DPM may act to cause allergenic effects has been examined in human cell culture studies. Takenaka et al. (1995)

reported that DPM extracts enhanced IgE production from purified human B cells. IgE production in these cells (stimulated by exogenous addition of interleukin-4 plus monoclonal antibody) was enhanced (i.e., further stimulated) 20% to 360% by the addition of DPM extracts (1-50 ng/mL) over a period of 10-14 days. DPM extracts in the absence of exogenously added IL-4 and/or monoclonal antibodies did not themselves induce IgE production or synergize with interleukin-4 alone to induce IgE from purified B cells, suggesting that the extracts were enhancing ongoing IgE production rather than inducing germline transcription or isotype switching. The authors concluded that enhancement of IgE production in the human airway resulting from the organic fraction of DPM may be an important factor in the increasing incidence of allergic airway disease.

Terada et al. (1997) examined the effects of DPM and DPM extract on eosinophil adhesion, survival rate, and degranulation. Eosinophils, human mucosal microvascular endothelial cells (HMMECs), and human nasal epithelial cells (HNECs) were preincubated in the presence of DPM and DPM extract. 35S-labeled eosinophils were allowed to adhere to monolayers of HMMECs and HNECs. Although neither DPM nor DPM extract affected the adhesiveness of HMMECs and HNECs to eosinophils, DPM and DPM extract each significantly increased eosinophil adhesiveness to HNECs; neither affected eosinophil adhesiveness to HMMECs. DPM extract also induced eosinophil degranulation without changing the eosinophil survival rate. These results indicate that DPM may play an important role in promoting the nasal hypersensitivity induced by enhanced eosinophil infiltration of epithelium and eosinophil degranulation. It should also be noted that eosinophils are major components of allergic inflammatory disorders, including asthma and nasal allergy.

Terada et al. (1999) examined the effects of DPM extract on the expression of histamine H1 receptor (H1R) mRNA in HNECs and HMMECs, and on the production of IL-8 and GM-CSF induced by histamine. HNECs and HMMECs, isolated from human nasal mucosa specimens, were cultured with DPM extract. DPM extract increased the expression of H1R mRNA in both HNECs and HMMECs. The amount of IL-8 and GM-CSF induced by histamine was also significantly higher in HNECs and HMMECs treated with DPM extract. These results strongly suggest that DPM accelerates the inflammatory change by not only directly upregulating H1R expression but also by increasing histamine-induced IL-8 and GM-CSF production. Histamine is the most important chemical mediator in the pathogenesis of nasal allergy.

Steerenberg et al. (1998) studied the effects of exposure to DPM on airway epithelial cells, the first line of defense against inhaled pollutants. Cells from a human bronchial cell line (BEAS-2B) were cultured in vitro and exposed to DPM (0.04-0.33 mg/mL) and the effects on IL-6 and IL-8 production were observed. Increases in IL-6 and IL-8 production compared to the

nonexposed cells (11- and 4-fold, respectively) were found after 24 or 48 h exposure to DPM. This increase was lower (17- and 3.3-fold) compared to silica and higher compared to titanium dioxide, which showed no increase for either IL-6 or IL-8. The study was extended to observe the effects of DPM on inflammation-primed cells. BEAS-2B cells were exposed to TNF-α followed by DPM. Additive effects on IL-6 and IL-8 production by BEAS-2B cells were found after TNF-α priming and subsequent exposure to DPM only at a low dose of DPM and TNF-α (0.05-0.2 ng/mL). The investigators concluded that BEAS-2B phagocytized DPM and produced an increased amount of IL-6 and IL-8, and that in TNF-α-primed BEAS-2B cells DPM increased interleukin production only at low concentrations of DPM and TNF-α.

Ohtoshi et al. (1998) studied the effect of suspended particulate matter (SPM), obtained from high-volume air samplers, and DPM obtained from exhaust of a stationary diesel engine on the production of IL-8 and granulocyte-colony stimulating factor (GM-CSF) by human airway epithelial cells in vitro. Nontoxic doses of DPMs stimulated production of IL-8 and GM-CSF by three kinds of human epithelial cells (nasal polyp-derived upper airway, normal bronchial, and transformed bronchial epithelial cells) in a dose- and time-dependent fashion at a DPM concentration as low as 10 μg/mL. SPM applied at 250 and 2,500 μg/mL had a stimulatory effect on GM-CSF, but not on IL-8 production. The effects could be blocked with a protein synthesis inhibitor, suggesting that the process required de novo protein synthesis, and appeared to be due to an extractable component because neither charcoal nor graphite showed such stimulatory effects. The authors concluded that SPM and DPM, a component of SPM, may be important air pollutants in the activation of airway cells for the release of cytokines relevant to allergic airway inflammation.

The mechanisms underlying DPM-induced injury to airway cells were investigated in human bronchial epithelial cells (HBECs) in culture (Bayram et al., 1998a). HBECs from bronchial explants obtained at surgery were cultured and exposed to DPM (10-100 μg/mL) suspended in a serum-free supplemented medium (SF-medium) or to a SF-medium filtrate of DPM. The filtrate was obtained by incubating DPM (50 μg/mL) in SF-medium for 24 h. The effects of DPM and DPM filtrate on permeability, ciliary beat frequency (CBF), and release of inflammatory mediators were observed. DPM and filtered solution of DPM significantly increased the electrical resistance of the cultures but did not affect movement of bovine serum albumin across cell cultures. DPM and filtered DPM solution significantly attenuated the CBF of these cultures and significantly increased the release of IL-8. DPM also increased the release by these cultures of GM-CSF and soluble intercellular adhesion molecule-1 (sICAM-1). These authors also observed that activated charcoal was not able to induce changes in electrical resistance, attenuate CBF, and increase the release of inflammatory mediators from HBEC, and proposed that these effects were due most likely to the compounds adsorbed onto the DPM

rather than the size of DPM. The authors concluded that exposure of airway cells to DPM may lead to functional changes and release of proinflammatory mediators and that these effects may influence the development of airway disease.

Bayram et al. (1998b) investigated the sensitivity of cultured airway cells from asthmatic patients to DPM. Incubation with DPM (10-100 μg/mL) significantly attenuated the CBF in both the asthmatic and nonasthmatic bronchial epithelial cell cultures. Cultured airway cells from asthmatic patients constitutively released significantly greater amounts of IL-8, GM-CSF, and sICAM-1 than cell cultures from nonasthmatic subjects. Only cultures from asthmatic patients additionally released RANTES. The authors concluded that cultured airway cells from asthmatic subjects differ with regard to the amounts and types of proinflammatory mediators they can release and that the increased sensitivity of bronchial epithelial cells of asthmatic subjects to DPM may result in exacerbation of their disease symptoms.

Devalia et al. (1999) investigated the potential sensitivity of HBECs biopsied from atopic mild asthmatic patients and non-atopic nonasthmatic subjects to DPM. HBECs from asthmatic patients constitutively released significantly greater amounts of IL-8, GM-CSF, and sICAM-1 than HBECs from nonasthmatic subjects. RANTES was only released by HBECs of asthmatic patients. Incubation of the asthmatic cultures with 10 μg/mL DPM significantly increased the release of IL-8, GM-CSF, and sICAM-1 after 24 h. In contrast, only higher concentrations (50-100 μg/mL DPM) significantly increased the release of IL-8 and GM-CSF from HBECs of nonasthmatics. The authors conclude that the increased sensitivity of the airways of asthmatics to DPM may be, at least in part, a consequence of greater constitutive and DPM-induced release of specific pro-inflammatory mediators from bronchial epithelial cells.

Abe and co-workers have demonstrated formation of increased cytokine levels in cultured human bronchial epithelial cells exposed to freshly generated DE, but not to filtered DE, i.e., particle-free DE (Abe et al., 2000). Cytokine IL-8 protein as well as transforming growth factor (TGF)-β1 mRNAs were induced in a time-dependent manner (from 0.5 to 14 h of exposure) in BET-1A human bronchial epithelial cells in response to exposure to freshly generated, cooled, humidified DE that was diluted to 2.9 mg DPM/m^3. The gas obtained by filtration of DE alone did not show any sustained increase in these indicators, suggesting that DE particles play a more important role in eliciting these responses than do the accompanying gases (10.6 ppm CO, 7.3 ppm NO_2, and 3.3 ppm SO_2).

To elucidate the intracellular signal transduction pathway regulating IL-8 and RANTES production, Hashimoto et al. (2000) examined the role of p38 mitogen-activated protein (MAP) kinase in DPM-induced (DPM = 10, 50, or 100 μg/mL) IL-8 and RANTES production by HBECs. They also examined the effect of a thiol-reducing agent, N-acetylcysteine (NAC), on DPM-induced p38 MAP kinase activation and cytokine production. The authors conclude that

p38 MAP kinase plays an important role in the DPM-activated signaling pathway that regulates IL-8 and RANTES production by HBECs and that the cellular redox state is critical for DPM-induced p38 MAP kinase activation leading to IL-8 and RANTES production.

Boland et al. (1999) compared the biological effects of carbon black and DPM (2.5 $\mu g/cm^2$ culture surface) collected from catalyst- and noncatalyst-equipped diesel vehicles in cultures of both human bronchial epithelial cells and human nasal epithelial cells. Transmission electron microscopy indicated that DPM was phagocytosed by epithelial cells and translocated through the epithelial cell sheet. The time and dose dependency of phagocytosis and its nonspecificity for different particles (DPM, carbon black, and latex particles) were established by flow cytometry. DPM also induced a time-dependent increase in interleukin-8, GM-CSF, and interleukin-1β release. The inflammatory response occurred later than phagocytosis and, because carbon black had no effect on cytokine release, its extent appeared to depend on the content of adsorbed organic compounds. Furthermore, treatment of the exhaust gas to decrease the adsorbed organic fraction reduced the DPM-induced increase in GM-CSF factor release. These results indicate that DPM can be phagocytosed by and induce a specific inflammatory response in airway epithelial cells.

5.1.1.1.5. ***Summary.*** In the available exposure studies, considerable variability is reported in DE detection threshold. The odor scales described in some of these studies have no general use at present because they are not objectively defined; however, the studies do clearly indicate substantial interindividual variability in the ability to detect odor and the level at which it becomes objectionable. Much of what is known about the acute effects of DE comes from case reports that lack clear measurements of exposure concentrations. The studies of pulmonary function changes in exposed humans have looked for changes occurring over a workshift or after a short-term exposure. The overall conclusion of these studies is that reversible changes in pulmonary function in humans can occur in relation to DE exposure, although it is not possible to relate these changes to specific exposure levels. Numerous studies described in this section, conducted in humans and in isolated cell systems derived from humans exposed to DPM, revealed various biochemical and pathophysiological alterations, such as IgE changes, altered levels of cytokines/chemokines, and goblet-cell hyperplasia, with nearly all these responses being key changes and markers of allergic inflammatory disorders of the airways such as asthma and nasal allergies (Nel et al., 1998). Thus, a major point of significance about these findings is that they indicate that DPM could be viewed as having the potential to elicit inflammatory and immunological responses and responses typical of asthma, and that DPM may be a likely factor in the increasing incidence of allergic hypersensitivity. These studies have also shown that effects are due primarily to the organic fraction and that DPM enhances the allergic response to

known allergens. Results from these studies, including those wih laboratory animals, indicate that DPM could be viewed as having the potential to influence the development of airway inflammation and disease through its adjuvant properties and by causing the release of proinflammatory mediators.

5.1.1.2. *Long-Term Exposures*

Several epidemiologic studies have evaluated the effects of chronic exposure to DE on occupationally exposed workers.

Battigelli et al. (1964) measured several indices of pulmonary function, including vital capacity, FEV_1, peak flow, nitrogen washout, and diffusion capacity in 210 locomotive repairmen exposed to DE in 3 engine houses. The average exposure of these locomotive repairmen to DE was 9.6 years. When compared with a control group matched for age, body size, "past extrapulmonary medical history" (no explanation given), and job status (154 railroad yard workers), no significant clinical differences were found in pulmonary function or in the prevalence of dyspnea, cough, or sputum between the DE-exposed and nonexposed groups. Exposure to DE showed marked seasonal variations because the doors of the engine house were open in the summer and closed in the winter. For the exposed group, the maximum daily workplace concentrations of air pollutants measured were 1.8 ppm NO_2, 1.7 ppm total aldehydes, 0.15 ppm acrolein, 4.0 ppm SO_2, and 5.0 ppm total hydrocarbons. The concentration of airborne particles was not reported.

Gamble et al. (1987b) examined 283 diesel bus garage workers from four garages in two cities to determine if there was excess chronic respiratory morbidity associated with exposure to DE. Tenure of employment was used as a surrogate of exposure; mean tenure of the study population was 9 years ± 10 years S.D. Exposure-effect relationships within the study population showed no detectable associations of symptoms with tenure. Reductions in FVC, FEV_1, peak flow, and FEF_{50} (but not FEF_{75}) were associated with increasing tenure. Compared with a control population (716 nonexposed blue-collar workers) and after indirect adjustment for age, race, and smoking, the exposed workers had a higher incidence of cough, phlegm, and wheezing; however, there was no correlation between symptoms and length of employment. Dyspnea showed an exposure-response trend but no apparent increase in prevalence. Mean FEV_1, FVC, FEF_{50}, and peak flow were not reduced in the total cohort compared with the reference population, but were reduced in workers with 10 years or more tenure.

Purdham et al. (1987) evaluated respiratory symptoms and pulmonary function in 17 stevedores employed in car ferry operations who were exposed to both diesel and gasoline exhausts and in a control group of 11 on-site office workers. Twenty-four percent of the exposed group and 36% of the controls were smokers. If a particular symptom was considered

to be influenced by smoking, smoking status was used as a covariate in the logistic regression analysis; pack-years smoked was a covariate for lung function indices. The frequency of respiratory symptoms was not significantly different between the two groups; however, baseline pulmonary function measurements were significantly different. The latter comparisons were measured by multiple regression analysis using the actual (not percentage predicted) results and correcting for age, height, and pack-years smoked. The stevedores had significantly lower FEV_1, FEV_1/FVC, FEF_{50}, and FEF_{75} ($p<0.021$, $p<0.023$, $p<0.001$, and $p<0.008$, respectively), but not FVC. The results from the stevedores were also compared with those obtained from a study of the respiratory health status of Sydney, Nova Scotia, residents. These comparisons showed that the dock workers had higher FVC, similar FEV_1, but lower FEV_1/FVC and flow rates than the residents of Sydney. Based on these consistent findings, the authors concluded that the lower baseline function measurements in the stevedores provided evidence of an obstructive ventilatory defect, but caution in interpretation was warranted because of the small sample size. There were no significant changes in lung function over the workshift, nor was there a difference between the two groups. The stevedores were exposed to significantly ($p<0.04$) higher concentrations of particulate matter (0.06 to 1.72 mg/m^3, mean 0.50 mg/m^3) than the controls (0.13 to 0.58 mg/m^3, mean not reported). Exposures of stevedores to SO_2, NO_2, aldehydes, and PAHs were very low; occasional CO concentrations in the 20 to 100 ppm range could be detected for periods up to 1 h in areas where blockers were chaining gasoline-powered vehicles.

Additional epidemiologic studies on the health hazards posed by exposure to DE have been conducted for mining operations. Reger et al. (1982) evaluated the respiratory health status of 823 male coal miners from six diesel-equipped mines compared with 823 matched coal miners not exposed to DE. The average tenure of underground work for the underground miners and their controls was only about 5 years; on average, the underground workers in diesel mines spent only 3 of those 5 years underground in diesel-use mines. Underground miners exposed to DE reported a higher incidence of symptoms of cough and phlegm but proportionally fewer symptoms of moderate to severe dyspnea than their matched counterparts. These differences in prevalence of symptoms were not statistically significant. The diesel-exposed underground miners, on the average, had lower FVC, FEV_1, FEF_{50}, FEF_{75}, and FEF_{90} but higher peak flow and FEF_{25} than their matched controls. These differences, however, were not statistically significant. Health indicators for surface workers and their matched controls were directionally the same as for matched underground workers. There were no consistent relationships between the findings of increased respiratory symptoms, decreased pulmonary function, smoking history, years of exposure, or monitored atmosphere pollutants (NO_x, CO, particles, and aldehydes). Mean concentrations of NO_x at the six mines ranged from 0 to 0.6 ppm for short-term area

samples, 0.13 to 0.28 ppm for full-shift personal samples, and 0.03 to 0.80 for full-shift area samples. Inhalable particles (less than 10 μm MMAD) averaged 0.93 to 2.73 mg/m^3 for personal samples and 0 to 16.1 mg/m^3 for full-shift area samples. Ames et al. (1984), using a portion of the miners studied by Reger, examined 280 diesel-exposed underground miners in 1977 and again in 1982. Each miner in this group had at least 1 year of underground mining work history in 1977. The control group was 838 miners with no exposure to DE. The miners were evaluated for prevalence of respiratory symptoms, chronic cough, phlegm, dyspnea, and changes in FVC, FEV_1, and FEF_{50}. No air monitoring data were reported; exposure to DE gases and mine dust particles were described as very low. These authors found no decrements in pulmonary function or increased prevalence of respiratory symptoms attributable to exposure to DE. In fact, the 5-year incidences of cough, phlegm, and dyspnea were greater in miners without exposure to DE.

Attfield (1978) studied 2,659 miners from 21 mines (8 metal, 6 potash, 5 salt, and 2 trona). Diesels were employed in only 18 of the mines, but the 3 mines not using diesels were not identified. The years of diesel usage, ranging from 8 in trona mines to 16 in potash mines, were used as a surrogate for exposure to DE. Based on a questionnaire, an increased prevalence of persistent cough was associated with exposure to aldehydes; this finding, however, was not supported by the pulmonary function data. No adverse respiratory symptoms or pulmonary function impairments were related to CO_2, CO, NO_2, inhalable dust, or inhalable quartz. The author failed to comment on whether the prevalence of cough was related to the high incidence (70%) of smokers in the cohort.

Questionnaire, chest radiograph, and spirometric data were collected by Attfield et al. (1982) on 630 potash miners from six potash mines. These miners were exposed for an average of 10 years (range 5 to 14 years) to 0.1 to 3.3 ppm NO_2, 0.1 to 4.0 ppm aldehyde, 5 to 9 ppm CO, and total dust concentrations of 9 to 23 mg/m^3. No attempt was made to measure diesel-derived particles separately from other dusts. The ratio of total to inhalable (<10 μm MMAD) dust ranged from 2 to 11. An increased prevalence of respiratory symptoms was related solely to smoking. No association was found between symptoms and tenure of employment, dust exposure, NO_2, CO, or aldehydes. A higher prevalence of symptoms of cough and phlegm was found, but no differences in pulmonary function (FVC and FEV_1) were found in these diesel-exposed potash miners when compared with the predicted values derived from a logistics model based on blue-collar workers working in nondusty jobs.

Gamble et al. (1983) investigated respiratory morbidity in 259 miners from 5 salt mines in terms of increased respiratory symptoms, radiographic findings, and reduced pulmonary function associated with exposure to NO_2, inhalable particles (<10 μm MMAD), or years worked underground. Two of the mines used diesel extensively; no diesels were used in one salt

mine. Diesels were introduced into each mine in 1956, 1957, 1963, or 1963 through 1967. Several working populations were compared with the salt miner cohort. After adjustment for age and smoking, the salt miners showed no increased prevalence of cough, phlegm, dyspnea, or airway obstruction (FEV_1/FVC) compared with aboveground coal miners, potash miners, or blue-collar workers. The underground coal miners consistently had an elevated level of symptoms. Forced expiratory volume at 1 s, FVC, FEF_{50}, and FEF_{75} were uniformly lower for salt miners in relation to all the comparison populations. There was, however, no association between changes in pulmonary function and years worked, estimated cumulative inhalable particles, or estimated NO_2 exposure. The highest average exposure to particulate matter was 1.4 mg/m^3 (particle size not reported, measurement includes NaCl). Mean NO_2 exposure was 1.3 ppm, with a range of 0.17 ppm to 2.5 ppm. In a continuation of these studies, Gamble and Jones (1983) grouped the salt miners into low-, intermediate-, and high-exposure categories based on tenure in jobs with DE exposure. Average concentrations of inhalable particles and NO_2 were 0.40, 0.60, and 0.82 mg/m^3 and 0.64, 1.77, and 2.21 ppm for the three diesel exposure categories, respectively. A statistically significant concentration-response association was found between the prevalence of phlegm in the salt miners and exposure to DE ($p<0.0001$) and a similar, but nonsignificant, trend for cough and dyspnea. Changes in pulmonary function showed no association with diesel tenure. In a comparison with the control group of nonexposed, blue-collar workers, adjusted for age and smoking, the overall prevalence of cough and phlegm (but not dyspnea) was elevated in the diesel-exposed workers. Forced expiratory volumes at 1 s and FVC were within 4% of expected, which was considered to be within the normal range of variation for a nonexposed population.

In a preliminary study of three subcohorts from bus company personnel (clerks [lowest exposure], bus drivers [intermediate exposure], and bus garage workers [highest exposure]) representing different levels of exposure to DE, Edling and Axelson (1984) found a fourfold higher risk ratio for cardiovascular mortality in bus garage workers, even after adjusting for smoking history and allowing for at least 10 years of exposure and 15 years or more of induction latency. Carbon monoxide was hypothesized as the etiologic agent for the increased cardiovascular disease but was not measured. However, in a more comprehensive epidemiologic study, Edling et al. (1987) evaluated mortality data covering a 32-year period for a cohort of 694 bus garage employees and found no significant differences between the observed and expected number of deaths from cardiovascular disease. Information on exposure components and their concentrations was not reported.

The absence of reported noncancerous human health effects, other than infrequently occurring effects related to respiratory symptoms and pulmonary function changes, is notable. Unlike studies in laboratory animals, to be described later in this chapter, studies of the impact

of DE on the defense mechanisms of the human lung have not been performed. No direct evidence is available in humans regarding doses of DE, gas phase, particulate phase, or total exhaust that lead to impaired particle clearance or enhanced susceptibility to infection. A summary of epidemiologic studies is presented in Table 5-1.

Table 5-1. Human studies of exposure to diesel exhaust

Study	Description	Findings
	Acute exposures	
Kahn et al. (1988)	13 cases of acute exposure, Utah and Colorado coal miners.	Acute reversible sensory irritation, headache, nervous system effects, bronchoconstriction were reported at unknown exposures.
El Batawi and Noweir (1966)	161 workers, two diesel bus garages.	Eye irritation (42%), headache (37%), dizziness (30%), throat irritation (19%), and cough and phlegm (11%) were reported in this order of incidence by workers exposed in the service and repair of diesel-powered buses.
Battigelli (1965)	Six subjects, eye exposure chamber, three dilutions.	Time to onset was inversely related and severity of eye irritation was associated with the level of exposure to DE.
Katz et al. (1960)	14 persons monitoring DE in a train tunnel.	Three occasions of minor eye and throat irritation; no correlation established with concentrations of DE components.
Hare and Springer (1971) Hare et al. (1974)	Volunteer panelists who evaluated general public's response to odor of DE.	Slight odor intensity, 90% perceived, 60% objected; slight to moderate odor intensity, 95% perceived, 75% objected; moderate odor intensity, 100% perceived, almost 95% objected.
Linnell and Scott (1962)	Odor panel under highly controlled conditions determined odor threshold for DE.	In six panelists, the volume of air required to dilute raw DE to an odor threshold ranged from a factor of 140 to 475.
Rudell et al. (1990, 1994)	Eight healthy nonsmoking subjects exposed for 60 min in chamber to DE (3.7 ppm NO, 1.5 ppm NO_2, 27 ppm CO, 0.5 mg/m^3 formaldehyde, particles (4.3 × 10^6/cm^3). Exercise, 10 of each 20 min (75 W).	Odor, eye and nasal irritation in 5/8 subjects. BAL findings: small decrease in mast cells, lymphocyte subsets and macrophage phagocytosis; small increase in PMNs.
Rudell et al. (1996)	Volunteers exposed to DE for 1 h while doing light work. Exposure concentrations uncertain.	Unpleasant smell along with irritation of eyes and nose reported. Airway resistance increased. Reduction of particle concentration by trapping did not affect results.
Battigelli (1965)	13 volunteers exposed to three dilutions of DE for 15 min to 1 h.	No significant effects on pulmonary resistance were observed as measured by plethysmography.
Wade and Newman (1993)	Three railroad workers acutely exposed to DE.	The workers developed symptoms of asthma.
Diaz-Sanchez et al. (1994)	Volunteers challenged by a nasal spray of 0.30 mg DPM.	Enhancement of IgE production reported due to a dramatic increase in IgE-secreting cells.

Table 5-1. Human studies of exposure to diesel exhaust (continued)

Study	Description	Findings
Takenaka et al. (1995)	Volunteers challenged by a nasal spray of 0.30 mg DPM.	DPM extracts enhanced interleukin-4 plus monoclonal antibody-stimulated IgE production as much as 360%, suggesting an enhancement of ongoing IgE production rather than inducing germline transcription or isotype switching.
Diaz-Sanchez et al. (1996)	Volunteers challenged by a nasal spray of 0.30 mg DPM.	A broad increase in cytokine expression predicted to contribute to enhanced local IgE production.
Diaz-Sanchez et al. (1997)	Ragweed-sensitive volunteers challenged by a nasal spray of 0.30 mg DPM alone or in combination with ragweed allergen.	Ragweed allergen plus DPM-stimulated ragweed-specific IgE to a much greater degree than ragweed alone, suggesting DPM may be a key feature in stimulating allergen-induced respiratory allergic disease.
Salvi et al. (1999)	Volunteers exposed to diluted DE (DPM 300 $\mu g/m^3$) for 1 h with intermittent exercise.	• No changes in pulmonary function, but significant increases in neutrophils, B lymphocytes, histamine, and fibronectin in airway lavage fluid. • Bronchial biopsies 6 h after exposure showed significant increase in neutrophils, mast cells, CD4+ and CD8+ T lymphocytes; upregulation of ICAM-1 and VCAM-1; increases in the number of LFA-1+ in bronchial tissue. • Significant increases in neutrophils and platelets observed in peripheral blood.
Salvi et al. (2000)	Volunteers exposed to diluted DE (DPM 300 $\mu g/m^3$) for 1 h.	• DPM enhanced gene transcription of IL-8 in bronchial tissue and bronchial wash cells • Increased expression of growth-regulated oncogene-α and IL-8 in bronchial epithelium; trend towards increased IL-5 mRNA gene transcripts.
Nightingale et al. (2000)	Volunteers exposed to resuspended DPM (200 ug/m^3) for 2 h at rest	• DPM increased exhaled levels of CO • DPM increased sputum neutrophils and myeloperoxidase
	Studies of cross-shift changes	
Reger (1979)	Five or more VC maneuvers by each of 60 coal miners exposed to DE at the beginning and end of a workshift.	FEV_1, FVC, and PEFR were similar between diesel and non-diesel-exposed miners. Smokers had an increased number of decrements over shift than nonsmokers.

Table 5-1. Human studies of exposure to diesel exhaust (continued)

Study	Description	Findings
Ames et al. (1982)	Pulmonary function of 60 diesel-exposed compared with 90 non-diesel-exposed coal miners over workshift.	Significant workshift decrements occurred in miners in both groups who smoked; no significant differences in ventilatory function changes between miners exposed to DE and those not exposed.
Jörgensen and Svensson (1970)	240 iron ore miners matched for diesel exposure, smoking, and age were given bronchitis questionnaires and spirometry pre- and postworkshift.	Among underground (surrogate for diesel exposure) miners, smokers, and older age groups, frequency of bronchitis was higher. Pulmonary function was similar between groups and subgroups except for differences accountable to age.
Gamble et al. (1979)	200 salt miners performed before- and after-workshift spirometry. Personal environmental NO_2 and inhalable particle samples were collected.	Smokers had greater but not significant reductions in spirometry than ex- or nonsmokers. NO_2 but not particulate levels significantly decreased FEV1, FEF_{25}, FEF_{50}, and FEF_{75} over the workshift.
Gamble et al. (1987a)	232 workers in 4 diesel bus garages administered acute respiratory questionnaire and before and after workshift spirometry. Compared to lead/acid battery workers previously found to be unaffected by their exposures.	Prevalence of burning eyes, headache, difficult or labored breathing, nausea, and wheeze were higher in diesel bus workers than in comparison population.
Ulfvarson et al. (1987)	Workshift changes in pulmonary function were evaluated in crews of roll-on/ roll-off ships and car ferries and bus garage staff. Pulmonary function was evaluated in six volunteers exposed to diluted DE, 2.1 ppm NO_2, and 0.6 mg/m^3 particulate matter.	Pulmonary function was affected during a workshift exposure to DE, but it normalized after a few days with no exposure. Decrements were greater with increasing intervals between exposures. No effect on pulmonary function was observed in the experimental exposure study.
	Cross-sectional and longitudinal studies	
Battigelli et al. (1964)	210 locomotive repairmen exposed to DE for an average of 9.6 years in railroad engine houses were compared with 154 railroad yard workers of comparable job status but no exposure to DE.	No significant differences in VC, FEV_1, peak flow, nitrogen washout, or diffusion capacity or in the prevalence of dyspnea, cough, or sputum were found between the DE-exposed and nonexposed groups.

Table 5-1. Human studies of exposure to diesel exhaust (continued)

Study	Description	Findings
Gamble et al. (1987b)	283 male diesel bus garage workers from four garages in two cities were examined for impaired pulmonary function (FVC, FEV_1, and flow rates). Study population with a mean tenure of 9 ± 10 years S.D. was compared to a nonexposed blue-collar population.	Analyses within the study population showed no association of respiratory symptoms with tenure. Reduced FEV_1 and FEF_{50} (but not FEF_{75}) were associated with increasing tenure. The study population had a higher incidence of cough, phlegm, and wheezing unrelated to tenure. Pulmonary function was not affected in the total cohort of diesel-exposed but was reduced with 10 or more years of tenure.
Purdham et al. (1987)	Respiratory symptoms and pulmonary function were evaluated in 17 stevedores exposed to both diesel and gasoline exhausts in car ferry operations; control group was 11 on-site office workers.	No differences between the two groups for respiratory symptoms. Stevedores had lower baseline lung function consistent with an obstructive ventilatory defect compared with controls and those of Sydney, Nova Scotia, residents. Caution in interpretation is warranted because of small sample size. No significant changes in lung function over workshift or difference between two groups.
Reger et al. (1982)	Differences in respiratory symptoms and pulmonary function were assessed in 823 coal miners from 6 diesel-equipped mines compared to 823 matched coal miners not exposed to DE.	Underground miners in diesel-use mines reported more symptoms of cough and phlegm and had lower pulmonary function. Similar trends were noted for surface workers at diesel-use mines. Pattern was consistent with small airway disease but factors other than exposure to DE thought to be responsible.
Ames et al. (1984)	Changes in respiratory symptoms and function were measured during a 5-year period in 280 diesel-exposed and 838 nonexposed U.S. underground coal miners.	No decrements in pulmonary function or increased prevalence of respiratory symptoms were found attributable to DE. In fact, 5-year incidences of cough, phlegm, and dyspnea were greater in miners without exposure to DE than in miners exposed to DE.
Attfield (1978)	Respiratory symptoms and function were assessed in 2,659 miners from 21 underground metal mines (1,709 miners) and nonmetal mines (950 miners). Years of diesel usage in the mines were surrogate for exposure to DE.	Questionnaire found an association between an increased prevalence of cough and aldehyde exposure; this finding was not substantiated by spirometry data. No adverse symptoms or pulmonary function decrements were related to exposure to NO_2, CO, CO_2, dust, or quartz.

Table 5-1. Human studies of exposure to diesel exhaust (continued)

Study	Description	Findings
Attfield et al. (1982)	Respiratory symptoms and function were assessed in 630 potash miners from 6 potash mines through a questionnaire, chest radiographs, and spirometry. A thorough assessment of the environment of each mine was made concurrently.	No obvious association indicative of diesel exposure was found between health indices, dust exposure, and pollutants. Higher prevalences of cough and phlegm but no differences in FVC and FEV_1 were found in these diesel-exposed potash workers when compared with predicted values from a logistic model based on blue-collar staff working in nondusty jobs.
Gamble et al. (1983)	Respiratory morbidity was assessed in 259 miners in 5 salt mines by respiratory symptoms, radiographic findings, and spirometry. Two mines used diesels extensively, two had limited use, and one used no diesels in 1956, 1957, 1963, or 1963 through 1967. Several working populations were compared with the salt-mine cohort.	After adjustment for age and smoking, salt miners showed no symptoms or increased prevalence of cough, phlegm, dyspnea, or air obstruction (FEV_1/FVC) compared with aboveground coal miners, potash workers, or blue-collar workers. FEV_1, FVC, FEF_{50}, and FEF_{75} were uniformly lower for salt miners in comparison with all the comparison populations. No changes in pulmonary function were associated with years of exposure or cumulative exposure to inhalable particles or NO_2.
Gamble and Jones (1983)	Same as above. Salt miners were grouped into low-, intermediate-, and high-exposure categories based on tenure in jobs with diesel exposure.	A statistically significant dose-related association of phlegm and diesel exposure was noted. Changes in pulmonary function showed no association with diesel tenure. Age- and smoking-adjusted rates of cough, phlegm, and dyspnea were 145%, 169%, and 93% of an external comparison population. Predicted pulmonary function indices showed small but significant reductions; there was no dose-response relationship.
Edling and Axelson (1984)	Pilot study of 129 bus company employees classified into 3 diesel-exhaust exposure categories: clerks (0), bus drivers (1), and bus garage workers.	The most heavily exposed group (bus garage workers) had a fourfold increase in risk of dying from cardiovascular disease, even after correction for smoking and allowing for 10 years of exposure and 14 years or more of induction latency time.
Edling et al. (1987)	Cohort of 694 male bus garage employees followed from 1951 through 1983 was evaluated for mortality from cardiovascular disease. Subcohorts categorized by levels of exposure were clerks (0), bus drivers (1), and bus garage employees (2).	No increased mortality from cardiovascular disease was found among the members of these five bus companies when compared with the general population or grouped as subcohorts with different levels of exposure.

To date, no large-scale epidemiologic study has looked for effects of chronic exposure to DE on pulmonary function. In the long-term longitudinal and cross-sectional studies, a relationship was generally observed between work in a job with diesel exposure and respiratory symptoms (such as cough and phlegm), but there was no consistent effect on pulmonary function. The interpretation of these results is hampered by lack of measured DE exposure levels and the short duration of exposure in these cohorts. The studies are further limited in that only active workers were included, and it is possible that workers who have developed symptoms or severe respiratory disease are likely to have moved away from these jobs. The relationship between work in a job with diesel exposure and respiratory symptoms may be due to short-term exposure.

5.1.2. Traffic Studies

The relationship between traffic density and respiratory health in children has been examined in a series of studies in Holland in children attending schools located near major freeways. Cough, wheeze, runny nose, and doctor-diagnosed asthma were reported more often for children living within 100 m of freeways carrying between 80,000 and 150,000 vehicles per day (van Vliet et al., 1997). Separate counts for truck traffic indicated a range from 8,000 to 17,500 trucks per day. Truck traffic intensity and concentration of "black smoke," considered by the authors to be a proxy for DPM, measured in schools were found to be significantly associated with chronic respiratory symptoms, with the relationships being more pronounced in girls than in boys.

Brunekreef et al. (1997) measured lung function in children in six areas located near major motorways and assessed their exposure to traffic-related air pollution using separate traffic counts for automobiles and trucks. They also measured air pollution in the children's schools. Although lung function was associated with truck traffic density, there was a lesser association with automobile traffic density. The association was stronger in those children living closest (300 m) to the roadways. Lung function was also associated with concentration of "black smoke" (source and constitution unclear from the study) measured inside the schools. The associations were stronger in girls than in boys. The authors conclude that exposure to vehicular pollution, in particular DPM, may lead to reduced lung function in children living near major motorways.

In a follow-up study of traffic-related air pollution and its effect on the respiratory health of children living near roadways, Brunekreef et al. (2000) showed that the intensity of truck traffic was significantly associated with the prevalence of wheeze, phlegm, bronchitis, eye symptoms, and allergy to dust and pets. Associations with yearly averaged $PM_{2.5}$ and "soot" concentrations measured inside and outside the schools showed similar patterns. Truck traffic

intensity was also significantly associated with a positive skin prick test or elevated IgE for outdoor allergens. There were no associations between traffic intensity or $PM_{2.5}$ and "soot" concentrations and lung function, bronchial responsiveness, and allergic reactions to indoor allergens. Further analysis of the data showed that the associations between traffic-related air pollution and symptoms were almost entirely related to children with bronchial hyperreactivity or sensitization to common allergens.

5.1.3. Laboratory Animal Studies

Because humans and laboratory animals show similar nonneoplastic responses to inhaled particles (ILSI, 2000), animal studies have been conducted to assess the pathophysiologic effects of DPM. Because of the large number of statistical comparisons made in the laboratory animal studies, and to permit uniform, objective evaluations within and among studies, data will be reported as significantly different (i.e., $p<0.05$) unless otherwise specified. The exposure regimens used and the resultant exposure conditions employed in the laboratory animal inhalation studies are summarized in Tables 5-2 through 5-16. Other than the pulmonary function studies performed by Wiester et al. (1980) on guinea pigs during their exposure in inhalation chambers, the pulmonary function studies performed by other investigators, although sometimes unreported, were interpreted as being conducted on the following day or thereafter and not immediately following exposure.

5.1.3.1. *Acute Exposures*

The acute toxicity of undiluted DE to rabbits, guinea pigs, and mice was assessed by Pattle et al. (1957). Four engine operating conditions were used, and 4 rabbits, 10 guinea pigs, and 40 mice were tested under each exposure condition for 5 h (no controls were used). Mortality was assessed up to 7 days after exposure. With the engine operating under light load, the exhaust was highly irritating but not lethal to the test species, and only mild tracheal and lung damage was observed in the exposed animals. The exhaust contained 74 mg/m^3 DPM (particle size not reported), 560 ppm CO, 23 ppm NO_2, and 16 ppm aldehydes. Exhaust containing 5 mg/m^3 DPM, 380 ppm CO, 43 ppm NO_2, and 6.4 ppm aldehydes resulted in low mortality rates (mostly below 10%) and moderate lung damage. Exhaust containing 122 mg/m^3 DPM, 418 ppm CO, 51 ppm NO_2, and 6.0 ppm aldehydes produced high mortality rates (mostly above 50%) and severe lung damage. Exhaust containing 1,070 mg/m^3 DPM, 1,700 ppm CO, 12 ppm NO_2, and 154 ppm aldehydes resulted in 100% mortality in all three species. High CO levels, which resulted in a carboxyhemoglobin value of 60% in mice and 50% in rabbits and guinea pigs, were considered to be the main cause of death in the latter case. High NO_2 levels

were considered to be the main cause of lung damage and mortality seen in the other three tests. Aldehydes and NO_2 were considered to be the main irritants in the light load test.

Kobayashi and Ito (1995) administered 1, 10, or 20 mg/kg DPM in phosphate-buffered saline to the nasal mucosa of guinea pigs. The administration increased nasal airway resistance, augmented increased airway resistance and nasal secretion induced by a histamine aerosol, increased vascular permeability in dorsal skin, and augmented vascular permeability induced by histamine. The increases in nasal airway resistance and secretion are considered typical responses of nasal mucosa against allergic stimulation. Similar results were reported for guinea pigs exposed via inhalation for 3 h to DE diluted to DPM concentrations of either 1 or 3.2 mg/m^3 (Kobayashi et al., 1997). These studies show that short-term exposure to DPM augments nasal mucosal hyperresponsiveness induced by histamine in guinea pigs.

5.1.3.2. *Short-Term and Subchronic Exposures*

A number of inhalation studies have employed a regimen of 20 h/day, 7 days/week for varying exposure periods up to 20 weeks to differing concentrations of airborne particulate matter, vapor, and gas concentrations of diluted DE. Exposure regimens and characterization of gas-phase components for these studies are summarized in Table 5-2.
Pepelko et al. (1980a) evaluated the pulmonary function of cats exposed under these conditions for 28 days to 6.4 mg/m^3 DPM. The only significant functional change observed was a decrease in maximum expiratory flow rate at 10% vital capacity. The excised lungs of the exposed cats appeared charcoal gray, with focal black spots visible on the pleural surface. Pathologic changes included a predominantly peribronchial localization of black-pigmented macrophages within the alveoli characteristic of focal pneumonitis or alveolitis.

The effects of a short-term DE exposure on arterial blood gases, pH, blood buffering, body weight changes, lung volumes, and deflation pressure-volume (PV) curves of young adult rats were evaluated by Pepelko (1982a). Exposures were 20 h/day, 7 days/week for 8 days to a concentration of 6.4 mg/m^3 DPM in the nonirradiated exhaust (RE) and 6.75 mg/m^3 in the irradiated exhaust (IE). In spite of the irradiation, levels of gaseous compounds were not substantially different between the two groups (Table 5-2). Body weight gains were significantly reduced in the RE-exposed rats and to an even greater degree in rats exposed to IE. Arterial blood gases and standard bicarbonate were unaffected, but arterial blood pH was significantly reduced in rats exposed to IE. Residual volume and wet lung weight were not affected by either exposure, but vital capacity and total lung capacity were increased significantly following exposure to RE. The shape of the deflation PV curves were nearly identical for the control, RE, and IE groups.

Table 5-2. Short-term effects of diesel exhaust on laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, F344, M; Mouse, A/J, M; Hamster, Syrian, M	20 h/day 7 days/week 10-13 weeks	1.5 0.19 µm MMD	2,100 to 2,730	6.9	0.49	—	Increase in lung wt; increase in thickness of alveolar walls; minimal species difference	Kaplan et al. (1982)
Rat, F344, M, F; Mouse, CD-1, M, F	7 h/day 5 days/week 19 weeks	0.21 1.0 4.4	140 665 2,926	— — —	— — —	— — —	No effects on lung function in rats (not done in mice); increase in PMNs and proteases and AM aggregation in both species	Mauderly et al. (1981)
Cat, Inbred, M	20 h/day 7 days/week 4 weeks	6.4	3,584	14.6	2.1	2.1	Few effects on lung function; focal pneumonitis or alveolitis	Pepelko et al. (1980a)
Rat, Sprague-Dawley, M	20 h/day 7 days/week 4 weeks	6.4 6.8[a]	3,584 3,808	16.9 16.1[a]	2.49 2.76[a] (<0.01 ppm O_3)[a]	2.10 1.86[a]	Decreased body wt; arterial blood pH reduced; vital capacity, total lung capacities increased	Pepelko (1982a)
Guinea Pig, Hartley, M, F	20 h/day 7 days/week 4 weeks	6.8[a]	3,808	16.7	2.9 (<0.01 ppm O_3)[a]	1.9	Exposure started when animals were 4 days old; increase in pulmonary flow; bardycardia	Wiester et al. (1980)
Rat, F344, M	20 h/day 5.5 days/week 4 weeks	6.0 6.8 µm MMD	2,640	—	—	—	Macrophage aggregation; increase in PMNs; Type II cell proliferation; thickened alveolar walls	White and Garg (1981)
Guinea Pig, Hartley, M	30 min	1-2 mg DPM Intranasally	—	—	—	—	Augmented increases in nasal airway resistance and vascular permeability induced by a histamine aerosol	Kobayashi and Ito (1995)
Guinea Pig, Hartley, M	3 h	1 3.2	0.5 1.6	5.9 12.9	1.4 4.4	0.13 0.34	Similar results to those reported in the previous study using intranasal challenge	Kobayashi et al. (1997)

Table 5-2. Short-term effects of diesel exhaust on laboratory animals (continued)

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Guinea Pig, Hartley, M, F	20 h/day 7 days/week 8 weeks	6.3	7,056	17.4	2.3	2.1	Increase in relative lung wt. AM aggregation; hypertrophy of goblet cells; focal hyperplasia of alveolar epithelium	Wiester et al. (1980)
Mouse ICR, M	6 weeks	100 μg DPM intranasally	—	—	—	—	DPM aggravated ovalbumin-induced airway inflammation and provided evidence that DPM can enhance manifestations of allergic asthma	Takano et al. (1997)
Rat, Sprague-Dawley, M	24 h	5-100 $\mu g/10^6$ AM/mL of DPM	—	—	—	—	Unchanged, but not organic-free DPM enhanced production of proinflammatory cytokines	Yang et al. (1997)

[a]Irradiated exhaust.
PMN = Polymorphonuclear leukocyte.
AM = Alveolar macrophage.

In related studies, Wiester et al. (1980) evaluated pulmonary function in 4-day-old guinea pigs exposed for 20 h/day, 7 days/week for 28 days to IE having a concentration of 6.3 mg/m^3 DPM. When housed in the exposure chamber, pulmonary flow resistance increased 35%, and a small but significant sinus bradycardia occurred as compared with controls housed and measured in control air chambers (p<0.002). Respiratory rate, tidal volume, minute volume, and dynamic compliance were unaffected, as were lead-1 electrocardiograms.

A separate group of adult guinea pigs was necropsied after 56 days of exposure to IE, to diluted RE, or to clean air (Wiester et al., 1980). Exposure resulted in a significant increase in the ratio of lung weight to body weight (0.68% for controls, 0.78% for IE, and 0.82% for RE). Heart/body weight ratios were not affected by exposure. Microscopically, there was a marked accumulation of black pigment-laden AMs throughout the lung, with a slight to moderate accumulation in bronchial and carinal lymph nodes. Hypertrophy of goblet cells in the tracheobronchial tree was frequently observed, and focal hyperplasia of alveolar lining cells was occasionally observed. No evidence of squamous metaplasia of the tracheobronchial tree, emphysema, peribronchitis, or peribronchiolitis was noted.

White and Garg (1981) studied pathologic alterations in the lungs of rats (16 exposed and 8 controls) after exposure to DE containing 6 mg/m^3 DPM. Two rats from the exposed group and one rat from the control group (filtered room air) were sacrificed after each exposure interval of 6 h and 1, 3, 7, 14, 28, 42, and 63 days; daily exposures were for 20 h and were 5.5 days/week. Evidence of AM recruitment and phagocytosis of diesel particles was found at the 6-h sacrifice; after 24 h of exposure there was a focal, scattered increase in the number of Type II cells. After 4 weeks of exposure, there were morphologic changes in size, content, and shape of AM, septal thickening adjacent to clusters of AMs, and an appearance of inflammatory cells, primarily within the septa. At 9 weeks of exposure, focal aggregations of particle-laden macrophages developed near the terminal bronchi, along with an influx of PMNs, Type II cell proliferation, and thickening of alveolar walls. The affected alveoli occurred in clusters that, for the most part, were located near the terminal bronchioles, but occasionally were focally located in the lung parenchyma. Hypertrophy of goblet cells in the tracheobronchial tree was frequently observed, and focal hyperplasia of alveolar lining cells was occasionally observed. No evidence of squamous metaplasia of the tracheobronchial tree, emphysema, peribronchitis, or peribronchiolitis was noted.

Mauderly et al. (1981) exposed rats and mice by inhalation to diluted DE for 545 h over a 19-week period on a regimen of 7 h/day, 5 days/week at concentrations of 0, 0.21, 1.02, or 4.38 mg/m^3 DPM. Indices of health effects were minimal following 19 weeks of exposure. There were no significant exposure-related differences in mortality or body weights of the rats or mice. There also were no significant differences in respiratory function (breathing patterns,

dynamic lung mechanics, lung volumes, quasi-static PV relationships, forced expirograms, and CO-diffusing capacity) in rats; pulmonary function was not measured in mice. No effect on tracheal mucociliary or deep lung clearances were observed in the exposed groups. Rats, but not mice, had elevated immune responses in lung-associated lymph nodes at the two higher exposure levels. Inflammation in the lungs of rats exposed to 4.38 mg/m^3 DPM was indicated by increases in PMNs and lung tissue proteases. Histopathologic findings included AMs that contained DPM, an increase in Type II cells, and the presence of particles in the interstitium and tracheobronchial lymph nodes.

Kaplan et al. (1982) evaluated the effects of subchronic exposure to DE on rats, hamsters, and mice. The exhaust was diluted to a concentration of 1.5 mg/m^3 DPM; exposures were 20 h/day, 7 days/week. Hamsters were exposed for 86 days, rats and mice for 90 days. There were no significant differences in mortality or growth rates between exposed and control animals. Lung weight relative to body weight of rats exposed for 90 days was significantly higher than the mean for the control group. Histological examination of tissues of all three species indicated particle accumulation in the lungs and mediastinal lymph nodes. Associated with the larger accumulations, there was a minimal increase in the thickness of the alveolar walls, but the vast majority of the particles elicited no response. After 6 mo of recovery, considerable clearance of the DPM from the lungs occurred in all three species, as evaluated by gross pathology and histopathology. However, no quantitative estimate of clearance was provided.

Toxic effects in animals from acute exposure to DE appear to be primarily attributable to the gaseous components (i.e., mortality from CO intoxication and lung injury caused by cellular damage resulting from NO_2 exposure). The results from short-term exposures indicate that rats experience minimal lung function impairment even at DE levels sufficiently high to cause histological and cytological changes in the lung. In subchronic studies of durations of 4 weeks or more, frank adverse health effects are not readily apparent and, when found, are mild and result from exposure to concentrations of about 6 mg/m^3 DPM and durations of exposures of 20 h/day. There is ample evidence that subchronic exposure to lower levels of DE affects the lung, as indicated by accumulation of particles, evidence of inflammatory response, AM aggregation and accumulation near the terminal bronchioles, Type II cell proliferation, and thickening of alveolar walls adjacent to AM aggregates. Little evidence exists, however, that subchronic exposure to DE impairs lung function.

5.1.3.3. *Chronic Exposures*

5.1.3.3.1. ***Effects on growth and longevity.*** Changes in growth, body weight, absolute or relative organ weights, and longevity can be measurable indicators of chronic toxic effects.

Such effects have been observed in some, but not all, of the long-term studies conducted on laboratory animals exposed to DE. There was limited evidence for an effect on survival in the published chronic animal studies; deaths occurred intermittently early in one study in female rats exposed to 3.7 mg/m^3 DPM; however, the death rate began to decrease after 15 mo, and the survival rate after 30 mo was slightly higher than that of the control group (Ishinishi et al., 1988). Studies of the effects of chronic exposure to DE on survival and body weight or growth are detailed in Table 5-3.

Increased lung weights and lung-to-body weight ratios have been reported in rats, mice, and hamsters. These data are summarized in Table 5-4. In rats exposed for up to 36 weeks to 0.25 or 1.5 mg/m^3 DPM, lung wet weights (normalized to body weight) were significantly higher in the 1.5 mg/m^3 exposure group than control values after 12 weeks of exposure (Misiorowski et al., 1980). Rats and Syrian hamsters were exposed for 2 years (five 16-h periods per week) to DE diluted to achieve concentrations of 0.7, 2.2, and 6.6 mg/m^3 DPM (Brightwell et al., 1986). At necropsy, a significant increase in lung weight was seen in both rats and hamsters exposed to DE compared with controls. This finding was more pronounced in the rats in which the increase was progressive with both duration of exposure and particulate matter level. The increase was greatest at 30 mo (after the end of a 6-mo observation period in the high-concentration male group where the lung weight was 2.7 times the control and at 24 mo in the high-concentration female group [3.9 times control]). Heinrich et al. (1986a,b; see also Stöber, 1986) found a significant increase in wet and dry weights of the lungs of rats and mice exposed at 4.24 mg/m^3 DPM for 1 year in comparison with controls. After 2 years, the difference was a factor of 2 (mice) or 3 (rats). After the same exposure periods, the hamsters showed increases of 50% to 75%, respectively. Exposure to equivalent filtered DE (i.e., without DPM) caused no significant effects in any of the species. Vinegar et al. (1980, 1981a,b) exposed hamsters to two levels of DE with resultant concentrations of about 6 and 12 mg/m^3 DPM for 8 h/day, 7 days/week for 6 mo. Both exposures significantly increased lung weight and lung-weight to body-weight ratios. The difference between lung weights of exposed and control hamsters exposed to 12 mg/m^3 DPM was approximately twice that of those exposed to 6 mg/m^3.

Heinrich et al. (1995) reported that rats exposed to 2.5 and 7 mg/m^3 DPM for 18 h/day, 5 days/week for 24 mo showed significantly lower body weights than controls starting at day 200 in the high-concentration group and at day 440 in the low-concentration group. Body weight in the low-concentration group was unaffected, as was mortality in any group. Lung weight was increased in the 7 mg/m^3 group starting at 3 mo and persisting throughout the study, while the 2.5 mg/m^3 group showed increased lung weight only at 22 and 24 mo of exposure. Mice (NMRI strain) exposed to 7 mg/m^3 in this study for 13.5 mo had no increase in mortality and insignificant decreases in body weight. Lung weights were dramatically affected, with

Table 5-3. Effects of chronic exposures to diesel exhaust on survival and growth of laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, F344, M, F; Monkey, Cynomolgus, M	7 h/day 5 days/week 104 weeks	2.0 0.23–0.36μ m MMD	7,280	11.5	1.5	0.8	No effects on growth or survival	Lewis et al. (1989)
Rat, F344, M; Guinea Pig, Hartley, M	20 h/day 5 days/week 106 weeks	0.25 0.75 1.5 0.19 μm MMD	2,650 7,950 15,900	2.7[a] 4.4[a] 7.1[a]	0.1[b] 0.27[b] 0.5[b]	— — —	Reduced body weight in rats at 1.5 mg/m^3	Schreck et al. (1981)
Hamster, Chinese, M	8 h/day 7 days/week 26 weeks	6.0 12.0	8,736 17,472	— —	— —	— —	No effect on growth	Vinegar et al. (1981a,b)
Rat, Wistar, M	6 h/day 5 days/week 87 weeks	8.3 0.71 μm MMD	21,663	50.0	4.0–6.0	—	No effect on growth or mortality rates	Karagianes et al. (1981)
Rat, F344, M, F; Mouse, CD-1, M, F	7 h/day 5 days/week 130 weeks	0.35 3.5 7.1 0.25 μm MMD	1,592 15,925 31,850	2.9 16.5 29.7	0.05 0.34 0.68	— — —	No effect on growth or mortality rates	Mauderly et al. (1984, 1987a)
Rat, Wistar, F; Mouse, MMRI, F	19 h/day 5 days/week 104 weeks	4.24 0.35 μm MMD	41,891	12.5	1.5	1.1	Reduced body wts; increased mortality in mice	Heinrich et al. (1986a)
Rat, F344 M, F	16 h/day 5 days/week 104 weeks	0.7 2.2 6.6	5,824 18,304 54,912	— — 32.0	— — —	— — —	Growth reduced at 2.2 and 6.6 mg/m^3	Brightwell et al. (1986)
Rat[c] F344/Jcl.	16 h/day 6 days/week 130 weeks	0.11[d] 0.41[d] 1.08[d] 2.31[d] 3.72[e] 0.2–0.3 μm MMD	1,373 5,117 13,478 28,829 46,426	1.23 2.12 3.96 7.10 12.9	0.08 0.26 0.70 1.41 3.00	0.38 1.06 2.42 4.70 4.57	Concentration-dependent decrease in body weight; earlier deaths in females exposed to 3.72 mg/m^3, stabilized by 15 mo	Research Committee for HERP Studies (1988)
Rat, Wistar, F; Mouse, NMRI, F (7 mg/m^3 only)	18 h/day 5 days/week 24 mo	0.84 2.5 6.98	7,400 21,800 61,700	2.6 8.3 21.2	0.3 1.2 3.8	0.3 1.1 3.4	Reduced body weight in rats at 2.5 and 6.98 mg/m^3 and no effect in mice	Heinrich et al. (1995)

Table 5-3. Effects of chronic exposures to diesel exhaust on survival and growth of laboratory animals (continued)

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Mice, NMRI, F; C57BL/6N, F	18 h/day 5 days/week 13.5 mo (NMRI) 24 mo (C57BL/N)	6.98	35,500 - NMRI 38,300 - C57	14.2	2.3	2.8	Reduced body weight in NMRI mice but not in C57BL/6N mice	Heinrich et al. (1995)
Rats, F344, M	16 h/day 5 days/week 23 mo	2.44 6.33	19,520 50,640	— —	— —	— —	Reduced survival in 6.33 mg/m^3 after 300 days. Body weight significantly lower at 6.33 mg/m^3	Nikula et al. (1995)
Mouse, CD-1, M,F	7 h/day 5 days/week 104 weeks	0.35 3.5 7.1 0.25 μm MDD	1,274 12,740 25,844	3 17 30	0.1 0.3 0.7	— — —	No effect on growth or mortality rates	Mauderly et al. (1996)

[a]Estimated from graphically depicted mass concentration data.
[b]Estimated from graphically presented mass concentration data for NO_2 (assuming 90% NO and 10% NO_2).
[c]Data for tests with light-duty engine; similar results with heavy-duty engine.
[d]Light-duty engine.
[e]Heavy-duty engine.

Table 5-4. Effects of chronic exposures to diesel exhaust on organ weights and organ-to-body-weight ratios

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, F344, M; Mouse, A/J, M; Hamster, Syrian, M	20 h/day 7 days/week 12-13 weeks	1.5 0.19 µm MMD	2,520-2,730	—	—	—	No effect on liver, kidney, spleen, or heart weights	Kaplan et al. (1982)
Rat, F344, M, F	7 h/day 5 days/week 52 weeks	2.0 0.23–0.36 µm MMD	3,640	12.7	1.6	0.83	No effects on weights of lungs, liver, heart, spleen, kidneys, and testes	Green et al. (1983)
Rat, F344, M	20 h/day 5.5 days/ week 36 weeks	0.25 1.5 0.19 µm MMD	990 5,940	— —	— —	— —	Increase in relative lung weight at 1.5 mg/m^3 only initially seen at 12 weeks	Misiorowski et al. (1980)
Rat, F344, F	7 h/day 5 days/week 104 weeks	2.0 0.23–0.36 µm MMD	7,280	11.5	1.5	0.81	No effects on heart weights	Vallyathan et al. (1986)
Rat, F344; M Guinea Pig, Hartley, M	20 h/day 5.5 days/ week 78 weeks	0.25 0.75 1.5 0.19 µm MMD	2,145 6,435 12,870	— — —	— — —	— — —	No effects on heart mass	Penney et al. (1981)
Hamster, Chinese, M	8 h/day 7 days/week 26 weeks	6.0 12.0	8,736 17,472	— —	— —	— —	Increase in lung weight and lung/body weight ratio	Vinegar et al. (1981a,b)
Rat, Wistar, F; Hamster, Syrian, M, F Mouse, NMRI, F	19 h/day 5 days/week 120-140 weeks	4.24 0.35 µm MMD	48,336-56,392	12.5	1.5	1.1	Increase in rat, mouse, and hamster lung weight and dry weights	Heinrich et al. (1986a,b) Stöber (1986)
Rat, F344, M, F; Hamster, Syrian, M, F	16 h/day 5 days/week 104 weeks	0.7[a] 2.2[b] 6.6	5,824 18,304 54,912	— — 32.0	— — —	— — —	Increase in lung weight concentration related in rats; heart weight/body weight ratio greater at 6.6 mg/m^3	Brightwell et al. (1986)
Cat, inbred, M	8 h/day 7 days/week 124 weeks	6.0[a] 12.0[b]	41,664 83,328	20.2 33.2	2.7 4.4	2.7 5.0	Decrease in lung and kidney weights	Pepelko et al. (1980b, 1981) Moorman et al. (1985)
Mouse, NMRI, F (7 mg/m^3 only)	18 h/day 5 days/week 24 mo	0.84 2.5 6.98	7,400 21,800 61,700	2.6 8.3 21.2	0.3 1.2 3.8	0.3 1.1 3.4	Increased rat and mouse lung weight at 7 mg/m^3 from 6 mo and at 2.5 mg/m^3 at 22 and 24 mo	Heinrich et al. (1995)

Table 5-4. Effects of chronic exposures to diesel exhaust on organ weights and organ-to-body-weight ratios (continued)

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Mouse, NMRI, F; C57BL/6N, F	18 h/day 5 days/week 13.5 mo (NMRI) 24 mo (C57BL/N)	6.98	35,500 - NMRI 38,300 - C57	14.2	2.3	2.8	Increased lung weight	Heinrich et al. (1995)
Rats, F344, M	16 h/day 5 days/week 23 mo	2.44 6.33	19,520 50,640	— —	— —	— —	Increase in lung weight was significant at 2 and 6 mg/m^3	Nikula et al. (1995)
Rat		0.8 2.5 6.98					Increased lung weight in rats and mice at 3.5 and 7.1 mg/m^3	Henderson et al. (1988a)
Mouse		6.98 4.5						

[a]1 to 61 weeks of exposure.
[b]62 to 124 weeks of exposure.

increases progressing throughout the study from 1.5-fold at 3 mo to 3-fold at 12 mo. Mice (NMRI and C57BL/6N strains) were also exposed to 4.5 mg/m^3 for 23 mo. In NMRI mice, the body weights were reported to be significantly lower than controls, but the magnitude of the change is not reported, so biological significance cannot be assessed. Mortality was slightly increased, but statistical significance is not reported. The C57BL/6N mice showed minimal effects on body weight and mortality, which were not statistically significant. Lung weights were dramatically affected in both strains.

Nikula et al. (1995) exposed male and female F344 rats to DPM concentrations of 2.4 and 6.3 mg/m^3 for 16 h/day, 5 days/week for 23 mo in a study designed to compare the effects of DPM with those of carbon black. Significantly reduced survival was observed in males exposed to 6.3 mg/m^3 but not in females or at the lower concentration. Body weights were decreased by exposure to 6.3 mg/m^3 DPM in both male and female rats throughout the exposure period. Significant increases in lung weight were first seen at 6 mo in the high-exposure group and at 12 to 18 mo in the low-exposure group.

No evidence was found in the published literature that chronic exposure to DE affected the weight of body organs other than the lung and heart (e.g., liver, kidney, spleen, or testes) (Table 5-4). Morphometric analysis of hearts from rats and guinea pigs exposed to 0.25, 0.75, or 1.5 mg/m^3 DPM 20 h/day, 5.5 days/week for 78 weeks revealed no significant alteration in mass at any exposure level or duration of exposure (Penney et al., 1981). The analysis included relative wet weights of the right ventricle, left ventricle, combined atria, and ratio of right to left ventricle. Vallyathan et al. (1986) found no significant differences in heart weights and the ratio of heart weight to body weight between rats exposed to 2 mg/m^3 DPM for 7 h/day, 5 days/week for 24 mo and their respective clean-air chamber controls. No significant differences were found in the lungs, heart, liver, spleen, kidney, and testes of rats exposed for 52 weeks, 7 h/day, 5 days/week to diluted DE containing 2 mg/m^3 DPM compared with their respective controls (Green et al., 1983).

5.1.3.3.2. ***Effects on pulmonary function.*** The effect of long-term exposure to DE on pulmonary function has been evaluated in laboratory studies of rats, hamsters, cats, and monkeys. These studies are summarized in Table 5-5, along with more details on the exposure characteristics, in general order of increasing dose (C × T) of DPM. The text will be presented using the same approach.

Lewis et al. (1989) evaluated functional residual capacity and airway resistance and conductance in 10 control and 10 diesel-exposed rats (2 mg/m^3 DPM, 7 h/day, 5 days/week for 52 or 104 weeks). At the 104-week evaluation, the rats were also examined for maximum flow volume impairments. No evidence of impaired pulmonary function as a result of the exposure to

Table 5-5. Effects of diesel exhaust on pulmonary function of laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, F344, M, F	7 h/day 5 days/week 104 weeks	2.0 0.23–0.36 µm MMD	7,280	11.5	1.5	0.8	No effect on pulmonary function	Lewis et al. (1989)
Monkey, Cynomolgus, M	7 h/day 5 days/week 104 weeks	2.0 0.23-0.36 µm MMD	7,280	11.5	1.5	0.8	Decreased expiratory flow; no effect on vital or diffusing capacities	Lewis et al. (1989)
Rat, F344, M	20 h/day 5.5 days/week 87 weeks	1.5 0.19 µm MMD	14,355	7.0	0.5	—	Increased functional residual capacity, expiratory volume, and flow	Gross (1981)
Rat, Wistar, F	7-8 h/day 5 days/week 104 weeks	3.9 0.1 µm MMD	14,196-16,224	18.5	1.2	3.1	No effect on minute volume, compliance, or resistance	Heinrich et al. (1982)
Hamster, Chinese, M	8 h/day 7 days/week 26 weeks	6.0 12.0	8,736 17,472	— —	— —	— —	Decrease in vital capacity, residual volume, and diffusing capacity; increase in static deflation lung volume	Vinegar et al. (1980, 1981a,b)
Rat, F344, M, F	7 h/day 5 days/week 130 weeks	0.35 3.5 7.1 0.23–0.26 µm MMD	1,593 15,925 31,850	2.9 16.5 29.7	0.05 0.34 0.68	— — —	Diffusing capacity, lung compliance reduced at 3.5 and 7.1 mg/m^3	Mauderly et al. (1988) McClellan et al. (1986)
Rat, F344, M, F; Hamster, Syrian, M, F	16 h/day 5 days/week 104 weeks	0.7 2.2 6.6	5,824 18,304 54,912	— — —	— — —	— — —	Large number of pulmonary function changes consistent with obstructive and restrictive airway diseases at 6.6 mg/m^3 (no specific data provided)	Brightwell et al. (1986)
Hamster, Syrian, M, F	19 h/day 5 days/week 120 weeks	4.24 0.35 µm MMD	48,336	12.5	1.5	1.1	Significant increase in airway resistance	Heinrich et al. (1986a)
Rat, Wistar, F	19 h/day 5 days/week 140 weeks	4.24 0.35 µm MMD	56,392	12.5	1.5	1.1	Decrease in dynamic lung compliance; increase in airway resistance	Heinrich et al. (1986a)
Cat, inbred, M	8 h/day 7 days/week 124 weeks	6.0[a] 12.0[b]	41,664 83,328	20.2 33.3	2.7 4.4	2.1 5.0	Decrease in vital capacity, total lung capacity, and diffusing capacity after 2 years; no effect on expiratory flow	Pepelko et al. (1980b, 1981) Moorman et al. (1985)

[a]1 to 61 weeks exposure.
[b]62 to 124 weeks of exposure.

DE was found in rats. Lewis et al. (1989) exposed male cynomolgus monkeys to DE for 7 h/day, 5 days/week for 24 mo. Groups of 15 monkeys were exposed to air, DE (2 mg/m^3), coal dust, or combined coal dust and DE. Pulmonary function was evaluated prior to exposure and at 6-mo intervals during the 2-year exposure, including compliance and resistance, static and dynamic lung volumes, distribution of ventilation, diffusing capacity, and maximum ventilatory performance. There were no effects on lung volumes, diffusing capacity, or ventilation distribution, so there was no evidence of restrictive disease. There was, however, evidence of obstructive airway disease as measured by low maximal flow rates in diesel-exposed monkeys. At 18 mo of exposure, forced expiratory flow at 25% of vital capacity and forced expiratory flow normalized to FVC were decreased. The measurement of forced expiratory flow at 40% of total lung capacity was significantly decreased at 12, 18, and 24 mo of exposure. The finding of an obstructive effect in monkeys contrasts with the finding of restrictive type effects in other laboratory animal species (Vinegar et al., 1980, 1981a; Mauderly et al., 1988; Pepelko et al., 1980b, 1981) and suggests a possible difference in effect between primate and small animal respiratory tracts. In these monkeys there were no specific histopathological effects reported (see next section), although particle aggregates were reported in the distal airways, suggesting more small airway deposition.

Gross (1981) exposed rats for 20 h/day, 5.5 days/week for 87 weeks to DE containing 1.5 mg/m^3 DPM. When the data were normalized (e.g., indices expressed in units of airflow or volume for each animal by its own forced expiratory volume), there were no apparent functionally significant changes occurring in the lungs at 38 weeks of exposure that might be attributable to the inhalation of DE. After 87 weeks of exposure, functional residual capacity (FRC) and its component volumes (expiratory reserve [ER] and residual volume [RV]), maximum expiratory flow (MEF) at 40% FVC, MEF at 20% FVC, and $FEV_{0.1}$ were significantly greater in the diesel-exposed rats. An observed increase in airflow at the end of the forced expiratory maneuver when a decreased airflow would be expected from the increased FRC, ER, and RV data (the typical scenario of human pulmonary disease) showed these data to be inconsistent with known clinically significant health effects. Furthermore, although the lung volume changes in the diesel-exposed rats could have been indicative of emphysema or chronic obstructive lung disease, this interpretation was contradicted by the airflow data, which suggest simultaneous lowering of the resistance of the distal airways.

Heinrich et al. (1982) evaluated the pulmonary function of rats exposed to a concentration of 3.9 mg/m^3 DPM for 7 to 8 h/day, 5 days/week for 2 years. When compared with a control group, no significant changes in respiratory rate, minute volume, compliance, or resistance occurred in the exposed group (number of rats per group was not stated).

Chinese hamsters (eight or nine per group) were exposed 8 h/day, 7 days/week, for 6 mo to concentrations of either about 6 mg/m^3 or about 12 mg/m^3 DPM (Vinegar et al., 1980,

1981a,b). Vital capacity, vital capacity/lung weight ratio, residual lung volume by water displacement, and CO_2 diffusing capacity decreased significantly in hamsters exposed to 6 mg/m^3 DPM. Static deflation volume-pressure curves showed depressed deflation volumes for diesel-exposed hamsters when volumes were corrected for body weight and even greater depressed volumes when volumes were corrected for lung weight. However, when volumes were expressed as percentage of vital capacity, the diesel-exposed hamsters had higher lung volumes at 0 and 5 cm H_2O. In the absence of confirmatory histopathology, the authors tentatively concluded that these elevated lung volumes and the significantly reduced diffusing capacity in the same hamsters were indicative of possible emphysematous changes in the lung. Similar lung function changes were reported in hamsters exposed at 12 mg/m^3 DPM, but detailed information was not reported. It was stated, however, that the decrease in vital capacity was 176% greater in the second experiment than in the first.

Mauderly et al. (1988; see also McClellan et al., 1986) examined the impairment of respiratory function in rats exposed for 7 h/day, 5 days/week for 24 mo to diluted DE with 0.35, 3.5, or 7.1 mg/m^3 DPM. After 12 mo of exposure to the highest concentration of DE, the exposed rats (n = 22) had lower total lung capacity (TLC), dynamic lung compliance (C_{dyn}), FVC, and CO diffusing capacity than controls (n = 23). After 24 mo of exposure to 7.1 mg/m^3 DPM, mean TLC, C_{dyn}, quasi-static chord compliance, and CO diffusing capacity were significantly lower than control values. Nitrogen washout and percentage of FVC expired in 0.1 s were significantly greater than control values. There was no evidence of airflow obstruction. The functional alterations were attributed to focal fibrotic and emphysematous lesions and thickened alveolar membranes observed by histological examination. Similar functional alterations and histopathologic lesions were observed in the rats exposed to 3.5 mg/m^3 DPM, but such changes usually occurred later in the exposure period and were generally less pronounced. There were no significant decrements in pulmonary function for the 0.35 mg/m^3 group at any time during the study nor were there reported histopathologic changes in this group.

Mauderly et al. (1989) examined the effects of DE on normal rats and on rats with experimentally induced pulmonary emphysema to see if emphysematous rats have increased susceptibility to DPM. The results from parallel lifetime exposures of these 2 groups of rats at 3.5 mg/m^3 DPM showed that only possibly 1 of 65 measured parameters gave results suggesting that rats with emphysematous lungs might be more susceptible than rats with normal lungs to the effects of DE exposure.

Additional studies were conducted by Heinrich et al. (1986a,b; see also Stöber, 1986) on the effects of long-term exposure to DE on the pulmonary function of hamsters and rats. The exhaust was diluted to achieve a concentration of 4.24 mg/m^3 DPM; exposures were for 19 h/day, 5 days/week for a maximum of 120 weeks (hamsters) or 140 weeks (rats). After 1 year of exposure to the DE, the hamsters exhibited a significant increase in airway resistance and a

nonsignificant reduction in lung compliance. For the same time period, rats showed increased lung weights, a significant decrease in C_{dyn}, and a significant increase in airway resistance. These indices did not change during the second year of exposure.

Syrian hamsters and rats were exposed to 0.7, 2.2, or 6.6 mg/m^3 DPM for five 16-h periods per week for 2 years (Brightwell et al., 1986). There were no treatment-related changes in pulmonary function in the hamster. Rats exposed to the highest concentration of DE exhibited changes in pulmonary function (data not presented) that were reported to be consistent with a concentration-related obstructive and restrictive disease.

Pepelko et al. (1980b; 1981; see also Pepelko, 1982b) and Moorman et al. (1985) measured the lung function of adult cats chronically exposed to DE. The cats were exposed for 8 h/day and 7 days/week for 124 weeks. Exposures were at 6 mg/m^3 for the first 61 weeks and 12 mg/m^3 from weeks 62 to 124. No definitive pattern of pulmonary function changes was observed following 61 weeks of exposure; however, a classic pattern of restrictive lung disease was found at 124 weeks. The significantly reduced lung volumes (TLC, FVC, FRC, and inspiratory capacity [IC]) and the significantly lower single-breath diffusing capacity, coupled with normal values for dynamic ventilatory function (mechanics of breathing), indicate the presence of a lesion that restricts inspiration but does not cause airway obstruction or loss of elasticity. This pulmonary physiological syndrome is consistent with an interstitial fibrotic response that was later verified by histopathology (Plopper et al., 1983).

Pulmonary function impairment has been reported in rats, hamsters, cats, and monkeys chronically exposed to DE. In all species but the monkey, the pulmonary function testing results have been consistent with restrictive lung disease. The monkeys demonstrated evidence of small airway obstructive responses. The disparity between the findings in monkeys and those in rats, hamsters, and cats could be in part the result of increased particle retention in the smaller species resulting from (1) exposure to DE that has higher airborne concentrations of gases, vapors, and particles and/or (2) longer duration of exposure. The nature of the pulmonary impairment is also dependent on the site of deposition and routes of clearance, which are determined by the anatomy and physiology of the test laboratory species and the exposure regimen. The data on pulmonary function effects raise the possibility that DE produces small airway disease in primates compared with primarily alveolar effects in small animals and that similar changes might be expected in humans and monkeys. The findings of Nikula et al. (1997a,b) suggest that a larger fraction of particles are translocated to the interstitium of the respiratory tract in primates that are heavily exposed than in rats that are heavily exposed, including the interstitium of the respiratory bronchioles, an anatomical site absent in rats. Nikula and co-workers' pulmonary histopathological findings may have a relationship to these functional findings (see Chapter 3 for a complete discussion). Unfortunately, the available data in primates are too limited to draw clear conclusions.

5.1.3.3.3. ***Lung morphology, biochemistry, and lung lavage analysis.*** Several studies have examined the morphological, histological, and histochemical changes occurring in the lungs of laboratory animals chronically exposed to DE. The histopathological effects of diesel exposure in the lungs of laboratory animals are summarized in Table 5-6, ranked in order of C × T. Table 5-6 also contains an expanded description of exposures.

Kaplan et al. (1982) performed macroscopic and microscopic examinations of the lungs of rats, mice, and hamsters exposed for 20 h/day, 7 days/week for 3 mo to DE containing 1.5 mg/m^3 DPM. Gross examination revealed diffuse and focal deposition of the diesel particles that produced a grayish overall appearance of the lungs with scattered, denser black areas. There was clearance of particles via the lymphatics to regional lymph nodes. Microscopic examination revealed no anatomic changes in the upper respiratory tract; the mucociliary border was normal in appearance. Most of the particles were in macrophages, but some were free as small aggregates on alveolar and bronchiolar surfaces. The particle-laden macrophages were often in masses near the entrances of the lymphatic drainage and respiratory ducts. Associated with these masses was a minimal increase in the thickness of the alveolar walls; however, the vast majority of the particles elicited no response. After 6 mo of recovery, the lungs of all three species contained considerably less pigment, as assessed by gross pathological and histopathological examinations.

Lewis et al. (1989; see also Green et al., 1983) performed serial histological examinations of rat lung tissue exposed to DE containing 2 mg/m^3 DPM for 7 h/day, 7 days/week for 2 years. Accumulations of black-pigmented AMs were seen in the alveolar ducts adjacent to terminal bronchioles as early as 3 mo of exposure, and particles were seen within the interstitium of the alveolar ducts. These macular lesions increased in size up to 12 mo of exposure. Collagen or reticulum fibers were seen only rarely in association with deposited particles; the vast majority of lesions showed no evidence of fibrosis. There was no evidence of focal emphysema with the macules. Multifocal histiocytosis (24% of exposed rats) was observed only after 24 mo of exposure. These lesions were most commonly observed subpleurally and were composed of collections of degenerating macrophages and amorphous granular material within alveoli, together with fibrosis and chronic inflammatory cells in the interstitium. Epithelial lining cells

Table 5-6. Histopathological effects of diesel exhaust in the lungs of laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, F344, M; Mouse, A/J, M; Hamster, Syrian, M	20 h/day 7 days/week 12-13 weeks	1.5 0.19 µm MDD	2,520-2,730	—	—	—	Inflammatory changes, increase in lung weight, increase in thickness of alveolar walls	Kaplan et al. (1982)
Monkey, Cynomolgus, M	7 h/day 5 days/week 104 weeks	2.0 0.23–0.36 µm MDD	7,280	11.5	1.5	0.8	AM aggregation; no fibrosis, inflammation, or emphysema	Lewis et al. (1989)
Rat, F344, M, F	7 h/day 5 days/week 104 weeks	2.0 0.23–0.36 µm MDD	3,640	11.5	1.5	0.8	Multifocal histiocytosis, inflammatory changes, Type II cell proliferation, fibrosis	Bhatnagar et al. (1980) Pepelko (1982a)
Rat, Sprague-Dawley, M; Mouse, A/HEJ, M	8 h/day 7 days/week 39 weeks	6.0	13,104	—	—	—	Increase in lung protein content and collagen synthesis but a decrease in overall lung protein synthesis in both species; prolylhydroxylase activity increased in rats in utero	Bhatnagar et al. (1980) Pepelko (1982a)
Hamster, Chinese, M	8 h/day 5 days/week 26 weeks	6.0 12.0	6,240 12,480	— —	— —	— —	Inflammatory changes, AM accumulation, thickened alveolar lining, Type II cell hyperplasia,edema, increase in collagen	Pepelko (1982b)
Hamster, Syrian, M, F	7-8 h/day 5 days/week 120 weeks	3.9 0.1 µm MDD	16,380-18,720	18.5	1.2	3.1	Inflammatory changes, 60% adenomatous cell proliferation	Heinrich et al. (1982)
Rat, Wistar, M	6 h/day 5 days/week 87 weeks	8.3 0.71 µm MDD	21,663	50.0	4.0-6.0	—	Inflammatory changes, AM aggregation, alveolar cell hypertrophy, interstitial fibrosis, emphysema (diagnostic methodology not described)	Karagianes et al. (1981)
Rat, F344, F	8 h/day 7 days/week 104 weeks	4.9	28,538	7.0	1.8	13.1	Type II cell proliferation, inflammatory changes, bronchial hyperplasia, fibrosis	Iwai et al. (1986)
Rat, F344, M, F; Mouse, CD-1, M, F	7 h/day 5 days/week 130 weeks	0.35 3.5 7.1 0.23 µm MDD	1,592 15,925 31,850	2.9 16.5 29.7	0.05 0.34 0.68	— — —	Alveolar and bronchiolar epithelial metaplasia in rats at 3.5 and 7.0 mg/m^3, fibrosis at 7.0 mg/m^3 in rats and mice, inflammatory changes	Mauderly et al. (1987a) Henderson et al. (1988a)

Table 5-6. Histopathological effects of diesel exhaust in the lungs of laboratory animals (continued)

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rats, SPF 344	7 h/day 5days/week 104 weeks	2 mg/m^3 coal dust (CD) 2 mg/m^3 DPM 1 mg/m^3 CD + 1 mg/m^3 DPM	—	—	—	—	• Assessed pharmacological responses of rat airway smooth muscle in vitro • Maximal contractile responses to acetylcholine of tissues from CD-, DPM-, and CD + DPM- exposed animals significantly increased; effects of CD and DPM were additive • Maximal relaxation response to isoproterenol increased significantly by CD + DPM exposure, but not by individual treatments • The results indicate that chronic exposure to CD, DPM, and CD + DPM produce differential modifications in the behavior of rat airway smooth muscle	Feden et al. (1985)
Rat, Wistar, F; Mouse, NMRI, F (7 mg/m^3 only)	18 h/day 5 days/week 24 mo	0.8 2.5 6.98	7,400 21,800 61,700	2.6 8.3 21.2	0.3 1.2 3.8	0.3 1.1 3.4	Bronchioalveolar hyperplasia, interstitial fibrosis in all groups. Severity and incidence increase with exposure concentration	Heinrich et al. (1995)
Mouse, NMRI, F; C57BL/6N, F	18 h/day 5 days/week 13.5 mo (NMRI) 24 mo (C57BL/N)	6.98	35,500 - NMRI 38,300 - C57	14.2	2.3	2.8	No increase in tumors. Noncancer effects not discussed	
Mouse		4.5					No increase in tumors Noncancer effects not discussed	
Rat, M, F, F344/Jcl.	16 h/day 6 days/week 130 weeks	0.11[a] 0.41[a] 1.08[a] 2.31[a] 3.72[b]	1,373 5,117 13,478 28,829 46,336	1.23 2.12 3.96 7.10 12.9	0.08 0.26 0.70 1.41 3.00	0.38 1.06 2.42 4.70 4.57	Inflammatory changes Type II cell hyperplasia and lung tumors seen at >0.4 mg/m^3; shortening and loss of cilia in trachea and bronchi	Research Committee for HERP Studies (1988)
Mouse, NMRI, F	19 h/day 5 days/week 120 weeks	4.24	48,336	12.5	1.5	1.1	Inflammatory changes, bronchiolo-alveolar hyperplasia, alveolar lipo-proteinosis, fibrosis	Heinrich et al. (1986a)

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Table 5-6. Histopathological effects of diesel exhaust in the lungs of laboratory animals (continued)

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, Wistar, F	19 h/day 5 days/week 140 weeks	4.24	56,392	12.5	1.5	1.1	Thickened alveolar septa; AM aggregation; inflammatory changes; hyperplasia; lung tumors	Heinrich et al. (1986a)
Guinea Pig, Hartley, M	20 h/day 5.5 days/week 104 weeks	0.25 0.75 1.5 6.0	2,860 8,580 17,160 68,640	— — — —	— — — —	— — — —	Minimal response at 0.25 and ultrastructural changes at 0.75 mg/m^3; thickened alveolar membranes; cell proliferation; fibrosis at 6.0 mg/m^3; increase in PMN at 0.75 mg/m^3 and 1.5 mg/m^3	Barnhart et al. (1981, 1982) Vostal et al. (1981) Wallace et al. (1987)
Cat, inbred, M	8 h/day 7 days/week 124 weeks	6.0[c] 12.0[d]	41,664 83,328	20.2 33.2	2.7 4.4	2.1 5.0	Inflammatory changes, AM aggregation, bronchiolar epithelial metaplasia, Type II cell hyperplasia, peribronchiolar fibrosis	Plopper et al. (1983) Hyde et al. (1985)
Rat, F344, M	16 h/day 5 days/week 23 mo	2.44 6.33	19,520 50,640	— —	— —	— —	AM hyperplasia, epithelial hyperplasia, inflammation, septal fibrosis, bronchoalveolar metaplasia	Nikula et al. (1995)
Mouse, CD-1, M,F	7 h/day 5 days/week 104 weeks	0.35 3.5 7.1 0.25 μm MDD	1,274 12,740 25,844	3 17 30	0.1 0.3 0.7	— — —	Exposure-related increase in lung soot, pigment-laden macrophages, lung lesions. Bronchiolization in alveolar ducts at 7.1 mg/m^3	Mauderly et al. (1996)

[a]Light-duty engine.
[b]Heavy-duty engine.
[c]1 to 61 weeks exposure.
[d]62 to 124 weeks of exposure.

AM = Alveolar macrophage.
PMN = Polymorphonuclear leukocyte.

adjacent to collections of pigmented macrophages showed a marked Type II cell hyperplasia; degenerative changes were not observed in Type I cells. Histological examination of lung tissue from monkeys exposed for 24 mo in the same regimen as used for rats revealed aggregates of black particles, principally in the distal airways of the lung. Particles were present within the cytoplasm of macrophages in the alveolar spaces as well as the interstitium. Fibrosis, focal emphysema, or inflammation was not observed. No specific histopathological lesions were reported for the monkey.

Nikula et al. (1997a,b) reevaluated the lung tissue from this study. They concluded that there were no significant differences in the amount of retained particulate matter between monkeys and rats exposed under the same conditions. The rats, however, retained a greater portion of the particulate matter in lumens of the alveolar ducts and alveoli than did the monkeys. Conversely, monkeys retained a greater portion of the particulate material in the interstitium than did rats. Aggregations of particle-laden macrophages in the alveoli were rare, and there were few signs of particle-associated inflammation in the monkeys. Minimal histopathologic lesions were detected in the interstitium.

Histopathological effects of DE on the lungs of rats have been investigated by the Health Effects Research Program on Diesel Exhaust (HERP) in Japan (Ishinishi et al., 1986, 1988). Both light-duty (LD) and heavy-duty (HD) diesel engines were used. The exhaust was diluted to achieve nominal concentrations of 0.1 (LD only), 0.4 (LD and HD), 1 (LD and HD), 2 (LD and HD), and 4 (HD only) mg/m^3 DPM. Rats were exposed for 16 h/day, 6 days/week for 30 mo. No histopathological changes were observed in the lungs of rats exposed to 0.4 mg/m^3 DPM or less. At concentrations above 0.4 mg/m^3 DPM, severe morphological changes were observed. These changes consisted of shortened and absent cilia in the tracheal and bronchial epithelium, marked hyperplasia of the bronchiolar epithelium, and swelling of the Type II cellular epithelium. These lesions appeared to increase in severity with increases in exhaust concentration and duration of exposure. There was no difference in the degree of changes in pulmonary pathology at the same concentrations between the LD and the HD series.

Heinrich et al. (1982) investigated histological changes occurring in the respiratory tract of hamsters exposed to DE. Exposures were for 7 to 8 h/day, 5 days/week for 104 weeks to DE diluted to achieve a concentration of 3.9 mg/m^3 DPM. Significantly higher numbers of hamsters in the group exposed to DE exhibited definite proliferative changes in the lungs compared with the groups exposed to particle-free DE or clean air. Sixty percent of these changes were described as adenomatous proliferations.

Heinrich et al. (1995) reported increased incidence and severity of bronchioloalveolar hyperplasia in rats exposed to 0.8, 2.5, and 7 mg/m^3. The lesion in the lowest concentration group was described as very slight to moderate. Slight to moderate interstitial fibrosis also increased in incidence and severity in all exposed groups, but incidences were not reported. This

chronic study also exposed NMRI mice to 7 mg/m^3 for 13.5 mo and both NMRI and C56BL/6N mice to 4.5 mg/m^3 for 24 mo. Noncancer histological endpoints are not discussed in any detail in the report, which is focused on the carcinogenicity of diesel as compared with titanium dioxide and carbon black.

Iwai et al. (1986) performed serial histopathology on the lungs of rats at 1, 3, 6, 12, and 24 mo of exposure to DE. Exposures were for 8 h/day, 7 days/week for 24 mo; the exposure atmosphere contained 4.9 mg/m^3 DPM. At 1 and 3 mo of exposure, there were minimal histological changes in the lungs of the exposed rats. After 6 mo of exposure, there were particle-laden macrophages distributed irregularly throughout the lung and a proliferation of Type II cells with adenomatous metaplasia in areas where the macrophages had accumulated. After 1 year of exposure, foci of heterotrophic hyperplasia of ciliated or nonciliated bronchiolar epithelium on the adjacent alveolar walls were more common, the quantity of deposited particulate matter increased, and the number of degenerative AMs and proliferative lesions of Type II or bronchiolar epithelial cells increased. After 2 years of exposure, there was a fibrous thickening of the alveolar walls, mast-cell infiltration with epithelial hyperplasia in areas where the macrophages had accumulated, and neoplasms.

Heinrich et al. (1986a; see also Stöber, 1986) performed histopathologic examinations of the respiratory tract of hamsters, mice, and rats exposed to DE that had 4 mg/m^3 DPM. Exposures were for 19 h/day, 5 days/week; the maximum exposure period was 120 weeks for hamsters and mice and 140 weeks for rats. Histological examination revealed different levels of response among the three species. In hamsters, the exhaust produced thickened alveolar septa, bronchioloalveolar hyperplasia, and what were termed emphysematous lesions (diagnostic methodology not described). In mice, bronchoalveolar hyperplasia occurred in 64% of the mice exposed to the exhaust and in 5% of the controls. Multifocal alveolar lipoproteinosis occurred in 71% and multifocal interstitial fibrosis occurred in 43% of the mice exposed to exhaust but in only 4% of the controls. In exposed rats, there were severe inflammatory changes in the lungs, as well as thickened septa, foci of macrophages, and hyperplastic and metaplastic lesions.

Nikula et al. (1995) reported in detail the nonneoplastic effects in male and female F344 rats exposed to 2.4 or 6.3 mg/m^3 of DPM. At 3 mo in the low-concentration group, enlarged particle-containing macrophages were found with minimal aggregation. With higher concentration and longer duration of exposure, the number and size of macrophages and aggregates increased. Alveolar epithelial hyperplasia was found starting at 3 mo and in all rats at 6 mo. These lesions progressed to chronic active inflammation, alveolar proteinosis, and septal fibrosis at 12 mo. Other lesions observed late in the study included bronchiolar-alveolar metaplasia, squamous metaplasia, and squamous cysts. This study reports in detail the progression of lesions in DE exposure and finds relatively little difference between the lesions caused by DE exposure and exposure to similar levels of carbon black particles.

The effects of DE on the lungs of rats exposed to 8.3 ± 2.0 mg/m^3 DPM were investigated by Karagianes et al. (1981). Exposures were for 6 h/day, 5 days/week, for 4, 8, 16, or 20 mo. Histological examinations of lung tissue noted focal aggregation of particle-laden AMs, alveolar histiocytosis, interstitial fibrosis, and alveolar emphysema (diagnostic methodology not described). Lesion severity was related to length of exposure. No significant differences were noted in lesion severity among the DE, the DE plus coal dust (5.8 ± 3.5 mg/m^3), or the high-concentration (14.9 ± 6.2 mg/m^3) coal dust exposure groups following 20 mo of exposure.

Histological changes in the lungs of guinea pigs exposed to diluted DE containing either 0.25, 0.75, 1.5, or 6.0 mg/m^3 DPM were reported by Barnhart et al. (1981; 1982). Exposures at 0.75 and 1.5 mg/m^3 for 2 weeks to 6 mo resulted in an uptake of exhaust particles by three alveolar cell types (AMs, Type I cells, and interstitial macrophages) and also by granulocytic leukocytes (eosinophils). The alveolar-capillary membrane increased in thickness as a result of an increase in the absolute tissue volume of interstitium and Type II cells. In a continuation of these studies, guinea pigs were exposed to DE (up to 6.0 mg/m^3 DPM) for 2 years (Barnhart et al., 1982). A minimal tissue response occurred at a concentration of 0.25 mg/m^3. After 9 mo of exposure, there was a significant increase, about 30%, in Type I and II cells, endothelial cells, and interstitial cells over concurrent age-matched controls; by 24 mo only macrophages and Type II cells were significantly increased. As in the earlier study, ultrastructural evaluation showed that Type I cells, AMs, and eosinophils phagocytized the diesel particles. Exposure to 0.75 mg/m^3 for 6 mo resulted in fibrosis in regions of macrophage clusters and in focal Type II cell proliferation. No additional information was provided regarding the fibrotic changes with increasing concentration or duration of exposure. With increasing concentration/duration of DE exposure, Type II cell clusters occurred in some alveoli. Intraalveolar debris was particularly prominent after exposures at 1.5 and 6.0 mg/m^3 and consisted of secretory products from Type II cells.

In studies conducted on hamsters, Pepelko (1982b) found that the lungs of hamsters exposed for 8 h/day, 7 days/week for 6 mo to 6 or 12 mg/m^3 DPM were characterized by large numbers of black AMs in the alveolar spaces, thickening of the alveolar epithelium, hyperplasia of Type II cells, and edema.

Lungs from rats and mice exposed to 0.35, 3.5, or 7.1 mg/m^3 (0.23 to 0.26 μm mass median diameter [MMD]) for 7 h/day and 5 days/week showed pathologic lesions (Mauderly et al., 1987a; Henderson et al., 1988a). After 1 year of exposure at 7.1 mg/m^3, the lungs of the rats exhibited focal areas of fibrosis; fibrosis increased with increasing duration of exposure and was observable in the 3.5-mg/m^3 group of rats at 18 mo. The severity of inflammatory responses and fibrosis was directly related to the exposure level. In the 0.35 mg/m^3 group of rats, there was no inflammation or fibrosis. Although the mouse lungs contained higher burdens

of diesel particles per gram of lung weight at each equivalent exposure concentration, there was substantially less inflammatory reaction and fibrosis than was the case in rats. Fibrosis was observed only in the lungs of mice exposed at 7.1 mg/m^3 and consisted of fine fibrillar thickening of occasional alveolar septa.

Histological examinations were performed on the lungs of cats initially exposed to 6 mg/m^3 DPM for 61 weeks and subsequently increased to 12 mg/m^3 for Weeks 62 to 124 of exposure. Plopper et al. (1983; see also Hyde et al., 1985) concluded from the results of this study that exposure to DE produced changes in both epithelial and interstitial tissue compartments and that the focus of these lesions in the peripheral lung was the centriacinar region where the alveolar ducts join the terminal conducting airways. This conclusion was based on the following evidence. The epithelium of the terminal and respiratory bronchioles in exposed cats consisted of three cell types (ciliated, basal, and Clara cells) compared with only one type (Clara cells) in the controls. The proximal acinar region showed evidence of peribronchial fibrosis and bronchiolar epithelial metaplasia. Type II cell hyperplasia was present in the proximal interalveolar septa. The more distal alveolar ducts and the majority of the rest of the parenchyma were unchanged from controls. Peribronchial fibrosis was greater at the end of 6 mo in clean air following exposure, whereas the bronchiolar epithelial metaplasia was most severe at the end of exposure. Following an additional 6 mo in clean air, the bronchiolar epithelium more closely resembled the control epithelial cell population.

Wallace et al. (1987) used transmission electron microscopy (TEM) to determine the effect of DE on the intravascular and interstitial cellular populations of the lungs of exposed rats and guinea pigs. Exposed animals and matched controls were exposed to 0.25, 0.75, 1.5, or 6.0 mg/m^3 DPM for 2, 6, or 10 weeks or 18 mo. The results inferred the following: (1) exposure to 6.0 mg/m^3 for 2 weeks was insufficient to elicit any cellular response, (2) both species demonstrated an adaptive multicellular response to DE, (3) increased numbers of fibroblasts were found in the interstitium from week 6 of exposure through month 18, and (4) there was no significant difference in either cell type or number in alveolar capillaries, but there was a significant increase at 18 mo in the mononuclear population in the interstitium of both species.

Additional means for assessing the adverse effects of DE on the lung are to examine biochemical and cytological changes in bronchoalveolar lavage fluid (BALF) and in lung tissue. Fedan et al. (1985) performed studies to determine whether chronic exposure of rats affected the pharmacologic characteristics of rat airway smooth muscle. Concentration-response relationships for tension changes induced with acetylcholine, 5-hydroxytryptamine, potassium chloride, and isoproterenol were assessed in vitro on isolated preparations of airway smooth muscle (trachealis). Chronic exposure to DE significantly increased the maximal contractile responses to acetylcholine compared with control values; exposure did not alter the sensitivity

(EC_{50} values) of the muscles to the agonists. Exposures were to DE containing 2 mg/m^3 DPM for 7 h/day, 5 days/week for 2 years.

Biochemical studies of BALF obtained from hamsters and rats revealed that exposures to DE caused significant increases in lactic dehydrogenase, alkaline phosphatase, glucose-6-phosphate dehydrogenase (G6P-DH), total protein, collagen, and protease (pH 5.1) after approximately 1 year and 2 years of exposure (Heinrich et al., 1986a). These responses were generally much greater in rats than in hamsters. Exposures were to DE containing 4.24 mg/m^3 DPM for 19 h/day, 5 days/week for 120 (hamsters) to 140 (rats) weeks.

Protein, β-glucuronidase activity, and acid phosphatase activity were significantly elevated in BALF obtained from rats exposed to DE containing 0.75 or 1.5 mg/m^3 DPM for 12 mo (Strom, 1984). Exposure for 6 mo resulted in significant increases in acid phosphatase activity at 0.75 mg/m^3 and in protein, β-glucuronidase, and acid phosphatase activity at the 1.5 mg/m^3 concentration. Exposure at 0.25 mg/m^3 DPM did not affect the three indices measured at either time period. The exposures were for 20 h/day, 5.5 days/week for 52 weeks.

Additional biochemical studies (Misiorowski et al., 1980) were conducted on laboratory animals exposed under the same conditions and at the same site as reported on by Strom (1984). In most cases, exposures at 0.25 mg/m^3 did not cause any significant changes. The DNA content in lung tissue and the rate of collagen synthesis were significantly increased at 1.5 mg/m^3 DPM after 6 mo. Collagen deposition was not affected. Total lung collagen content increased in proportion to the increase in lung weight. The activity of prolyl hydroxylase was significantly increased at 12 weeks at 0.25 and 1.5 mg/m^3; it then decreased with age. Lysal oxidase activity did not change. After 9 mo of exposure, there were significant increases in lung phospholipids in rats and guinea pigs exposed to 0.75 mg/m^3 and in lung cholesterol in rats and guinea pigs exposed to 1.5 mg/m^3. Pulmonary prostaglandin dehydrogenase activity was stimulated by an exposure at 0.25 mg/m^3 but was not affected by exposure at 1.5 mg/m^3 (Chaudhari et al., 1980, 1981). Exposures for 12 or 24 weeks resulted in a concentration-dependent lowering of this enzyme activity. Exposure of male rats and guinea pigs at 0.75 mg/m^3 for 12 weeks did not cause any changes in glutathione levels of the lung, heart, or liver. Rats exposed for 2 mo at 6 mg/m^3 showed a significant depletion of hepatic glutathione, whereas the lung showed an increase of glutathione (Chaudhari and Dutta, 1982). Schneider and Felt (1981) reported that similar exposures did not substantially change adenylate cyclase and guanylate cyclase activities in lung or liver tissue of exposed rats and guinea pigs.

Bhatnagar et al. (1980; see also Pepelko, 1982a) evaluated changes in the biochemistry of lung connective tissue of diesel-exposed rats and mice. The mice were exposed for 8 h/day and 7 days/week for up to 9 mo to exhaust containing 6 mg/m^3 DPM. Total lung protein content was measured, as was labeled proline and labeled leucine. Leucine incorporation is an index of total protein synthesis, although collagen is very low in leucine. Proline incorporation reflects

collagen synthesis. Amino acid incorporation was measured in vivo in the rat and in short-term organ culture in mice. Both rats and mice showed a large increase in total protein (41% to 47% in rats), while leucine incorporation declined and proline incorporation was unchanged. These data are consistent with an overall depression of protein synthesis in diesel-exposed animals and also with a relative increase in collagen synthesis compared to other proteins. The increase in collagen synthesis suggested proliferation of connective tissue and possible fibrosis (Pepelko, 1982a).

A number of reports (McClellan et al., 1986; Mauderly et al., 1987a, 1990a; Henderson et al., 1988a) have addressed biochemical and cytological changes in lung tissue and BALF of rodents exposed for 7 h/day, 5 days/week for up to 30 mo at concentrations of 0, 0.35, 3.5, or 7.1 mg/m^3 DPM. At the lowest exposure level (0.35 mg/m^3), no biochemical or cytological changes occurred in the BALF or in lung tissue in either Fischer 344 rats or CD-1 mice. Henderson et al. (1988a) provide considerable time-course information on inflammatory events taking place throughout a chronic exposure. A chronic inflammatory response was seen at the two higher exposure levels in both species, as evidenced by increases in inflammatory cells (macrophages and neutrophils), cytoplasmic and lysosomal enzymes (lactate dehydrogenase, glutathione reductase, and β-glucuronidase), and protein (hydroxyproline) in BALF. Analysis of lung tissue indicated similar changes in enzyme levels as well as an increase in total lung collagen content. After 18 mo of exposure, lung tissue glutathione was depleted in a concentration-dependent fashion in rats but was slightly increased in mice. Lavage fluid levels of glutathione and glutathione reductase activity increased in a concentration-dependent manner and were higher in mice than in rats.

Rats exposed for up to 17 days to diluted DE (3.5 mg/m^3 DPM) had a fivefold increase in the bronchoconstrictive prostaglandin $PGF_{2\alpha}$ and a twofold increase in the inflammatory leukotriene LTB_4. In similarly exposed mice, there was a twofold increase in both parameters. These investigators (Henderson et al., 1988a,b) concluded that the release of larger amounts of such mediators of inflammation from the alveolar phagocytic cells of rats accounted for the greater fibrogenic response seen in that species.

Biochemical analysis of lung tissue from cats exposed for 124 weeks and held in clean air for an additional 26 weeks indicated increases of lung collagen; this finding was confirmed by an observed increase in total lung wet weight and in connective tissue fibers estimated morphometrically (Hyde et al., 1985). Exposures were for 7 h/day, 5 days/week at 6 mg/m^3 DPM for 61 weeks and at 12 mg/m^3 for weeks 62 to 124.

Heinrich et al. (1995) reported on bronchoalveolar lavage in animals exposed for 24 mo and found exposure-related increases in lactate dehydrogenase, β-glucuronidase, protein, and hydroxyproline in groups exposed to 2.5 or 7 mg/m^3, although detailed data are not presented. Lavage analyses were not carried out in concurrent studies in mice.

The pathogenic sequence following the inhalation of DE as determined histopathologically and biochemically begins with the interaction of diesel particles with airway epithelial cells and phagocytosis by AMs. The airway epithelial cells and activated macrophages release chemotactic factors that attract neutrophils and additional AMs. As the lung burden of DPM increases, there is an aggregation of particle-laden AMs in alveoli adjacent to terminal bronchioles, increases in the number of Type II cells lining particle-laden alveoli, and the presence of particles within alveolar and peribronchial interstitial tissues and associated lymph nodes. The neutrophils and macrophages release mediators of inflammation and oxygen radicals that deplete a biochemical defense mechanism of the lung (i.e., glutathione). As will be described later in more detail, other defense mechanisms are affected, particularly the decreased viability of AMs, which leads to decreased phagocytic activity and death of the macrophage. The latter series of events may result in the presence of pulmonary inflammatory, fibrotic, or emphysematous lesions. The data suggest that there may be a threshold of exposure to DE below which adverse structural and biochemical effects may not occur in the lung; however, differences in the anatomy and pathological responses of laboratory animals coupled with their lifespans compared with humans make a determination of human levels of exposure to DE without resultant pulmonary injury a difficult and challenging endeavor.

5.1.3.3.4. ***Effects on pulmonary defense mechanisms.*** The respiratory system has a number of defense mechanisms that negate or compensate for the effects produced by the injurious substances that repeatedly insult the upper respiratory tract, the tracheobronchial airways, and the alveoli. The effects of exposure to DE on the pulmonary defense mechanisms of laboratory animals as well as more details on exposure atmosphere are summarized in Table 5-7 and ranked by cumulative exposure (C × T).

Several studies have been conducted investigating the effect of inhaled DE on the deposition and fate of inert tracer particles or diesel particles themselves. Lung clearance of deposited particles occurs in two distinct phases: a rapid phase (hours to days) from the tracheobronchial region via the mucociliary escalator and a much slower phase (weeks to months) from the nonciliated pulmonary region via, primarily but not solely, AMs. Battigelli et al. (1966) reported impaired tracheal mucociliary clearance in vitro in excised trachea from rats exposed for single or repeated exposures of 4 to 6 h at two dilutions of DE that resulted in exposures of approximately 8 and 17 mg/m^3 DPM. The exposure to 17 mg/m^3 resulted in

Table 5-7. Effects of exposure to diesel exhaust on the pulmonary defense mechanisms of laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
				Alveolar macrophage status				
Guinea Pig, Hartley	20 h/day 5.5 days/week 8 weeks	0.25 1.5 0.19 µm MDD	220 1,320	2.9 7.5	— —	— —	No significant changes in absolute numbers of AMs	Chen et. al. (1980)
Rat, F344, M	7 h/day 5 days/week 104 weeks	2.0 0.23–0.36 µm MDD	7,280	11.5	1.5	0.81	Little effect on viability, cell number, oxygen consumption, membrane integrity, lyzomal enzyme activity, or protein content of AMs; decreased cell volume and ruffling of cell membrane and depressed luminescence of AM	Castranova et al. (1985)
Rat, F344, M	20 h/day 5.5 days/week 26, 48, or 52 weeks	0.25[a] 0.75[a] 1.5[b] 0.19 µm MDD	715-8,580	2.9 4.8 7.5	— — —	— — —	AM cell counts proportional to concentration of DPM at 0.75 and 1.5 mg/m^3; AM increased in lungs in response to rate of DPM mass entering lung rather than total DPM burden in lung; increased PMNs were proportional to inhaled concentrations and/or duration of exposure; PMNs affiliated with clusters of aggregated AM rather than DPM	Strom (1984) Vostal et al. (1982)
Rat F344/Crl, M, F Mouse, CD, M, F	7 h/day 5 days/week 104 weeks (rat), 78 weeks (mouse)	0.35 3.5 7.0 0.25 µm MDD	1,274[c] 12,740[c] 25,480[c]	2.9 16.5 29.7	0.05 0.34 0.68	— — —	Significant increases of AM in rats and mice exposed to 7.0 mg/m^3 DPM for 24 and 18 mo, respectively, but not at concentrations of 3.5 or 0.35 mg/m^3 DPM for the same exposure durations; PMNs increased in a dose-dependent fashion in both rats and mice exposed to 3.5 or 7.0 mg/m^3 DPM and were greater in mice than in rats	Henderson et al. (1988a)
Rat, Wistar, F	18 h/day 5 days/week 24 mo	0.8 2.5 7.1	7,400 21,800 61,700	2.6 8.3 21.2	0.3 1.1 3.4	— — —	Changes in differential cell counts in lung lavage	Heinrich et al. (1995)
Rat, F344/Crl, M	7 h/day 5 days/week 24 mo	3.49	12,704	9.8	1.2	—	Significantly reduced AM in lavage at 24 mo	Mauderly et al. (1990a)

Table 5-7. Effects of exposure to diesel exhaust on the pulmonary defense mechanisms of laboratory animals (continued)

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
					Clearance			
Rat, M, F	7 h/day 5 days/week 12 weeks	0.2 1.0 4.5 0.25µm MDD	84 420 1,890	— — —	— — —	— — —	Evidence of apparent speeding of tracheal clearance at the 4.5 mg/m^3 level after 1 week of ^{99m}Tc macroaggregated-albumin and reduced clearance of tracer aerosol in each of the three exposure levels at 12 weeks; indication of a lower percentage of ciliated cells at the 1.0 and 4.5 mg/m^3 levels	Wolff and Gray (1980)
Rat, Wistar, F	18 h/day 5 days/week 24 mo	0.8 2.5 7.1	7,400 21,800 61,700	2.6 8.3 21.2	0.3 1.2 3.8	0.3 1.1 3.4	Significant increase in clearance half-time of inhaled labeled aerosols in all groups at 3-18 mo	Heinrich et al. (1995)
Rat, F344, M, developing 0-6 mo adult 6-12 mo	7 h/day 5 days/week 6 mo	3.55	3,321	7.9	9.5		Clearance of 2 µm, aluminosilicate particles. Half-time significantly increased in adult, not different in developing rats	Mauderly et al. (1987b)
Rat, F344, M, F	7 h/day 5 days/week 18 weeks	0.15 0.94 4.1 <0.5 µm MDD	94.5 592 2,583	— — —	— — —	— — —	Lung burdens of DPM were concentration-related; clearance half-time of DPM almost double in 4.1 mg/m^3 group compared to 0.15 mg/m^3 group	Griffis et al. (1983)
Rat, F344, M	7 h/day 5 days/week 26-104 weeks	2.0 0.23-0.36 µm MDD	1,820-7,280	11.5	1.5	0.8	No difference in clearance of $^{59}Fe_3O_4$ particles 1 day after tracer aerosol administration; 120 days after exposure tracer aerosol clearance was enhanced; lung burden of DPM increased significantly between 12 and 24 mo of exposure	Lewis et al. (1989)
Rat, Sprague-Dawley, M	4-6 h/day 7 days/week 0.1 to 14.3 weeks	0.9 8.0 17.0	2.5-10,210	— — —	5.0 2.7 8.0	0.2 0.6 1.0	Impairment of tracheal mucociliary clearance in a concentration-response manner	Battigelli et al. (1966)

Table 5-7. Effects of exposure to diesel exhaust on the pulmonary defense mechanisms of laboratory animals (continued)

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, F344, M, F	7 h/day 5 days/week 130 weeks	0.35 3.5 7.1 0.25 µm MDD	1,593 15,925 31,850	2.9 16.5 29.7	0.1 0.3 0.7	— — —	No changes in tracheal mucociliary clearance after 6, 12, 18, 24, or 30 mo of exposure; increases in lung clearance half-times as early as 6 mo at 7.0 mg/m^3 level and 18 mo at 3.5 mg/m^3 level; no changes seen at 0.35 mg/m^3 level; after 24 mo of diesel exposure, long-term clearance half-times were increased in the 3.5 and 7.0 mg/m^3 groups	Wolff et al. (1987)
Rat, F344/Crl, M	7 h/day 5 days/week 24 mo	3.49	12,704	9.8	1.2	—	Doubling of long-term clearance half-time for clearance of 1.0 µm aluminosilicate particles. Less effect on clearance in animals with experimentally induced emphysema	Mauderly et al. (1990a)
				Microbial-induced mortality				
Mice CD-1, F	7 h/day 5 days/week 4, 12, or 26 weeks	2.0 0.23–0.36 µm MDD	280-1,820	11.5	1.5	0.8	Mortality similar at each exposure duration when challenged with Ao/PR/8/34 influenza virus; in mice exposed for 3 and 6 mo, but not 1 mo, there were increases in the percentages of mice having lung consolidation, higher virus growth, depressed interferon levels, and a fourfold reduction in hemagglutinin antibody levels	Hahon et al. (1985)
Mice, CR/CD-1, F	8 h/day 7 days/week 2 h up to 46 weeks	5.3 to 7.9	11-20,350	19 to 22	1.8 to 3.6	0.9 to 2.8	Enhanced susceptibility to lethal effects of *S. pyogenes* infections at all exposure durations (2 and 6 h; 8, 15, 16, 307, and 321 days); inconclusive results with *S. typhimurium* because of high mortality rates in controls; no enhanced mortality when challenged with A/PR8-3 influenza virus	Campbell et al. (1980, 1981)

[a]Chronic exposure lasted 52 weeks.
[b]Chronic exposure lasted 48 weeks.
[c]Calculated for 104-week exposure.
DPM = Diesel particulate matter.
AM = Alveolar macrophage.
PMN = Polymorphonuclear leukocyte.

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decreased clearance after a single exposure as well as after a cumulative exposure of 34 or 100 h. Clearance was reduced to a lesser extent and in fewer tracheas from animals exposed to 8 mg/m^3 for a cumulative exposure of 40 h. Lewis et al. (1989) found no difference in the clearance of $^{59}Fe_3O_4$ particles (1.5 μm MMAD, σ_g 1.8) 1 day after dosing control and DE-exposed rats (2 mg/m^3, 7 h/day, 5 days/week for 8 weeks).

Wolff et al. (1987) and Wolff and Gray (1980) studied the effects of both subchronic and chronic DE exposure on the tracheal clearance of particles. Tracheal clearance assessments were made by measuring the retention of radiolabeled technetium macroaggregated-albumin remaining 1 h after instillation in the distal trachea of rats. In the subchronic studies, rats were exposed to 0.2, 1.0, or 4.5 mg/m^3 DPM on a 7 h/day, 5 days/week schedule for up to 12 weeks. After 1 week there was an apparent speeding of tracheal clearance at the 4.5 mg/m^3 exposure level (p=0.10), which returned toward baseline after 6 weeks and was slightly below the baseline rate at 12 weeks. In the 1.0 mg/m^3 group, there was a progressive significant reduction in the clearance rate at 6 and 12 weeks of exposure. There was a trend toward reduced clearance in the 0.2 mg/m^3 group. Scanning electron micrographs indicated minimal changes in ciliary morphology; however, there was an indication of a lower percentage of ciliated cells at the 1.0 and 4.5 mg/m^3 levels. In the chronic studies, rats were exposed to 0, 0.35, 3.5, or 7.1 mg/m^3 for 7 h/day, 5 days/week for 30 mo. There were no significant differences in tracheal clearance rates between the control group and any of the exposure groups after 6, 12, 18, 24, or 30 mo of exposure. The preexposure measurements for all groups, however, were significantly lower than those during the exposure period, suggesting a possible age effect. The preexposure value for the 3.5-mg/m^3 group was also significantly lower than the control group.

There is a substantial body of evidence for an impairment of particle clearance from the bronchiole-alveolar region of rats following exposure to DE. Griffis et al. (1983) exposed rats 7 h/day, 5 days/week for 18 weeks to DE at 0.15, 0.94, or 4.1 mg/m^3 DPM. Lung burdens of the 0.15, 0.94, and 4.1 mg/m^3 levels were 35, 220, and 1,890 μg/g lung, respectively, 1 day after the 18-week exposure. The clearance half-time of the DPM was significantly greater, almost double, for the 4.1 mg/m^3 exposure group than for those of the lower exposure groups, 165 ± 8 days versus 99 ± 8 days (0.94 mg/m^3) and 87 ± 28 days (0.15 mg/m^3), respectively.

Chan et al. (1981) showed a dose-related slowing of ^{14}C-diesel particle clearance in rats preexposed to DE at 0.25 or 6 mg/m^3 particulate matter for 20 h/day, 7 days/week for 7 to 112 days. Clearance was inhibited in the 6 mg/m^3 group when compared by length of exposure or compared with the 0.25 mg/m^3 or control rats at the same time periods.

Heinrich et al. (1982) evaluated lung clearance in rats exposed for approximately 18 mo at 3.9 mg/m^3 DPM for 7 to 8 h/day, 5 days/week. Following exposure to $^{59}Fe_2O_3$-aerosol, the rats were returned to the DE exposure and the radioactivity was measured over the thoracic area

at subsequent times. The biological half-life of the iron oxide deposited in the rats' lungs was nearly twice that of controls.

Heinrich also used labeled iron oxide aerosols to study clearance in rats exposed to 0.8, 2.5, or 7 mg/m^3 diesel DPM for 24 mo (Heinrich et al., 1995). Clearance measurements were carried out at 3, 12, and 18 mo of exposure. Half-times of clearance were increased in a concentration- and duration-related manner in all exposed groups, with a range of a 50% increase in the 0.8 mg/m^3 group at 3 mo to an 11-fold increase in the 7 mg/m^3 group at 19 mo. The differential cell counts in these animals were stated to have shown clear effects in the 2.5 and 7 mg/m^3 groups, but specific information about the changes is not reported.

Wolff et al. (1987) investigated alterations in DPM clearance from the lungs of rats chronically exposed to DE at 0, 0.35, 3.5, or 7.1 mg/m^3 DPM for 7 h/day, 5 days/week for up to 24 mo. Progressive increases in lung burdens were observed over time in all groups; levels of DPM in terms of milligrams per lung were 0.60, 11.5, and 20.5 after 24 mo of exposure at the 0.35, 3.5, or 7.1 mg/m^3 exposure levels, respectively. There were significant increases in 16-day clearance half-times of inhaled radiolabeled particles of $^{67}Ga_2O_3$ (0.1 μm MMD) as early as 6 mo at the 7.1 mg/m^3 level and 18 mo at the 3.5 mg/m^3 level; no significant changes were seen at the 0.35 mg/m^3 level at any time point examined. Rats inhaled fused aluminosilicate particles (2 μm MMAD) labeled with ^{134}Cs after 24 mo of DE exposure; long-term clearance half-times were 79, 81, 264, and 240 days for the 0, 0.35, 3.5, and 7.1 mg/m^3 groups, respectively. Differences were significant between the control and the 3.5 and 7.1 mg/m^3 groups ($p < 0.01$), but not between the control and the 0.35 mg/m^3 group.

Mauderly et al. (1987b) compared the effects of DE in the developing lung to the adult lung by exposing groups of male F344 rats to 3.5 mg/m^3 for 7 h/day, 5 days/week for 6 mo. One group (adult) was exposed between 6 and 12 mo of age, and the other was exposed beginning in utero and until 6 mo of age. Clearance of an inhaled monodisperse 2 μm aluminosilicate particle was measured after exposure for 6 mo. The clearance half-time of the slow phase was found to be doubled in the diesel-exposed adult rats compared with age-matched controls and was not significantly affected in developing rat lungs.

Mauderly et al. (1990a) compared the effects of DE in normal lungs with rats in which emphysema had been induced experimentally by instillation of elastase 6 weeks before DE exposures. The rats were exposed to 3.5 mg/m^3 DPM for 7 h/day, 5 days/week for 24 mo. Measurements included histopathology, clearance, pulmonary function, lung lavage, and immune response. In the rats that were not pretreated with elastase, there was a significant reduction in the number of macrophages recovered by pulmonary lavage in contrast to the increases in macrophages reported by Strom (1984) and Henderson et al. (1988). The half-time of the slow phase of clearance of inhaled, 1 μm, monodisperse particles was doubled in the animals without elastase pretreatment. The elastase pretreatment did not affect clearance in

unexposed animals but significantly reduced the effect of diesel. The clearance half-time was significantly less in elastase-pretreated, diesel-exposed animals than in diesel-exposed normal animals. Many other effects measured in this study were also less affected by diesel exposure in elastase-treated animals. Measurements of lung burden of DPM showed that elastase-pretreated animals accumulated less than half as much DPM mass as normal animals exposed at the same time, suggesting that the difference in effect could be explained by differences in dose to the lung. The composite results of this study indicate that, at least in a murine laboratory animal species, the presence of a pulmonary restrictive disease such as emphysema does not seem to exacerbate the effects of chronic exposure to diesel.

Lewis et al. (1989) conducted lung burden and $^{59}Fe_3O_4$ tracer studies in rats exposed for 12 and 24 mo to 2 mg/m^3 DPM (7 h/day, 5 days/week). The slope of the Fe_3O_4 clearance curve of the DPM-exposed animals was significantly steeper than that of the controls, indicating a more rapid alveolar clearance of the deposited $^{59}Fe_3O_4$. After 120 days from the inhalation of the tracer particle, 19% and 8% of the initially deposited $^{59}Fe_3O_4$ were present in the lungs of control and DE-exposed rats, respectively. The lung burden of DPM, however, increased significantly between 12 and 24 mo of exposure (0.52 to 0.97% lung dry weight), indicating a later dose-dependent inhibition of clearance.

Alveolar macrophages, because of their phagocytic and digestive capabilities, are one of the prime defense mechanisms of the alveolar region of the lung against inhaled particles. Thus, characterization of the effects of DE on various properties of AMs provides information on the integrity or compromise of a key pulmonary defense mechanism. The physiological viability of AMs from diesel-exposed rats was assessed after 2 years of exposure by Castranova et al. (1985). The 7 h/day, 5 days/week exposure at 2 mg/m^3 DPM had little effect on the following: viability, cell number, oxygen consumption, membrane integrity, lysosomal enzyme activity, or protein content of the AMs. A slight decrease in cell volume, a decrease in chemiluminescence indicative of a decreased secretion of reactive oxygen species, and a decrease in ruffling of the cell membrane were observed. These latter findings could be reflective of an overall reduction in phagocytic activity.

Exposure to DE has been reported both to increase the number of recoverable AMs from the lung (Strom, 1984; Vostal et al., 1982; Henderson et al., 1988a) or to produce no change in numbers (Chen et al., 1980; Castranova et al., 1985). Strom (1984) found that in rats exposed to 0.25 mg/m^3 DPM for 20 h/day, 5.5 days/week for 6 mo or 1 year, as well as in the controls, BAL cells consisted entirely of AMs, with no differences in the cell counts in the lavage fluid. At the higher concentrations, 0.75 or 1.5 mg DPM/m^3, the count of AM increased proportionally with the exposure concentration; the results were identical for AMs at both 6 and 11 or 12 mo of exposure. The increase in AM counts was much larger after exposure to 1.5 mg/m^3 DPM for 6 mo than after exposure to 0.75 mg/m^3 for 1 year, although the total mass (calculated as C × T)

of deposited particulate burden was the same. These data suggested to the authors that the number of lavaged AMs was proportional to the mass influx of particles rather than to the actual DPM burden in the lung. These results further implied that there may be a threshold for the rate of mass influx of DPM into the lungs of rats above which there was an increased recruitment of AMs. Henderson et al. (1988a) reported similar findings of significant increases of AMs in rats and mice exposed to 7.1 mg/m^3 DPM for 18 and 24 mo, respectively, for 7 h/day, 5 days/week, but not at concentrations of 3.5 or 0.35 mg/m^3 for the same exposure durations. Chen et al. (1980), using an exposure regimen of 0.25 and 1.5 mg/m^3 DPM for 2 mo and 20 h/day and 5.5 days/week, found no significant changes in absolute numbers of AMs from guinea pig BALF, nor did Castranova et al. (1985) in rat BALF following exposure to 2 mg/m^3 DPM for 7 h/day, 5 days/week for 2 years.

A similar inflammatory response was noted by Henderson et al. (1988a) and Strom (1984), as evidenced by an increased number of PMNs present in BALF from rodents exposed to DE. Henderson et al. (1988) found these changes in rats and mice exposed to 7.1 and 3.5 mg/m^3 DPM for 7 h/day, 5 days/week. Significant increases in BALF PMNs were observed in mice at 6 mo of exposure and thereafter at the 7.1 and 3.5 mg/m^3 exposure levels, but in rats only the 7.1 mg/m^3 exposure level showed an increase in BALF PMNs at 6 mo of exposure and thereafter. Significant increases in BALF PMNs occurred in rats at 12, 18, and 24 mo of exposure to 3.5 mg/m^3 DPM. Although increases in PMNs were usually greater in mice in terms of absolute numbers, the PMN response in terms of increase relative to controls was only about one-third that of rats. Strom (1984) reported that the increased numbers of PMNs in BALF were proportional to the inhaled concentrations and/or duration of exposure. The PMNs also appeared to be affiliated with clusters of aggregated AMs rather than to the diesel particles per se. Proliferation of Type II cells likewise occurred in response to the formed aggregates of AMs (White and Garg, 1981).

The integrity of pulmonary defense mechanisms can also be ascertained by assessing if exposure to DE affects colonization and clearance of pathogens and alters the response of the challenged animals to respiratory tract infections. Campbell et al. (1980, 1981) exposed mice to DE followed by infectious challenge with *Salmonella typhimurium, Streptococcus pyogenes*, or A/PR8-3 influenza virus and measured microbial-induced mortality. Exposures to DE were to 6 mg/m^3 DPM for 8 h/day, 7 days/week for up to 321 days. Exposure to DE resulted in enhanced susceptibility to the lethal effects of *S. pyogenes* infection at all exposure durations (2 h, 6 h; 8, 15, 16, 307, and 321 days). Tests with *S. typhimurium* were inconclusive because of high mortality rates in the controls. Mice exposed to DE did not exhibit an enhanced mortality when challenged with the influenza virus. Hatch et al. (1985) found no changes in the susceptibility of mice to Group C *Streptococcus* sp. infection following intratracheal injection of 100 μg of DPM suspended in unbuffered saline.

Hahon et al. (1985) assessed virus-induced mortality, virus multiplication with concomitant IFN levels (lungs and sera), antibody response, and lung histopathology in mice exposed to DE prior to infectious challenge with Ao/PR/8/34 influenza virus. Weanling mice were exposed to DE containing 2 mg/m^3 DPM for 7 h/day, 5 days/week. In mice exposed for 1, 3, and 6 mo, mortality was similar between the exposed and control mice. In mice exposed for 3 and 6 mo, however, there were significant increases in the percentage of mice having lung consolidation, higher virus growth, depressed IFN levels, and a fourfold reduction in hemagglutinin antibody levels; these effects were not seen after the 1-mo exposure.

The effects of DE on the pulmonary defense mechanisms appear to be determined by three critical factors related to exposure: the concentrations of the pollutants, the exposure duration, and the exposure pattern. Higher doses of DE as determined by an increase in one or more of these three variables have been reported to increase the numbers of AMs, PMNs, and Type II cells in the lung, whereas lower doses fail to produce such changes. In rats, the single most significant contributor to the impairment of the pulmonary defense mechanisms appears to be an excessive accumulation of DPM, particularly as particle-laden aggregates of AMs. Such an accumulation would result from an increase in deposition and/or a reduction in clearance. The deposition of particles does not appear to change significantly following exposure to equivalent DE doses over time. Because of the significant nonlinearity in particle accumulation between low and high doses of DE exposure, coupled with no evidence of increased particle deposition, an impairment in one or more of the mechanisms of pulmonary defense appears to be responsible for the DPM accumulation and subsequent pathological sequelae. The time of onset of pulmonary clearance impairment was dependent both on the magnitude and on the duration of exposures. For example, for rats exposed for 7 h/day, 5 days/week for 104 weeks, the concentration needed to induce pulmonary clearance impairment appears to lie between 0.35 and 2.0 mg/m^3 DPM.

5.1.3.3.5. ***Effects on the immune system—inhalation studies.*** The effects of DE on the immune system of guinea pigs were investigated by Dziedzic (1981). Exposures were to 1.5 mg/m^3 DPM for 20 h/day, 5.5 days/week for up to 8 weeks. There was no effect of diesel exposure when compared with matched controls for the number of B and T lymphocytes and null cells isolated from the tracheobronchial lymph nodes, spleen, and blood. Cell viability as measured by trypan blue exclusion was comparable between the exposed and control groups. The results of this study and others on the effects of exposure to DE on the immune system are summarized in Table 5-8.

Mentnech et al. (1984) examined the effect of DE on the immune system of rats. Exposures were to 2 mg/m^3 DPM for 7 h/day, 5 days/week for up to 2 years. Rats exposed for 12 and 24 mo were tested for immunocompetency by determining antibody-producing cells in

the spleen 4 days after immunization with sheep erythrocytes. The proliferative response of splenic T-lymphocytes to the mitogens concanavalin A and phytohemagglutinin was assessed in rats exposed for 24 mo. There were no significant differences between the exposed and control animals. Results obtained from these two assays indicate that neither humoral immunity (assessed by enumerating antibody-producing cells) nor cellular immunity (assessed by the lymphocyte blast transformation assay) were markedly affected by the exposures.

Bice et al. (1985) evaluated whether or not exposure to DE would alter antibody immune responses induced after lung immunization of rats and mice. Exposures were to 0.35, 3.5, or 7.1 mg/m^3 DPM for 7 h/day, 5 days/week for 24 mo. Chamber controls and exposed animals were immunized by intratracheal instillation of SRBCs after 6, 12, 18, or 24 mo of exposure. No suppression in the immune response occurred in either species. After 12, 18, and 24 mo of exposure, the total number of anti-SRBC IgM antibody forming cells (AFCs) was elevated in rats, but not in mice, exposed to 3.5 or 7.1 mg/m^3 DPM; after 6 mo of exposure, only the 7.1 mg/m^3 level was found to have caused this response in rats. The number of AFCs per 10^6 lymphoid cells in lung-associated lymph nodes and the levels of specific IgM, IgG, or IgA in rat sera were not significantly altered. The investigators concluded that the increased cellularity and the presence of DPM in the lung-associated lymph nodes had only a minimal effect on the immune and antigen filtration function of these tissues.

The effects of inhaled DE and DPM have been studied in a murine model of allergic asthma (Takano et al., 1998a,b). ICR mice were exposed for 12 h/day, 7 days/week for 40 weeks to DE (0.3, 1.0, or 3.0 mg/m^3). The mice were sensitized with ovalbumin (OA) after 16 weeks exposure and subsequently challenged with aerosol allergen (1% OA in isotonic saline for 6 min) at 3-week intervals during the last 24 weeks of exposure. Exposure to DE enhanced allergen-related eosinophil recruitment to the submucosal layers of the airways and to the bronchoalveolar space, and increased protein levels of GM-CSF and IL-5 in the lung in a dose-dependent manner. In the DE-exposed mice, increases in eosinophil recruitment and local cytokine expression were accompanied by goblet-cell proliferation in the bronchial epithelium and airwayhyperresponsiveness to inhaled acetylcholine. In contrast, mice exposed to clean air or DE without allergen provocation showed no eosinophil recruitment to the submucosal layers of the airways or to the bronchoalveolar space, and few goblet-cells in the bronchial epithelium. The

Table 5-8. Effects of inhalation of diesel exhaust on the immune system of laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Guinea Pig, Hartley, M	20 h/day 5.5 days/week 4 or 8 weeks	1.5 0.19 µm MDD	660 or 7,280	7.5	—	—	No alterations in numbers of B, T, and null lymphocytes or cell viability among lymphocytes isolated from tracheobronchial lymph nodes, spleen, or blood	Dziedzic (1981)
Rat, F344, M	7 h/day 5 days/week 52 or 104 weeks	2.0 0.23–0.36 µm MDD	3,640 or 7,280	11.5	1.5	0.8	Neither humoral immunity (assessed by enumerating antibody-producing cells) nor cellular immunity (assessed by the lymphocyte blast transformation assay) were markedly affected	Mentnech et al. (1984)
Rat, F344; Mouse, CD-I	7 h/day 5 days/week 104 weeks	0.35 3.5 7.1 0.25 µm MDD	1,274 12,740 25,480	2.9 16.5 29.7	0.05 0.34 0.68	— — —	Total number of anti-sheep red blood cell IgM AFC in the lung-associated lymph nodes was elevated in rats exposed to 3.5 or 7.0 mg/m^3 DPM (no such effects in mice); total number of AFC per 10^6 lymphoid cells in lung-associated lymph nodes and level of specific IgM, IgG, or IgA in rat sera were not altered	Bice et al. (1985)
Mouse, BALB/C, M	12 h/day, 7 days/week, 3 weeks Mice administered OA intranasally before, immediately after, and 3 weeks after exposure	3.0 6.0 0.4 µm	756 1,512	— —	2.8 4.1	1.7 2.7	Spleen weights in mice exposed to DE (6 mg/m^3) increased significantly. Serum anti-OA IgE antibody titers in mice exposed to 6 mg/m^3 significantly higher than control. Antigen-stimulated IL-4 and IL-10 production increased while IFN-g production decreased significantly in spleen cells from DE-exposed (6 mg/m^3) mice stimulated with OA in vitro. DE inhalation may affect antigen-specific IgE antibody production through alteration of the cytokine network.	Fujimaki et al. (1997)
Mouse, C3H/Hen, M	12 h /day, for 12 weeks. Before exposure mice injected IP with OA. After 3 weeks and every 3 weeks thereafter, mice challenged with OA aerosol.	1.0 3.0	1,008 3,024	—	1.42 4.02	0.87 1.83	DE + antigen challenge induced airway hyperresponsiveness and inflammation with increased eosinophils, mast cells, and goblet cells. DE alone induced airway hyperresponsiveness, but not eosinophilic infiltration or increased goblet cells. DE inhalation enhanced airway hyperresponsiveness and airway inflammation caused by OA sensitization.	Miyabara et al. (1998a)

Table 5-8. Effects of inhalation of diesel exhaust on the immune system of laboratory animals (continued)

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Mouse, C3H/HeN, M	12 h/day, for 5 weeks. After 7 days mice injected IP with OA. At end of exposure mice challenged with OA aerosol for 15 minutes.	3.0	1,260	—	4.08	1.26	DE alone increased neutrophils and macrophages in BAL fluid; after DE + OA challenge eosinophils increased. OA alone increased eosinophils but the increase was enhanced by DE. DE + OA, but not DE alone, increased goblet cells, respiratory resistance, production of OA-specific IgE and Ig1 in the serum, and overexpression of IL-5 in lung tissue.	Miyabara et al. (1998b)
Mouse, ICR (murine model of allergic asthma)	12 h/day, 7days/week, 40 weeks. After 16 weeks sensitized to OA and challenged with OA aerosol for 6 min, at 3-week intervals during the last 24 weeks of exposure.	0.3 1.0 3.0	1,008 3,360 10,080	—	—	—	DE exposure enhanced allergen-related recruitment to the submucosal layers of the airways and the bronchoalveolar space, and increased GM-CSF and IL-5 in the lung in a dose-dependent manner. Increases in eosinophil recruitment and local cytosine expression accompanied by goblet cell proliferation in the bronchial epithelium and airway hyperresponsiveness to inhaled acetylcholine. Mice exposed to clean air or DE without allergen provocation showed no eosinophil recruitment to the submucosal layers of the airways nor to the bronchoalveolar space, and few goblet cells in the bronchial epithelium. Daily inhalation of DE may enhance allergen-related respiratory diseases such as allergic asthma, and effect may be mediated by the enhanced local expression of IL-5 and GM-CSF.	Takano et al. (1998a)

DPM = Diesel particulate matter.
AFC = Antibody-forming cells.

authors concluded that daily inhalation of DE can enhance allergen-related respiratory diseases such as allergic asthma, and that this effect may be mediated by the enhanced local expression of IL-5 and GM-CSF. The effect of DPM on a second characteristic of allergic asthma, airway hyperresponsiveness, was examined by Takano et al. (1998b). Laboratory mice were administered OA, DPM, or OA and DPM combined by intratracheal instillation for 6 wk. Respiratory resistance (Rrs) after acetylcholine challenge was measured 24 h after the final instillation. Rrs was significantly greater in the mice treated with OA and DPM than in the other treatments. The authors concluded that DPM can enhance airway responsiveness associated with allergen exposure.

In a series of inhalation studies following earlier instillation studies, Miyabara and co-workers investigated whether inhalation of DE could enhance allergic reactions in laboratory mice. C3H/HeN mice were exposed to DE (3 mg DPM/m^3) by inhalation for 5 weeks (Miyabara et al., 1998b) and, after 7 days of exposure, were sensitized to OA injected intraperitoneally. At the end of the DE exposure, the mice were challenged with an OA aerosol for 15 min. DE caused an increase in the numbers of neutrophils and macrophages in bronchoalveolar lavage fluid independent of OA sensitization, whereas a significant increase in eosinophil numbers occurred only after DE exposure was combined with antigen challenge. Even though OA alone caused an increase in eosinophil numbers in lung tissue, this response was enhanced further by DE. DE exposure combined with OA sensitization enhanced the number of goblet-cells in lung tissue, respiratory resistance, production of OA-specific IgE and IgG_1 in the serum, and overexpression of IL-5 in lung tissue. In a second study, C3H/HeN mice were sensitized with OA injected intraperitoneally and then exposed to DE by inhalation for 12 h/day for 3 mo at either 1 or 3 mg/m^3 (Miyabara et al., 1998a). After 3 weeks of DE exposure, and every 3 weeks thereafter, the mice were challenged with an OA aerosol. Exposure to DE with antigen challenge induced airway hyperresponsiveness and airway inflammation, which was characterized by increased numbers of eosinophils and mast cells in lung tissue. The increase in inflammatory cells was accompanied by an increase in goblet cells in the bronchial epithelium. Airway hyperresponsiveness, but not eosinophilic infiltration or increased goblet cells, was increased by DE exposure alone. These workers concluded that inhalation of DE can enhance airway hyperresponsiveness and airway inflammation caused by OA sensitization in mice.

The effects of DE on IgE antibody production were investigated in BALB/c mice sensitized with OA and exposed by inhalation to DE (3.0 and 6.0 mg/m^3) for 3 weeks (Fujimaki et al., 1997). The mice were sensitized by intranasal administration of OA alone before, immediately after, and 3 weeks after DE inhalation. While body and thymus weights were unchanged in the DE-exposed and control mice, spleen weights in mice exposed to 6 mg/m^3 DE increased significantly. Anti-OA IgE antibody titers in the sera of mice exposed to 6 mg/m^3 DE were significantly higher than control. Total IgE and anti-OA IgG in sera from DE-exposed and

control mice remained unchanged. Cytokine production was measured in vitro stimulated with OA in spleen cells from mice exposed to DE (6 mg/m^3). Antigen-stimulated interleukin-4 (IL-4) and -10 (IL-10) production increased significantly in vitro in spleen cells from DE-exposed mice compared with controls, while IFN-γ production decreased markedly. The authors concluded that DE inhalation in mice may affect antigen-specific IgE antibody production through alteration of the cytokine network.

5.1.3.3.6. ***Effects on the immune system—noninhalation studies.*** The immune response of laboratory animals to DPM has been studied in various noninhalation models, and the results of these studies are presented in Table 5-9. Takafuji et al. (1987) evaluated the IgE antibody response of mice inoculated intranasally at intervals of 3 weeks with either 0.5 or 25 μg of DPM in ovalbumin per mouse. Antiovalbumin IgE antibody titers, assayed by passive cutaneous anaphylaxis, were enhanced by doses as low as 1 μg of particles compared with immunization with ovalbumin alone.

Muranaka et al. (1986) studied the effects of DPM on IgE antibody production in immunized mice. A greater IgE antibody response was noted in mice immunized by ip injection of ovalbumin (OA) mixed with DPM, either 0.02, 0.2, or 2mg per mouse, than in animals immunized with OA alone. This effect of DPM on IgE antibody production in mice was also demonstrated in mice immunized with repeated injections of dinitrophenylated-OA. Moreover, a persistent IgE-antibody response to Japanese cedar pollen (JCPA), a common pollen allergen causing allergic rhinitis in Japan, was observed in mice immunized with JCPA mixed with DPM but not in animals immunized with JCPA alone. The results suggest an association between the adjuvant activity of DPM and allergic rhinitis caused by JCPA.

Takano et al. (1997) designed a study to evaluate the effects of DPM on the manifestations of allergic asthma in mice, with emphasis on antigen-induced airway inflammation; the local expression of IL-5, GM-CSF, IL-2, and IFN-γ; and the production of antigen-specific IgE and IgG. Male ICR mice were intratracheally instilled with ovalbumin (OVA), DPM, and DPM+OVA. DPM was obtained from a 4JB1-type, light-duty 2.74 L, four-cylinder Isuzu diesel engine operated at a steady speed of 1,500 rpm under a load of 10 torque (kg/m). The OVA-group mice were instilled with 1 μg OVA at 3 and 6 weeks. The mice receiving DPM alone were instilled with 100 μg DPM weekly for 6 weeks. The OVA + DPM group received the combined treatment in the same protocol as the OVA and the DPM groups, respectively. Additional groups were exposed for 9 weeks. DPM aggravated OVA-induced airway inflammation, characterized by infiltration of eosinophils and lymphocytes and an

Table 5-9. Effects of diesel particulate matter on the immune response of laboratory animals

Model	Treatment	Effects	Reference
Mouse, BDFI, F		Intranasally delivered doses of DPM as low as 1 mg exerted an adjuvant activity for IgE antibody production.	Takafuji et al. (1987)
Mouse, ICR, w/w, M	Intratracheal instillation of DPM, once/week for 16 weeks	Infiltration of inflammatory cells, proliferation of goblet cells, increased mucus secretion, respiratory resistance, and airway constriction. Increased eosinophils in the submucosa of the proximal bronchi and medium bronchioles. Eosinophil infiltration suppressed by pretreatment with PEG-SOD. Bound sialic acid, an index of mucus secretion, in bronchial alveolar lavage fluids increased, but was suppressed by PEG-SOD. Increased respiratory resistance suppressed by PEG-SOD. Oxygen radicals produced by instilled DPM may cause features characteristic of bronchial asthma in mice.	Sagai et al. (1996)
Mouse, A/J, M	Mice immunized intranasally with Der f II + pyrene, or Der f II + DPM 7 times at 2-week intervals	IgE antibody responses to Der f II enhanced in mice immunized with Der f II+ pyrene or Der f II + DPM compared with Der f II alone. Response was dose related. DPM and pyrene contained in DPM have adjuvant activity on IgE and IgG1 antibody production in mice immunized with house dust mite allergen.	Suzuki et al. (1996)
Mouse, BDF_1, M	Mice were administered 25 mg of each of 5 fine particles (Kanto loam dust, fly ash, CB, DPM, and aluminum hydroxide [alum]) intranasally and exposed to aerosolized Japanese cedar pollen allergens (JCPA) for intervals up to 18 wk	Measurements were made of JCPA-specific IgE and IgG antibody titers, the protein-adsorbing capacity of each type of particle, and nasal rubbing movements (a parameter of allergic rhinitis in mice). The increases in anti-JPCA IgE and IgG antibody titers were significantly greater in mice treated with particles and aerosolized JCPA than in mice treated with aerosolized JCPA alone. In a subsequent experiment, the mice received the particles as before, but about 160,000 grains of Japanese cedar pollen (JCP) were dropped onto the tip of the nose of each mouse twice a week for 16 wk. After 18 wk there were no significant differences in the anti-JCPA IgE and IgG production, nasal rubbing, or histopathological changes. The workers concluded that the nature of the particle, the ability of the particle to absorb antigens, and/or particle size is not related to the enhancement of IgE antibody production or symptoms of allergic rhinitis. However, IgE antibody production did appear to occur earlier in mice treated with particles than in mice immunized with allergens alone.	Maejima et al. (1997)
Mouse, BALB/C, nu/nu, F	Inoculated OA with DPM or CB into hind footpad measured response using popliteal lymph node assay	Increased response (increased weight, cell numbers, cell proliferation) and longer response observed with DPM and OA, compared to DPM or OA alone. Response was specific and not an unspecific inflammatory response. CB was slightly less potent than DPM. Nonextractable carbon core contributes substantially to adjuvant activity of DPM.	Løvik et al. (1997)
Mouse, BALB/cA, F	Intranasal administration of DPM. Mice immunized with OA or OA combined with DPM or CB	Increased response to antigen in animals receiving DPM or CB. Increased number of responding animals and increased serum anti OA IgE antibody. Both DPM and CB have adjuvant activity for IgE production. DPM response more pronounced than CB, indicating both organic matter adsorbed to DPM and the nonextractable carbon core responsible for adjuvant activity.	Nilsen et al. (1997)
Mouse, ICR, M	Intratracheal instillation of OA, DPM, or OVA and DPM combined, once/week for 6 wk	Respiratory resistance (Rrs) measured 24 h after the final instillation. Rrs after acetylcholine challenge was significantly greater in the mice treated with OVA and DPM than other treatments. DPM can enhance airway responsiveness associated with allergen exposure.	Takano et al. (1998b)

OA - Ovalbumin.
DPM - Diesel particulate matter.
CB - Carbon black.

PEG-SOD - Polyethyleneglycol-conjugated superoxide dismutase.
IL-4 - Interleukin-4.
IL-5 - Interleukin-5.
IL-10 - Interleukin-10.
IFN - Interferon-g.
GM-CSF -Granulocyte-colony stimulating factor.
IP - Intraperitoneally.

increase in goblet cells in the bronchial epithelium. DPM in combination with antigen markedly increased IL-5 protein levels in lung tissue and bronchoalveolar lavage supernatants compared with either antigen or DPM alone. The combination of DPM and antigen induced significant increases in local expression of IL-4, GM-CSF, and IL-2, whereas expression of IFN-γ was not affected. In addition, DPM exhibited adjuvant activity for the antigen-specific production of IgG and IgE.

The potential role of oxygen radicals in injury caused by DPM was investigated by Sagai et al. (1996). These workers reported that repeated intratracheal instillation of DPM (either 0.1 or 0.2 mg per mouse, once/week for 16 weeks) in mice caused marked infiltration of inflammatory cells, proliferation of goblet cells, increased mucus secretion, respiratory resistance, and airway constriction. Eosinophils in the submucosa of the proximal bronchi and medium bronchioles increased eightfold following instillation. Eosinophil infiltration was significantly suppressed by pretreatment with polyethyleneglycol-conjugated superoxide dismutase (PEG-SOD), an inhibitor of oxygen radicals. Bound sialic acid concentrations in bronchial alveolar lavage fluids, an index of mucus secretion, increased with DPM, but were also suppressed by pretreatment with PEG-SOD. Goblet cell hyperplasia, airway narrowing, and airway constriction also were observed with DPM.

Respiratory resistance to acetylcholine in the DPM group was 11 times higher than in controls, and the increased resistance was significantly suppressed by PEG-SOD pretreatment. These findings indicate that oxygen radicals caused by intratracheally instilled DPM elicit responses characteristic of bronchial asthma.

Potential adjuvant effects of DPM on the response to the model allergen OA were investigated in BALB/c mice using the popliteal lymph node (PLN) assay (Løvik et al., 1997). DPM inoculated together with OA into one hind footpad (0.02 mL of a 5 mg/mL DPM suspension) gave a significantly augmented response (increase in weight, cell numbers, and cell proliferation) in the draining popliteal lymph node as compared to DPM or OA alone. The duration of the local lymph node response was also longer when DPM was given with the allergen. The lymph node response appeared to be of a specific immunologic character and not an unspecific inflammatory reaction. The OA-specific response IgE was increased in mice receiving OA together with DPM as compared with the response in mice receiving OA alone. Further studies using carbon black (CB) as a surrogate for the nonextractable core of DPM found that while CB resembled DPM in its capacity to increase the local lymph node response and serum-specific IgE response to OA, CB appeared to be slightly less potent than DPM. The results indicate that the nonextractable particle core contributes substantially to the adjuvant activity of DPM.

Nilsen et al. (1997) investigated which part of the particle was responsible, the carbon core and/or the adsorbed organic substances, for the adjuvant activity of DPM. Female

BALB/cA mice were immunized with OA alone or in combination with DPM or CB particles by intranasal administration a total of four times, once weekly, at 25 μg/inoculation. There was an increased response to the antigen in animals receiving OA together with DPM or CB, compared with animals receiving OA alone. The response was seen as both an increased number of responding animals and increased serum anti OA IgE response. The workers concluded that both DPM and CB have an adjuvant activity for specific IgE production, but that the activity of DPM may be more pronounced than that of CB. The results suggest that both the organic matter adsorbed to DPM and the nonextractable carbon are responsible for the observed adjuvant effect of DPM.

The effects of DPM and its components (extracted particles and particle extracts) on the release of proinflammatory cytokines, interleukin-1 (IL-1), and tumor necrosis factor-α (TNF-α) by alveolar macrophages (AMs) were investigated by Yang et al. (1997). Rat AMs were incubated with 0, 5, 10, 20, 50, or 100 μg/10^6 AM/mL of DPM, methanol-extracted DPM, or equivalent concentrations of DPM at 37 °C for 24 h. At high concentrations, both DPM and DPM extracts were shown to increase IL-1-like activity secreted by AMs, whereas extracted particles had no effect. Neither particles, particle extracts, or extracted particles stimulated secretion of TNF-α. DPM inhibited lipid polysaccharide (LPS)-stimulated production of IL-1 and TNF-α. In contrast, interferon (IFN)-γ-stimulated production of TNF-α was not affected by DPM. Results of this study indicate that the organic fraction of exhaust particles is responsible for the effects noted. Stimulation of IL-1 but not TNF-α suggests that IL-1, but not TNF-α, may play an important role in the development of DPM-induced inflammatory and immune responses. The cellular mechanism involved in inhibiting increased release of IL-1 and TNF-α by LPS is unknown, but may be a contributing factor to the decreased AM phagocytic activity and increased susceptibility to pulmonary infection after prolonged exposure to DPM.

Fujimaki et al. (1994) investigated the relationship between DPM and IgE antibody production, interleukin 4 (IL-4) production in BALB/c mice treated with DPM mixed with antigen OA or JCP antigen by intratracheal instillation. BALB/c mice were injected with DPM (300 μg) plus OA or OA alone and, after the last instillation, the proliferative response and lymphokine production by mediastinal lymph node cells (LNC) were examined in vitro. The proliferative response to OA in mediastinal LNC from mice injected with DPM plus OA was enhanced to 4-17 times that of control mice. IL-4 production by OA stimulation was also enhanced in mediastinal LNC from mice injected with DPM plus OA. A significantly larger amount of anti-OA IgE antibody was detected in sera from DPM- and OA-injected mice compared with those from control mice. The levels of IL-4, estimated by JCP antigen in mediastinal LNC, from mice injected with DPM plus JCP antigen were twofold higher than those from mice injected with JCP antigen alone. These results suggest that intratracheal

instillation of DPM affects antigen-specific IgE antibody responses via local T-cell activation, especially enhanced IL-4 production.

Suzuki et al. (1993) investigated the adjuvant activity of pyrene, one of many PAHs contained in DPM, on IgE antibody production in mice. In the first experiment, mice were immunized with 1 mg of OA alone, 1 mg of OA plus 1 mg of pyrene, or 1 mg of OA plus 1 mg of DPM, respectively. The IgE antibody responses to OA in mice immunized with OA plus pyrene or OA plus DPM were enhanced as compared to those in mice immunized with OA alone; the highest responses were observed in mice immunized with OA plus DPM. In the second experiment, mice were immunized with 10 mg of JCPA alone or 10 mg of JCPA plus 5 mg of pyrene. The IgE antibody responses to JCPA in mice immunized with JCPA plus pyrene were higher than those in mice immunized with JCPA alone. The results indicate that pyrene contained in DPM acts as an adjuvant in IgE antibody production in immunized mice.

Suzuki et al. (1996) investigated the effect of pyrene on IgE and IgG1 antibody production in mice to clarify the relation between mite allergy and adjuvancy of the chemical compounds in DPM. The mite allergen was Der f II, one of the major allergens of house dust mite (*Dermatophagoides farinae*). Allergen mice were grouped and immunized with Der f II (5 μg), Der f II (5 μg) plus pyrene (200 μg), and Der f II (5 μg) plus DPM (100 μg) intranasally seven times at 2-week intervals. The separate groups of mice were also immunized with Der f II (10 μg) plus the same dose of adjuvants in the same way. The IgE antibody responses to Der f II in mice immunized with Der f II plus pyrene or Der f II plus DPM were markedly enhanced compared with those immunized with Der f II alone. The anti-Der f II IgE antibody production increased with increasing the dose of Der f II from 5 μg to 10 μg in mice immunized with Der f II plus the same dose of adjuvants. The IgG1 antibody responses to Der f II in mice immunized with Der f II (10 μg) plus pyrene (200 μg) or Der f II (10 μg) plus DPM (100 μg) were greater than those immunized with 10 μg of Der f II alone. In addition, when peritoneal macrophages obtained from normal mice were incubated with pyrene or DPM in vitro, an enhanced IL-1a production by the macrophages was observed. When spleen lymphocytes obtained from the mice immunized with Der f II (10 μg) plus DPM (100 μg) or Der f II (10 μg) plus pyrene (200 μg) were stimulated with 10 μg of Der f II in vitro, an enhanced IL-4 production of the lymphocytes was also observed compared with those immunized with Der f II alone. This study indicates that DPM and pyrene (one of the many PAHs adsorbed onto DPM) have an adjuvant activity on IgE and IgG1 antibody production in mice immunized intranasally with a house dust mite allergen.

Maejima et al. (1997) examined the potential adjuvant activity of several different fine particles. These workers administered 25 μg of each of 5 particles (Kanto loam dust, fly ash, CB, DPM, and aluminum hydroxide [alum]) intranasally in mice and exposed them to aerosolized JCPA for intervals up to 18 weeks. Measurements were made of JCPA-specific IgE

and IgG antibody titers, the protein-adsorbing capacity of each type of particle, and nasal rubbing movements (a parameter of allergic rhinitis in mice). The increases in anti-JPCA IgE and IgG antibody titers were significantly greater in mice treated with particles and plus aerosolized JCPA than in mice treated with aerosolized JCPA alone. In a subsequent experiment, the mice received the particles as before, but about 160,000 grains of JCP were dropped onto the tip of the nose of each mouse twice a week for 16 weeks. After 18 weeks there were no significant differences in the anti-JCPA IgE and IgG production, nasal rubbing, or histopathological changes. The workers concluded that the nature of the particle, the ability of the particle to absorb antigens, and particle size are not related to the enhancement of IgE antibody production or symptoms of allergic rhinitis. However, IgE antibody production did appear to occur earlier in mice treated with particles than in mice immunized with allergens alone.

The potential for DPM to modulate cytokine production has been demonstrated in cultured mouse bone marrow-derived mast cells (BMMC). Saneyoshi et al. (1997) examined the production of cytokines in BMMC treated with DPM (0.8, 2 and 4 mg/mL). Production of interleukin-4 (IL-4) and IL-6 was higher in BMMC stimulated with A23187 and treated with low concentrations of DPM than in controls, but no increase was seen in BMMC treated with high DPM. After pretreatment with low DPM for 24 h, IL-4 production in BMMC stimulated with A23187 was lower than in controls. Antigen-induced IL-4 production increased significantly in BMMC treated with 0.4 or 0.8 mg/mL DPM, but did not increase with low DPM. Although the enhancement of IL-4 production of BMMC stimulated with A23187 plus DPM was not completely inhibited by 2-mercaptoethanol, treatment with dexamethasone inhibited further IL-4 production. Thus, DPM may affect the immune response via the modulation of cytokine production in mast cells.

Ormstad et al. (1998) investigated the potential for DPM as well as other suspended particulate matter (SPM) to act as a carrier for allergens into the airways. These investigators found both Can f 1 (dog) and Bet v 1 (birch pollen) on the surface of SPM collected in air from different homes. In an extension of the study, they found that DPM adhered to polycarbonate filters had the potential of binding both of these allergens as well as Fel d 1 (cat) and Der p 1 (house mite). The authors conclude that soot particles in indoor air house dust may act as carrier of several allergens in indoor air.

Knox et al. (1997) investigated whether free grass pollen allergen molecules, released from pollen grains by osmotic shock (Suphioglu et al., 1992) and dispersed in microdroplets of water in aerosols, can bind to DPM mounted on copper grids in air. Using natural highly purified Lol p 1, immunogold labeling with specific monoclonal antibodies, and a high-voltage transmission electron-microscopic imaging technique, these workers demonstrated binding of the major grass pollen allergen, Lol p 1, to DPM in vitro. These workers conclude that binding of

DPM with Lol p 1 might be a mechanism by which allergens can become concentrated in air and trigger attacks of asthma.

Murphy et al. (1999) examined the comparative toxicities to the lung of four different-sized CB particles and DPM, in primary cultures of mouse Clara and rat type II epithelial cells. Particle toxicity was assessed by cell attachment to an extracellular matrix substratum. The CB particles varied in toxicity to Clara and type II cells. DPM stored for 2 weeks was equally toxic to both cell types. DPM became progressively less toxic to type II cells with time of storage. Both primary epithelial cell types internalized the particles in culture. These workers concluded that bioreactivity was related to CB particle size and surface area, with the smaller particles having the larger surface area being the more toxic. Although freshly prepared DPM was equally toxic to type II and Clara cells, DPM became progressively less toxic to the type II cells with time.

Exposure studies in laboratory animals and isolated cell systems derived from animals also indicate that DPM can elicit both inflammatory and immunological changes. Moreover, the effects appear to be due to both the nonextractable carbon core and the adsorbed organic fraction of the diesel particle. Changes in IgE, goblet cell hyperplasia, mast cell influx, and cytokines in various animal models and in vitro model systems are all key markers of asthma. The data further indicate a role for oxygen radicals in DPM injury because the extent of the injury can be reduced by treatment with antioxidants. DPM also has the capacity to bind and transport airborne allergens.

5.1.3.3.7. ***Effects on the liver***. Meiss et al. (1981) examined alterations in the hepatic parenchyma of hamsters by using thin-section and freeze-fracture histological techniques. Exposures to DE were for 7 to 8 h/day, 5 days/week, for 5 mo at about 4 or 11 mg/m^3 DPM. The livers of the hamsters exposed to both concentrations of DE exhibited moderate dilatation of the sinusoids, with activation of the Kupffer cells and slight changes in the cell nuclei. Fatty deposits were observed in the sinusoids, and small fat droplets were occasionally observed in the peripheral hepatocytes. Mitochondria often had a loss of cristae and exhibited a pleomorphic character. Giant microbodies were seen in the hepatocytes, which were moderately enlarged, and gap junctions between hepatocytes exhibited a wide range in structural diversity. The results of this study and others on the effect of exposure of DE on the liver of laboratory animals are summarized in Table 5-10.

Table 5-10. Effects of exposure to diesel exhaust on the liver of laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, F344, M, F	7 h/day 5 days/week 52 weeks	2.0 0.23–0.36 µm MDD	3,640	12.7	1.6	0.83	No changes in absolute liver weight or liver/body weight ratio	Green et al. (1983)
Hamster, Syrian	7-8 h/day 5 days/week 22 weeks	4.0 8.0 11.0	3,080-9,680	12.0 19.0 25.0	0.5 1.0 1.5	3.0 6.0 7.0	Enlarged sinusoids, with activated Kupffer's cells and slight changes of nuclei; fatty deposits; mitochondria, loss of cristae and pleomorphic character; gap junctions between hepatocytes had wide range in structural diversity	Meiss et al. (1981)
Cat, inbred, M	8 h/day 7 days/week 124 weeks	6.0[a] 12.0[b]	41,664 83,328	20.2 33.3	2.7 4.4	2.1 5.0	No change in the absolute liver weight	Plopper et al. (1983)

[a]1 to 61 weeks of exposure.
[b]62 to 124 weeks of exposure.

Green et al. (1983) and Plopper et al. (1983) reported no changes in liver weights of rats exposed to 2 mg/m^3 DPM for 7 h/day, 5 days/week for 52 weeks or of cats exposed to 6 to 12 mg/m^3, 8 h/day, 7 days/week for 124 weeks. The use of light and electron microscopy revealed that long-term inhalation of varying high concentrations of DE caused numerous alterations to the hepatic parenchyma of guinea pigs. A less sensitive index of liver toxicity, increased liver weight, failed to detect an effect of DE on the liver of the rat and cat following long-term exposure to DE. These results are too limited to understand potential impacts on the liver.

5.1.3.3.8. ***Blood and cardiovascular systems.*** Several studies have evaluated the effects of DE exposure on hematological and cardiovascular parameters of laboratory animals. These studies are summarized in Table 5-11. Standard hematological indices of toxicological effects on red and white blood cells failed to detect dramatic and consistent responses. Erythrocyte (RBC) counts were reported as being unaffected in cats (Pepelko and Peirano, 1983), rats and monkeys (Lewis et al., 1989), guinea pigs and rats (Penney et al., 1981), and rats (Karagianes et al., 1981); lowered in rats (Heinrich et al., 1982); and elevated in rats (Ishinishi et al., 1988; Brightwell et al., 1986). Mean corpuscular volume was significantly increased in monkeys, 69 versus 64 (Lewis et al., 1989), and hamsters (Heinrich et al., 1982), and lowered in rats (Ishinishi et al., 1988). The only other parameters of erythrocyte status and related events were lowered mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration in1 rats (Ishinishi et al., 1988), a 3% to 5% increase in carboxyhemoglobin saturation in rats (Karagianes et al., 1981), and a suggestion of an increase in prothrombin time (Brightwell et al., 1986). The biological significance of these findings regarding adverse health effects is deemed to be inconsequential.

Three investigators (Pepelko and Peirano, 1983; Lewis et al., 1989; Brightwell et al., 1986) reported an increase in the percentage of banded neutrophils in cats and rats. This effect was not observed in monkeys (Lewis et al., 1989). The health implications of an increase in abnormal maturation of circulating neutrophils are uncertain but indicate a toxic response of leukocytes following exposures to DE. Leukocyte counts were reported to be reduced in hamsters (Heinrich et al., 1982); increased in rats (Brightwell et al., 1986); and unaffected in cats, rats, and monkeys (Pepelko and Peirano, 1983; Ishinishi et al., 1988; Lewis et al., 1989). These inconsistent findings indicate that the leukocyte counts are more indicative of the clinical status of the laboratory animals than any direct effect of exposure to DE.

No significant changes in heart mass were found in guinea pigs or rats exposed to DE (Wiester et al., 1980; Penney et al., 1981; Lewis et al., 1989). Rats exposed to DE showed a greater increase in the medial wall thickness of pulmonary arteries of differing diameters and

Table 5-11. Effects of exposure to diesel exhaust on the hematological and cardiovascular systems of laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Monkey, Cynomolgus, M	7 h/day 5 days/week 104 weeks	2 0.23–0.36 µm MDD	7,280	11.5	1.5	0.8	Increased MCV	Lewis et al. (1989)
Rat, F344, M, F	7 h/day 5 days/week 104 weeks	2 0.23–0.36 µm MDD	7,280	11.5	1.5	0.8	Increase in banded neutrophils; no effect on heart or pulmonary arteries	Lewis et al. (1989) Vallyathan et al. (1986)
Guinea Pig, Hartley, M, F	20 h/day 7 days/week 8 weeks	6.3[a] 6.8[b]	7,056 7,616	17.4 16.7	2.3 2.9	2.1 1.9	No effect on heart mass or ECG; small decrease in heart rate (IE only)	Wiester et al. (1980)
Hamster, Syrian, M, F	7-8 h/day 5 days/week 75 weeks	3.9 0.1 µm MDD	10,238-11,700	18.5	1.2	3.1	At 29 weeks, lower erythrocyte count; increased MCV; reduced leukocyte count	Heinrich et al. (1982)
Rat, F344; Guinea Pig, Hartley	20 h/day 5.5 days/week 78 weeks	0.25 0.75 1.5 0.19 µm MDD	2,145 6,435 12,870	3.0 4.8 6.9	0.11 0.27 0.49	— — —	No changes in heart mass or hematology at any exhaust level or duration of exposure in either species	Penney et al. (1981)
Rat, Wistar, M	6 h/day 5 days/week 78 weeks	8.3 0.71 µm MDD	19,422	50.0	4-6	—	3% increase in COHb	Karagianes et al. (1981)
Rat, F3444/Jcl, M, F	16 h/day 6 days/week 130 weeks	0.11[c] 0.41[c] 1.08[c] 2.31[c] 3.72[d] 0.1 µm MDD	1,373 5,117 13,478 28,829 46,426	1.23 2.12 3.96 7.10 12.9	0.08 0.26 0.70 1.41 3.00	0.38 1.06 2.42 4.70 4.57	At higher concentrations, RBC, Hb, Hct slightly elevated; MCV and mean corpuscular hemoglobin and concentration were lowered	Ishinishi et al. (1988)
Rat, F344	16 h/day 5 days/week 104 weeks	0.7 2.2 6.6	5,824 18,304 54,912	— — 32.0	— — —	— — —	Increases in RBC, Hb, Hct, and WBC, primarily banded neutrophils; suggestion of an increase in prothrombin time; increased heart/body weight and right ventricular/heart ratios and decreased left ventricular contractility in 6.6 mg/m^3 group	Brightwell et al. (1986)
Cat, Inbred, M	8 h/day 7 days/week 124 weeks	6.0[e] 12.0[f]	41,664 83,328	20.2 33.3	2.7 4.4	2.1 5.0	Increases in banded neutrophils; significant at 12 mo, but not 24 mo	Pepelko and Peirano (1983)

[a]Nonirradiated DE.
[b]Irradiated DE.
[c]Light-duty engine.
[d]Heavy-duty engine.
[e]1 to 61 weeks of exposure.
[f]62 to 124 weeks of exposure.

Key: MCV = Mean corpuscular volume.

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right ventricular wall thickness; these increases, however, did not achieve statistically significant levels (Vallyathan et al., 1986). Brightwell et al. (1986) reported increased heart/body weight and right ventricular/heart weight ratios and decreased left ventricular contractility in rats exposed to 6.6 mg/m^3 DPM for 16 h/day, 5 days/week for 104 weeks.

The effects of DPM on the endothelium-dependent relaxation (EDR) of vascular smooth muscle cells have been investigated (Ikeda et al., 1995, 1998). Incubation of rat thoracic aortae with suspensions of DPM (10-100 μg/mL) markedly attenuated acetylcholine-induced EDR. The mechanism of this effect was studied further in cultured porcine endothelial cells (CPE). A 10-min incubation of CPE with DPM (0.1-100 μg/mL) inhibited endothelium-dependent relaxing factor (EDRF) or nitric oxide (NO) release. A 10-min incubation of DPM with NO synthase inhibited formation of NO_2^-, a product of NO metabolism. The authors concluded that DPM, at the concentrations tested, neither induced cell damage nor inhibited EDRF release from CPE, but scavenged and thereby blocked the physiological action of NO.

5.1.3.3.9. ***Serum chemistry.*** A number of investigators have studied the effects of exposure to DE on serum biochemistry, and no consistent effects have been found. Such studies are summarized in Table 5-12.

The biological significance of changes in serum chemistry reported by Lewis et al. (1989) in female but not male rats exposed at 2 mg/m^3 DPM for 7 h/day, 5 days/week for 104 weeks is difficult to interpret. Not only were the effects noted in one sex (females) only, but the serum enzymes, lactate dehydrogenase (LDH), serum glutamic-oxaloacetic transaminase (SGOT), and serum glutamic-pyruvic transaminase (SGPT), were elevated in the control group, a circumstance contrary to denoting organ damage in the exposed female rats. The elevations of liver-related serum enzymes in the control versus the exposed female rats appear to be a random event among these aged subjects. The incidence of age-related disease, such as mononuclear cell leukemia, can markedly affect such enzyme levels, seriously compromising the usefulness of a comparison to historical controls. The serum sodium values of 144 versus 148 mmol/L in control and exposed rats, respectively, although statistically different, would have no biological significance.

The increased serum enzyme activities, alkaline phosphatase, SGOT, SGPT, gamma-glutamyl transpeptidase, and decreased cholinesterase activity suggest an impaired liver; however, such an impairment was not established histopathologically (Heinrich et al., 1982; Ishinishi et al., 1988; Brightwell et al., 1986). The increased urea nitrogen, electrolyte levels, and gamma globulin concentration and reduction in total blood proteins are indicative of impaired kidney function. Again, there was no histopathological confirmation of impaired kidneys in these studies.

Table 5-12. Effects of chronic exposures to diesel exhaust on serum chemistry of laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, F344, M, F	7 h/day 5 days/week 104 weeks	2.0 0.23 0.36 µm MDD	7,280	11.5	1.5	0.8	Decreased phosphate, LDH, SGOT, and SGPT; increased sodium in females but not males	Lewis et al. (1989)
Hamster, Syrian, M, F	7-8 h/day 5 days/week 75 weeks	3.9 0.1 µm MDD	10,238-11,700	18.5	1.2	3.1	After 29 weeks, increases in SGOT, LDH, alkaline phosphatase, gamma-glutamyl transferase, and BUN	Heinrich et al. (1982)
Rat, F344/JcL, M, F	16 h/day 6 days/week 130 weeks	0.11[a] 0.41[a] 1.08[a] 2.31[a] 3.72[b] 0.19–0.28 µm MDD	1,373 5,117 13,478 28,829 46,426	1.23 2.12 3.96 7.10 12.9	0.08 0.26 3.96 7.10 3.00	0.38 1.06 2.42 4.70 4.57	Lower cholinesterase activity in males in both the light-and heavy-duty series and elevated gamma globulin and electrolyte levels in males and females in both series	Research Committee for HERP Studies (1988)
Rat, F344; Hamster, Syrian	16 h/day 5 days/week 104 weeks	0.7 2.2 6.6	5,824 18,304 54,912	— — 32.0	— — —	— — —	Rats, 6.6 mg/m^3, reduction in blood glucose, blood proteins, triglycerides, and cholesterol; increase in BUN, alkaline phosphate alamine, and aspartate aminotransferases (SGPT and SGOT); hamsters, 6.6 mg/m^3, decrease in potassium, LDH, aspartate amino-transferase; increase in albumin and gamma-glutamyl transferase	Brightwell et al. (1986)
Cat inbred, M	8 h/day 7 days/week 124 weeks	6.0[c] 12.0[d]	41,664 83,328	20.2 33.3	2.7 4.4	2.1 5.0	BUN unaltered; SGOT and SGPT unaffected; LHD increase after 1 year of exposure	Pepelko and Peirano (1983)

[a]Light-duty engine.
[b]Heavy-duty engine.
[c]1 to 61 weeks of exposure.
[d]62 to 124 weeks of exposure.

Key:
LDH = Lactate dehydrogenase.
SGOT = Serum glutamic-oxaloacetic transaminase.
BUN = Blood urea nitrogen.
SGPT = Serum glutamic-pyruvic transaminase.

Clinical chemistry studies suggest impairment of both liver and kidney functions in rats and hamsters chronically exposed to high concentrations of DE. The absence of histopathological confirmation, the appearance of such effects near the end of the lifespan of the laboratory animal, and the failure to find such biochemical changes in cats exposed to a higher dose, however, tend to discredit the probability of hepatic and renal hazards to humans exposed at atmospheric levels of DE.

5.1.3.3.10. ***Effects on microsomal enzymes.*** Several studies have examined the effects of DE exposure on microsomal enzymes associated with the metabolism and possible activation of xenobiotics, especially polynuclear aromatic hydrocarbons (PAH). These studies are summarized in Table 5-13. Lee et al. (1980) measured the activities of aryl hydrocarbon hydroxylase (AHH) and epoxide hydrase (EH) in liver, lung, testis, and prostate gland of adult male rats exposed to 6.32 mg/m^3 DPM 20 h/day for 42 days. Maximal significant AHH activities (pmol/min/mg microsomal protein) occurred at different times during the exposure period, and differences between controls and exposed rats, respectively, were as follows: prostate 0.29 versus 1.31, lung 3.67 versus 5.11, and liver 113.9 versus 164.0. There was no difference in AHH activity in the testis between exposed and control rats. Epoxide hydrase activity was not significantly different from control values for any of the organs tested.

Pepelko and Peirano (1983) found no statistically significant differences in liver microsomal cytochrome P448-450 levels and liver microsomal AHH between control and diesel-exposed mice at either 6 or 8 mo of exposure. Small differences were noted in the lung microsomal AHH activities, but these were believed to be artifactual differences, due to increases in nonmicrosomal lung protein present in the microsomal preparations. Exposures to 6 mg/m^3 DPM were for 8 h/day, 7 days/week.

Rabovsky et al. (1984) investigated the effect of chronic exposure to DE on microsomal cytochrome P450-associated benzo[*a*]pyrene (B[*a*]P) hydroxylase and 7-ethoxycoumarin deethylase activities in rat lung and liver. Male rats were exposed for 7 h/day, 5 days/week for 104 weeks to 2 mg/m^3 DPM. The exposure had no effect on B[*a*]P hydroxylase or 7-ethoxycoumarin deethylase activities in lung or liver. In related studies, Rabovsky et al. (1986) examined the effects of DE on viral induced enzyme activity and interferon production in female mice. The mice were exposed for 7 h/day, 5 days/week for 1 mo to DE diluted to achieve a concentration of 2 mg/m^3 DPM. After the exposure, the mice were inoculated intranasally with influenza virus. Changes in serum levels of interferon and liver microsomal activities of 7-ethoxycoumarin, ethylmorphine demethylase, and nicotinamide adenine dinucleotide phosphate

Table 5-13. Effects of chronic exposures to diesel exhaust on microsomal enzymes of laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × t ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, F344, M	—	—	—	—	—	—	Intratracheal administration of DPM extract required doses greater than 6 mg/m^3 before the lung AHH was barely doubled; liver AHH activity was unchanged	Chen (1986)
Mouse, CD-1, F	7 h/day 5 days/week 4 weeks	2.0 0.2–0.36 μm mdd	280	11.5	1.5	0.8	Mice inoculated intranasally with influenza virus had smaller increases in ethylmorphine demethylase activity on days 2 to 4 postvirus infection and abolition of day 4 postinfection increase in NADPH-dependent cytochrome c reductase	Rabovsky et al. (1986)
Rat, Sprague-Dawley, M	20 h/day 7 days/week 1-7 weeks	6.3	882-6,174	17.4	2.3	2.1	AHH induction occurred in lung, liver, and prostate gland but not in testes; maximum significant activities occurred at different times; liver has greatest overall activity, percent increase highest in prostate; expoxide hydrase activity was unaffected	Lee et al. (1980)
Rat, F344, M	20 h/day 5.5 days/week 4, 13, 26, or 39 weeks	0.75 1.5 0.19 μm mdd	330-6,435	4.8 7.5	— —	— —	Inhalation exposure had no significant effect on liver AHH activity; lung AHH activity was slightly reduced after 6-mo exposure to 1.5 mg/m^3 DPM; an ip dose of dp extract, estimated to be equivalent to inhalation exposure, had no effect on AHH activity in liver and lungs; cyt. P-50 was unchanged in lungs and liver following inhalation or ip administration	Chen and Vostal (1981)
	20 h/day 5.5 days/week 4, 13, 26, or 39 weeks	0.75 1.5 0.19 μm mdd	330-6,435	4.8 7.5	— —	— —		
Rat, F344, F	7 h/day 5 days/week 12, 26, or 104 weeks	2.0 0.23-0.36 μm mdd	840-7,280	11.5	1.5	0.8	No effect on B[*a*]p hydrolase or 7-exthoxycoumarin deethylase activities in the liver	Rabovsky et al. (1984)
Rat, F344, M	20 h/day 5.5 days/week 8-53 weeks	0.25 1.5 0.19 μm mdd	220-8,745	2.9 7.5	— —	— —	After 8 weeks, no induction of cyt. P-450, cyt. P-448, or NADPH-dependent cyt. c reductase; after 1 year of exposure, liver microsomal oxidation of B[*a*]p was not increased; 1 year of exposure to either 0.25 or 1.5 mg/m^3 DPM impaired lung microsomal metabolism of B[*a*]p	Navarro et al. (1981)
Mouse, A/J, M	8 days/week 7 days/week 26 or 35 weeks	6.0	17.4	17.4	2.3	2.1	No differences in lung and liver AHH activities and liver P-448, P-450 levels	Pepelko and Peirano (1983)

AHH = aryl hydrocarbon hydroxylase.
B[*a*]p = benzo[*a*]pyrene.

(NADPH)-dependent cytochrome c reductase were measured. In the absence of viral inoculation, exposure to DE had no significant effects on the activity levels of the two liver microsomal monooxygenases and NADPH-dependent cytochrome c reductase. Exposure to DE produced smaller increases in ethylmorphine demethylase activity on days 2 to 4 postvirus infection and also abolished the day 4 postinfection increase in NADPH-dependent cytochrome c reductase when compared with nonexposed mice. These data suggested to the authors that the relationship that exists between metabolic detoxification and resistance to infection in unexposed mice was altered during a short-term exposure to DE.

Chen and Vostal (1981) measured the activity of AHH and the content of cytochrome P450 in the lungs and livers of rats exposed by inhalation of DE or intraperitoneal (i.p.) injection of a dichloromethane extract of DPM. In the inhalation exposures, the exhaust was diluted to achieve concentrations of 0.75 or 1.5 mg/m^3 DPM, and the exposure regimen was 20 h/day, 5.5 days/week for up to 9 mo. The concentration of total hydrocarbons and particle-phase hydrocarbons was not reported. Parenteral administration involved repeated injections at several dose levels for 4 days. Inhalation exposure had no significant effect on liver microsomal AHH activity; however, lung AHH activity was slightly reduced after 6 mo exposure to 1.5 mg/m^3. An i.p. dose of DPM extract, estimated to be equivalent to the inhalation exposure, had no effect on AHH activity in liver or lungs. No changes were observed in cytochrome P450 contents in lungs or liver following inhalation exposure or i.p. treatment. Direct intratracheal administration of a dichloromethane DPM extract required doses greater than 6 mg/kg body weight before the activity of induced AHH in the lung was barely doubled; liver AHH activity remained unchanged (Chen, 1986).

In related studies, Navarro et al. (1981) evaluated the effect of exposure to DE on rat hepatic and pulmonary microsomal enzyme activities. The same exposure regimen was employed (20 h/day, 5.5 days/week, for up to 1 year), and the exhaust was diluted to achieve concentrations of 0.25 and 1.5 mg/m^3 DPM (a few studies were also conducted at 0.75 mg/m^3). After 8 weeks of exposure, there was no evidence for the induction of cytochrome P450, cytochrome P448, or NADPH-dependent cytochrome c reductase in rat liver microsomes. One year of exposure had little, if any, effect on the hepatic metabolism of B[*a*]P. However, 1 year of exposure to 0.25 and 1.5 mg/m^3 significantly impaired the ability of lung microsomes to metabolize B[*a*]P (0.15 and 0.02 nmole/30 min/mg protein, respectively, versus 0.32 nmole/30 min/mg protein for the controls).

There are conflicting results regarding the induction of microsomal AHH activities in the lungs and liver of rodents exposed to DE. One study reported induction of AHH activity in the lungs, liver, and prostate of rats exposed to DE containing 6.32 mg/m^3 DPM for 20 h/day for 42 days; however, no induction of AHH was observed in the lungs of rats and mice exposed to 6 mg/m^3 DPM for 8 h/day, 7 days/week for up to 8 mo or to 0.25 to 2 mg/m^3 for periods up to 2

years. Exposure to DE has not been shown to produce adverse effects on microsomal cytochrome P450 in the lungs or liver of rats or mice. The weight of evidence suggests that the absence of enzyme induction in the rodent lung exposed to DE is caused either by the unavailability of the adsorbed hydrocarbons or by their presence in quantities insufficient for enzyme induction.

5.1.3.3.11. ***Effects on behavior and neurophysiology***. Studies on the effects of exposure to DE on the behavior and neurophysiology of laboratory animals are summarized in Table 5-14. Laurie et al. (1978) and Laurie et al. (1980) examined behavioral alterations in adult and neonatal rats exposed to DE. Exposure for 20 h/day, 7 days/week, for 6 weeks to exhaust containing 6 mg/m^3 DPM produced a significant reduction in adult spontaneous locomotor activity (SLA) and in neonatal pivoting (Laurie et al., 1978). In a follow-up study, Laurie et al. (1980) found that shorter exposure (8 h/day) to 6 mg/m^3 DPM also resulted in a reduction of SLA in adult rats. Laurie et al. (1980) conducted additional behavioral tests on adult rats exposed during their neonatal period. For two of three exposure situations (20 h/day for 17 days postparturition, or 8 h/day for the first 28 or 42 days postparturition), significantly lower SLA was observed in the majority of the tests conducted on the adults after week 5 of measurement. When compared with control rats, adult 15-month-old rats that had been exposed as neonates (20 h/day for 17 days) also exhibited a significantly slower rate of acquisition of a bar-pressing task to obtain food. The investigators noted that the evidence was insufficient to determine whether the differences were the result of a learning deficit or due to some other cause (e.g., motivational or arousal differences).

These data are difficult to interpret in terms of health hazards to humans under ambient environmental conditions because of the high concentration of DE to which the laboratory rats were exposed. Additionally, there are no further concentration-response studies to assess at what exposure levels these observed results persist or abate. A permanent alteration in both learning ability and activity resulting from exposures early in life is a health hazard whose significance to humans should be pursued further.

Neurophysiological effects from exposure to DE were investigated in rats by Laurie and Boyes (1980, 1981). Rats were exposed to diluted DE containing 6 mg/m^3 DPM for 8 h/day, 7 days/week from birth up until 28 days of age. Somatosensory evoked potential, as elicited by a 1 mA electrical pulse to the tibial nerve in the left hind limb, and visual evoked potential, as elicited by a flash of light, were the endpoints tested. An increased pulse latency was reported for the rats exposed to DE, and this was thought to be caused by a reduction in the degree of

Table 5-14. Effects of chronic exposures to diesel exhaust on behavior and neurophysiology

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, Sprague-Dawley, M	8 h/day 7 days/week 1-4 weeks	6	336-1,344	19	2.5	1.8	Somatosensory and visual evoked potentials revealed longer pulse latencies in pups exposed neonatally	Laurie and Boyes (1980, 1981)
Rat, Sprague Dawley, F	20 h/day 7 days week 6 weeks	6	5,040	19	2.5	1.8	Reduction in adult SLA and in neonatal pivoting	Laurie et al. (1978)
Rat, Sprague-Dawley, F	8 or 20 h/day 7 days/week 3, 4, 6, or 16 weeks	6	1,008-13,440	19	2.5	1.8	Reduction in SLA in adults; neonatal exposures for 20 or 8 h/day caused reductions in SLA. Neonatal exposures for 20 h/day for 17 days resulted in a slower rate of a bar-pressing task to obtain food	Laurie et al. (1980)

SLA = Spontaneous locomotor activity.

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nerve myelinization. There was no neuropathological examination, however, to confirm this supposition.

Based on the data presented, it is not possible to specify the particular neurological impairment(s) induced by the exposure to DE. Again, these results occurred following exposure to a high level of DE and no additional concentration-response studies were performed.

5.1.3.3.12. ***Effects on reproduction and development.*** Studies of the effects of exposure to DE on reproduction and development are summarized in Table 5-15. Twenty rats were exposed 8 h/day on days 6 through 15 of gestation to diluted DE containing 6 mg/m^3 DPM (Werchowski et al., 1980a,b; Pepelko and Peirano, 1983). There were no signs of maternal toxicity or decreased fertility. No skeletal or visceral teratogenic effects were observed in 20-day-old fetuses (Werchowski et al., 1980a). In a second study, 42 rabbits were exposed to 6 mg/m^3 DPM for 8 h/day on gestation days 6 through 18. No adverse effects on body weight gain or fertility were seen in the does exposed to DE. No visceral or skeletal developmental abnormalities were observed in the fetuses (Werchowski et al., 1980b).

Pepelko and Peirano (1983) evaluated the potential for DE to affect reproductive performance in mice exposed from 100 days prior to exposure throughout maturity of the F_2 generation. The mice were exposed for 8 h/day, 7 days/week to 12 mg/m^3 DPM. In general, treatment-related effects were minimal. Some differences in organ and body weights were noted, but overall fertility and survival rates were not altered by exposure to DE. The only consistent change, an increase in lung weights, was accompanied by a gross pathological diagnosis of anthracosis. These data denoted that exposure to DE at a concentration of 12 mg/m^3 did not affect reproduction. See Section 5.3, which reports a lack of effects of exposure to DE on rat lung development (Mauderly et al., 1987b).

Several studies have evaluated the effect of exposure to DE on sperm. Lewis et al. (1989) found no adverse sperm effects (sperm motility, velocity, densities, morphology, or incidence of abnormal sperm) in monkeys exposed for 7 h/day, 5 days/week for 104 weeks to 2 mg/m^3 DPM. In another study in which A/Strong mice were exposed to DE containing 6 mg/m^3 DPM for 8 h/day for 31 or 38 weeks, no significant differences were observed in sperm morphology between exposed and control mice (Pereira et al., 1981). It was noted, however, that there was a high rate of spontaneous sperm abnormalities in this strain of mice, and this may have masked any small positive effect. Quinto and De Marinis (1984) reported a statistically significant and dose-related increase in sperm abnormalities in mice injected intraperitoneally for 5 days with 50, 100, or 200 mg/kg of DPM suspended in corn oil. A significant decrease in sperm number was seen at the highest dose, but testicular weight was unaffected by the treatment.

Table 5-15. Effects of chronic exposures to diesel exhaust on reproduction and development in laboratory animals

Species/sex	Exposure period	Particles (mg/m^3)	C × T ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Mouse, [C57BL]/6XC3H]F_1, M	5 days	50, 100, or 200 mg/kg in corn oil; i.p. injection	—	—	—	—	Dose-related increase in sperm abnormalities; decrease in sperm number at highest dose; testicular weights unaffected	Quinto and De Marinis (1984)
Rat, Sprague-Dawley, F	8 h/day 7 days/week 1.7 weeks	6	571	20	2.7	2.1	No signs of maternal toxicity or decreased fertility; no skeletal or visceral teratogenic effects in 20-day-old fetuses	Werchowski et al. (1980a) Pepelko and Peirano (1983)
Rabbit, New Zealand Albino, F	8 h/day 7 days/week 1.9 weeks	6	638	20	2.7	2.1	No adverse effects on maternal weight gain or fertility; no skeletal or visceral teratogenic effects in the fetuses	Werchowski et al. (1980a) Pepelko and Peirano (1983)
Monkey, Cynomolgus, M	7 h/day 5 days/week 104 weeks	2	7,280	11.5	1.5	0.8	No effects on sperm motility, velocity, density, morphology, or incidence of abnormalities	Lewis et al. (1989)
Mouse, A/Strong, M	8 h/day 7 days/week 31 or 38 weeks	6	10,416-12,768	20	2.7	2.1	No effect on sperm morphology; high rate of spontaneous sperm abnormalities may have masked small effects	Pereira et al. (1981)
Mouse, CD-1, M, F	8 h/day 7 days/week 6 to 28 weeks	12	4,032-18,816	33	4.4	5.0	Overall fertility and survival rates were unaffected in the three-generation reproductive study; only consistent change noted, an increase in lung weights, was diagnosed as anthracosis	Pepelko and Peirano (1983)

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Watanabe and Oonuki (1999) investigated the effects of diesel engine exhaust on reproductive endocrine function in growing rats. The rats were exposed to whole diesel engine exhaust (5.63 mg/m^3 DPM, 4.10 ppm NO_2, and 8.10 ppm NO_x); a group was exposed to filtered exhaust without DPM, and a group was exposed to clean air. Exposures were for 3 mo beginning at birth (6 h/day for 5 days/week).

Serum levels of testosterone and estradiol were significantly higher and follicle-stimulating hormone significantly lower in animals exposed to whole DE and filtered exhaust compared to controls. Luteinizing hormone was significantly decreased in the whole-exhaust-exposed group as compared to the control and filtered groups. Sperm production and activity of testicular hyaluronidase were significantly reduced in both exhaust-exposed groups as compared to the control group. This study suggests that DE stimulates hormonal secretion of the adrenal cortex, depresses gonadotropin-releasing hormone, and inhibits spermatogenesis in rats. Because these effects were not inhibited by filtration, the gaseous phase of the exhaust appears more responsible than particulate matter for disrupting the endocrine system.

The effects of freshly generated DE particles on the reproductive system of male Fischer 344 rats were investigated by Tsukue et al. (2001). Groups (n=25) of 13-mo-old male rats were exposed to whole DE diluted to 0.33, 0.99 or 3.24 mg/m^3 (MMAD = 0.4 μm) for 8 months 12/h/d, 7 d/wk. Subsequent to this exposure, evaluation of potential reproductive effect was performed, including measurement of reproductive organ weights, sperm characteristics and number, gonadotrophins, testosterone, and inhibin. Results showed either no effect or effects with an inconsistent dose-response character that typically were not different from controls even at the highest exposure concentration.

No teratogenic, embryotoxic, fetotoxic, or female reproductive effects were observed in mice, rats, or rabbits at exposure levels up to 12 mg/m^3 DPM. Effects on sperm morphology and number were reported in hamsters and mice exposed to high doses of DPM; however, no adverse effects were observed in sperm obtained from monkeys exposed at 2 mg/m^3 for 7 h/day, 5 days/week for 104 weeks. Concentrations of 12 mg/m^3 DPM did not affect male rat reproductive fertility in the F_0 and F_1 generation breeders. Thus, exposure to DE would not appear to be a reproductive or developmental hazard.

5.2. MODE OF ACTION OF DIESEL EXHAUST-INDUCED NONCANCER EFFECTS

5.2.1. Comparison of Health Effects of Filtered and Unfiltered Diesel Exhaust

There exist a total of four chronic toxicity studies of DE, in which the experimental protocol included exposing test animals to exhaust containing no particles. Comparisons were then made between the effects caused by whole, unfiltered exhaust and those caused by the gaseous components of the exhaust. Concentrations of components of the exposure atmospheres in these four studies are given in Table 5-16.

Heinrich et al. (1982) compared the toxic effects of whole and filtered DE on hamsters and rats. Exposures were at 3.9 mg/m^3 for 7 to 8 h/day and 5 days/week. Rats exposed for 24 mo to either whole or filtered exhaust exhibited no significant changes in respiratory frequency, respiratory minute volume, compliance or resistance as measured by a whole-body plethysmography, or heart rate. In the hamsters, histological changes (adenomatous proliferations) were seen in the lungs of animals exposed to either whole or filtered exhaust; however, in all groups exposed to the whole exhaust the number of hamsters exhibiting such lesions was significantly higher than for the corresponding groups exposed to filtered exhaust or clean air. Severity of the lesions was, however, not reported.

In a second study, Heinrich et al. (1986a, see also Stöber, 1986) compared the toxic effects of whole and filtered DE on hamsters, rats, and mice. The test animals (96 per test group) were exposed to 4.24 mg DPM/m^3 for 19 h/day, 5 days/week for 120 (hamsters and mice) or 140 (rats) weeks. Body weights of hamsters were unaffected by either exposure. Body weights of rats and mice were reduced by the whole exhaust but not by the filtered exhaust. Exposure-related higher mortality rates occurred in mice after 2 years of exposure to whole exhaust. After 1 year of exposure to the whole exhaust, hamsters exhibited increased lung weights, a significant increase in airway resistance, and a nonsignificant reduction in lung compliance. For the same time period, rats exhibited increased lung weights, a significant decrease in dynamic lung compliance, and a significant increase in airway resistance. Test animals exposed to filtered exhaust did not exhibit such effects. Histopathological examination indicated that different levels of response occurred in the three species. In hamsters, filtered exhaust caused no significant histopathological effects in the lung; whole exhaust caused thickened alveolar septa, bronchioloalveolar hyperplasia, and emphysematous lesions. In mice, whole exhaust, but not filtered exhaust, caused multifocal bronchioloalveolar hyperplasia, multifocal alveolar lipoproteinosis, and multifocal interstitial fibrosis. In rats, there were no significant morphological changes in the lungs following exposure to filtered exhaust. In rats exposed to whole exhaust, there were severe inflammatory changes in the lungs, thickened alveolar septa, foci of macrophages, crystals of cholesterol, and hyperplastic and metaplastic lesions. Biochemical studies of lung lavage fluids of hamsters and mice indicated that exposure to filtered exhaust caused fewer changes than did exposure to whole exhaust. The latter produced significant increases in lactate dehydrogenase, alkaline phosphatase, glucose-6-phosphate dehydrogenase (G6PDH), total protein, protease (pH 5.1), and collagen. The filtered exhaust had a slight but nonsignificant effect on G6PDH, total protein, and collagen. Similarly, cytological studies showed that while the filtered exhaust had no effect on differential cell counts, the whole

Table 5-16. Composition of exposure atmospheres in studies comparing unfiltered and filtered diesel exhaust[a]

Species/sex	Exposure[b] period		Particles (mg/m^3)	C × t ($mg \cdot h/m^3$)	CO (ppm)	NO_2 (ppm)	SO_2 (ppm)	Effects	Study
Rat, Wistar, F; Hamster, Syrian	7 h/day 5 days/week 104 weeks	Uf F C	3.9 — —	14,196	18.5 18.0 —	1.2 1.0 —	3.1 2.8 —	No effect on pulmonary function or heart rate in rats; increases in pulmonary adenomatous proliferations in hamsters, UF significantly higher than F or C	Heinrich et al. (1982)
Rat, F344, F	8 h/day 7 days/week 104 weeks	Uf F[c] C	4.9 — —	28,538	7.0 — —	1.8 — —	13.1 — —	Body weight decrease after 6 mo in UF, 18 mo in f; lung/body rate weight rate higher in both groups at 24 mo; at 2 years, fibrosis and epithelial hyperplasia in lungs of uf; nominal lung and spleen histologic changes	Iwai et al. (1986)
Rat, F344, M, F; Hamster, Syrian, M, F	16 h/day 5 days/week 104 weeks	Uf Uf Uf F[d] C	0.7 2.2 6.6 — —	5,824 18,304 54,912	— — 32.0 32.0 1.0	— — — — —	— — — — —	Uf: elevated red and white cell counts, hematocrit and hemoglobin; increased heart/body weight and right ventricular/heart weight ratios; lower left ventricular contractility; changes in blood chemistry; obstructive and restrictive lung disease; F: no effects	Brightwell et al. (1986)
Rat, Wistar, F; Hamster, Syrian, F; Mouse NMRI, F	19 h/day 5 days/week 120 to 140 weeks	Uf F[d] C	4.24 — —	48,336 56,392	12.5 11.1 0.16	1.5 1.2 —	3.1 1.02 —	Uf: decreased body wt in rats and mice but not hamsters; increased mortality, mice only; decreased lung compliance and increased airway resistance, rats and hamsters; species differences in lung lavage enzymes and cell counts and lung histopathology and collagen content, most pronounced in rats; F: no effect on glucose-6-phosphate dehydrogenase, total protein, and lung collagen	Heinrich et al. (1986a)
Mouse, NMRI, F, C57BL/6N, F	18 h/day 5 days/week 23 mo (NMRI) 24 mo (C57BL/6N)	Uf F C	4.5 0.01 0.01	40,365	14.2 14.2 0.2	2.3 2.9 0.01	2.8 2.4 0.1	Uf: increased lung wet weight starting at 3 mo F: no noncancer effects reported	Heinrich et al. (1995)

[a]Man values.
[b]UF= unfiltered whole exhaust, F = filtered exhaust, C = control.
[c]Reported to have the same component concentrations as the unfiltered, except particles were present in undetectable amounts.
[d]Concentrations reported for high concentration level only.

exhaust resulted in an increase in leukocytes (161 ± 43.3/μL versus 55.7 ± 12.8/μL in the controls), a decrease in AMs (30.0 ± 12.5 versus 51.3 ± 12.5/μL in the controls), and an increase in granulocytes (125 ± 39.7 versus 1.23 ± 1.14/μL in the controls). All values presented for this study are the mean with its standard deviation. The differences were significant for each cell type. There was also a small increase in lymphocytes (5.81 ± 4.72 versus 3.01 ± 1.23/μL in the controls).

Iwai et al. (1986) exposed rats (24 per group) to whole or filtered DE 8 h/day, 7 days/week for 24 mo. The whole exhaust was diluted to achieve a concentration of 4.9 ± 1.6 mg/m^3 DPM. Body weights in the whole exhaust group began to decrease after 6 mo and in both exposed groups began to decrease after 18 mo when compared with controls. Lung-to-body weight ratios of the rats exposed to the whole exhaust showed a significant increase ($p<0.01$) after 12 mo in comparison with control values. Spleen-to-body weight ratios of both exposed groups were higher than control values after 24 mo. After 6 mo of exposure to whole exhaust, DPM accumulated in AMs, and Type II cell hyperplasia was observed. After 2 years of exposure, the alveolar walls had become fibrotic with mast cell infiltration and epithelial hyperplasia. In rats exposed to filtered exhaust, after 2 years there were only minimal histologic changes in the lungs, with slight hyperplasia and stratification of bronchiolar epithelium and infiltration of atypical lymphocytic cells in the spleen.

Brightwell et al. (1986) evaluated the toxic effects of whole and filtered DE on rats and hamsters. Three exhaust dilutions were tested, producing concentrations of 0.7, 2.2, and 6.6 mg/m^3 DPM. The test animals (144 rats and 312 hamsters per exposure group) were exposed for five 16-h periods per week for 2 years. The four exposure types were gasoline, gasoline catalyst, diesel, and filtered diesel. The results presented were limited to statistically significant differences between exhaust-exposed and control animals. The inference from the discussion section of the paper was that there was a minimum of toxicity in the animals exposed to filtered DE: "It is clear from the results presented that statistically significant differences between exhaust-exposed and control animals are almost exclusively limited to animals exposed to either gasoline or unfiltered diesel exhaust." Additional results are described in Section 5.1.3.3.

Heinrich et al. (1995) exposed female NMRI and C57BL/6N mice to a DE dilution that resulted in a DPM concentration of 4.5 mg/m^3 and to the same dilution after filtering to remove the particles. This study is focused on the carcinogenic effects of DPM exposure, and inadequate information was presented to compare noncancer effects in filtered versus unfiltered exhaust.

A comparison of the toxic responses in laboratory animals exposed to whole exhaust or filtered exhaust containing no particles demonstrates across studies that when the exhaust is sufficiently diluted to limit the concentrations of gaseous irritants (NO_2 and SO_2), irritant vapors (aldehydes), CO, or other systemic toxicants, the diesel particles are the prime etiologic agents

of noncancer health effects, although additivity or synergism with the gases cannot be ruled out. These toxic responses are both functional and pathological and represent cascading sequelae of lung pathology based on concentration and species. The diesel particles plus gas exposures produced biochemical and cytological changes in the lung that are much more prominent than those evoked by the gas phase alone. Such marked differences between whole and filtered DE are also evident from general toxicological indices, such as decreases in body weight and increases in lung weights, pulmonary function measurements, and pulmonary histopathology (e.g., proliferative changes in Type II cells and respiratory bronchiolar epithelium, fibrosis). Hamsters, under equivalent exposure regimens, have lower levels of retained DPM in their lungs than rats and mice do and, consequently, less pulmonary function impairment and pulmonary pathology. These differences may result from lower DPM inspiration and deposition during exposure, greater DPM clearance, or lung tissue less susceptible to the cytotoxicity of deposited DPM.

5.2.2. Mode of Action for the Noncarcinogenic Effects of DPM

As noted in Chapter 2, diesel emissions are a complex mixture that includes both a vapor phase and a particle phase. The particle phase consists of poorly soluble carbon particles on the surfaces of which are adsorbed a large number of organic and inorganic compounds. Although the effects to be discussed are considered attributable to the particle phase (termed diesel particulate matter or DPM), additive or synergistic effects due to the vapor phase cannot be totally discounted. This may be especially so in the human studies and the animal toxicology studies where exposure is to various dilutions of diesel emissions, or in the in vitro studies in which the test material was captured by filtration.

The mechanisms by which DPM is inhaled, deposited, and cleared from the respiratory tract are discussed in Chapter 3. DPM deposited upon airway surfaces may be cleared from the respiratory tract completely, or may be translocated to other sites within the respiratory system. In rats, the pathogenic sequence following the deposition of inhaled DPM begins with the interaction of DPM with airway epithelial cells and phagocytosis by AMs. The airway epithelial cells and activated AMs release chemotactic factors that attract neutrophils and additional AMs. As the lung burden of DPM increases, there is an aggregation of particle-laden AMs in alveoli adjacent to terminal bronchioles, increases in the number of Type II cells lining particle-laden alveoli, and the presence of particles within alveolar and peribronchial interstitial tissues and associated lymph nodes.

The macrophages engulfing the DPM may release cytokines, growth factors, and proteases, which may cause inflammation, cell injury, cell proliferation, hyperplasia, and fibrosis. This is especially true under lung overload conditions occurring in laboratory rats when the rate of deposition exceeds the rate of alveolar clearance. This phenomenon is described in

Chapter 3. The mechanisms leading to the generation of oxygen radicals and subsequent lung injury are described in Chapter 7, Section 7.4.3.

DPM is a poorly soluble particle whose rate of clearance by dissolution is likely insignificant compared to its rate of clearance as an intact particle. The organic material adsorbed to the surface is desorbed from the DPM and may enter into metabolic reactions and be activated and enter into reactions with other macromolecules or be detoxified and excreted (Figure 7-1). The diesel particle may be cleared directly by the clearance mechanisms described in Chapter 3.

The organic material desorbed from the particle (described in Chapter 7, Section 7.4.7) appears to be associated with the immunological changes described above. The potential adjuvant effects of DPM have also been studied. The results indicate that the nonextractable particle core and the organic matter adsorbed to the core both contribute to the adjuvant activity of DPM. Further, it is possible that any of the plethora of compounds present in the organic fraction of DPM, including various PAH, may elicit this response.

Thus, the available evidence indicates that DPM has the potential to produce pathological and immunological changes in the respiratory tract. Moreover, the magnitude of these responses is determined by the dose delivered to the respiratory tract and is attributable to both the carbon core and the adsorbed organic materials.

5.3. INTERACTIVE EFFECTS OF DIESEL EXHAUST

A multitude of factors may influence the susceptibility to exposure to DE as well as the resulting response. Some of these have already been discussed in detail (e.g., the composition of DE and concentration-response data); others will be addressed in this section (e.g., the interaction of DE with factors particular to the exposed individual and the interaction of DE components with other airborne contaminants).

In a study discussed already in this chapter, Mauderly et al. (1990a) compared the susceptibility of normal rats and rats with preexisting laboratory-induced pulmonary emphysema exposed for 7 h/day, 5 days/week for 24 mo to DE containing 3.5 mg/m^3 DPM or to clean air (controls). Emphysema was induced in one-half of the rats by intratracheal instillation of elastase 6 weeks before exhaust exposure. Measurements included lung burdens of DPM, respiratory function, bronchoalveolar lavage, clearance of radiolabeled particles, pulmonary immune responses, lung collagen, excised lung weight and volume, histopathology, and mean linear intercept of terminal air spaces. None of the data for the 63 parameters measured suggest that rats with emphysematous lungs were more susceptible than rats with normal lungs to the effects of DE exposure. In fact, each of the 14 emphysema-exhaust interactions detected by statistical analysis of variance indicated that emphysema acted to reduce the effects of DE exposure. DPM accumulated much less rapidly in the lungs of emphysematous rats than in those

of normal rats. The mean lung burdens of DPM in the emphysematous rats were 39%, 36%, and 37% of the lung burdens of normal rats at 12, 18, and 24 mo, respectively. No significant interactions were observed among lung morphometric parameters. Emphysema prevented the exhaust-induced increase for three respiratory indices of expiratory flow rate at low lung volumes, reduced the exhaust-induced increase in nine lavage fluid indicators of lung damage, prevented the expression of an exhaust-induced increase in lung collagen, and reduced the exhaust-induced delay in DPM clearance.

Mauderly et al. (1987b) evaluated the relative susceptibility of developing and adult rat lungs to damage by exposure to DE. Rats (48 per test group) were exposed to DE containing 3.5 mg/m^3 DPM and about 0.8 ppm NO_2. Exposures were for 7 h/day, 5 days/week through gestation to the age of 6 mo, or from the age of 6 to 12 mo. Comparative studies were conducted on respiratory function, immune response, lung clearance, airway fluid enzymes, protein and cytology, lung tissue collagen, and proteinases in both age groups. After the 6-mo exposure, adult rats, compared with controls, exhibited (1) more focal aggregates of particle-containing AMs in the alveolar ducts near the terminal bronchioles, (2) a sixfold increase in the neutrophils (as a percentage of total leukocytes) in the airway fluids, (3) a significantly higher number of total lymphoid cells in the pulmonary lymph nodes, (4) delayed clearance of DPM and radiolabeled particles ($t_{1/2}$ = 90 days versus 47 days for controls), and (5) increased lung weights. These effects were not seen in the developing rats. On a weight-for-weight (milligrams of DPM per gram of lung) basis, DPM accumulation in the lungs was similar in developing and adult rats immediately after the exposure. During the 6-mo postexposure period, DPM clearance was much more rapid in the developing rats, approximately 2.5-fold. During postexposure, diesel particle-laden macrophages became aggregated in the developing rats, but these aggregations were located primarily in a subpleural position. The authors concluded that exposure to DE, using pulmonary function, structural (qualitative or quantitative) biochemistry as the indices, did not affect the developing rat lung more severely than the adult rat lung.

As a result of the increasing trend of using diesel-powered equipment in coal mining operations and the concern for adverse health effects in coal miners exposed to both coal dust or coal mine dust and DE, Lewis et al. (1989) and Karagianes et al. (1981) investigated the interaction of coal dust and DE. Lewis et al. (1989) exposed rats, mice, and cynomolgus monkeys to (1) filtered ambient air, (2) 2 mg/m^3 DPM, (3) 2 mg/m^3 respirable coal dust, and (4) 1 mg/m^3 of both DPM and respirable coal dust. Gaseous and vapor concentrations were identical in both DE exposures. Exposures were for 7 h/day, 5 days/week for up to 24 mo. Synergistic effects between DE and coal dust were not demonstrated; additive toxic effects were the predominant effects noted.

Karagianes et al. (1981) exposed rats (24 per group) to DE containing 8.3 mg/m^3 of DPM alone or in combination with about 6 mg/m^3 of coal dust. No synergistic effects were found

between DE and coal dust; additive effects in terms of visual dust burdens in necropsied lungs were related to dose (i.e., length of exposure and airborne particulate concentrations).

The health effects of airborne contaminants from sources other than diesel engines may be altered in the presence of DPM by their adsorption onto the diesel particles. When adsorbed onto diesel particles, the gases and vapors can be transported and deposited deeper into the lungs, and because they are more concentrated on the particle surface, the resultant cytotoxic effects or physiological responses may be enhanced. Nitrogen dioxide adsorbed onto carbon particles caused pulmonary parenchymal lesions in mice, whereas NO_2 alone produced edema and inflammation but no lesions (Boren, 1964). Exposure to formaldehyde and acrolein adsorbed onto carbon particles (1 to 4 μm) resulted in the recruitment of PMNs to tracheal and intrapulmonary epithelial tissues but not when the aldehydes were tested alone (Kilburn and McKenzie, 1978).

Madden et al. (2000) observed that O_3 exposure increased the bioactivity of DPM. DPM, preexposed to O_3 for 48 h or nonozone-exposed DPM (1 to 500 μg), was instilled into the lungs of laboratory rats. Lung inflammation and injury were examined 24 h after instillation by lung lavage. DPM pre-exposed to 0.1 PPM O_3 was more potent in increasing neutrophilia, lavage total protein, and LDH compared to unexposed DPM. Treatment of DPM with higher concentrations of O_3 (1.0 PPM) decreased the bioactivity of the particles.

There is no direct evidence that DE, at concentrations found in the ambient environment, interacts with other substances in the exposure environment or the physiological status of the exposed subject other than impaired resistance to respiratory tract infections. Although there is experimental evidence that gases and vapors can be adsorbed onto carbonaceous particles, enhancing the toxicity of these particles when deposited in the lung, there is no evidence for an increased health risk from such interactions with DPM under urban atmospheric conditions. Likewise, there is no experimental evidence in laboratory animals that the youth or preexisting emphysema of an exposed individual enhances the risk of exposure to DE.

5.4. COMPARATIVE RESPONSIVENESS AMONG SPECIES TO THE HISTOPATHOLOGIC EFFECTS OF DIESEL EXHAUST

There is some evidence indicating that species may differ in pulmonary responses to DE. Mauderly (1994) compared the pulmonary histopathology of rats and mice after 18 mo of exposure to DE. There was less aggregation of macrophages in mice. Diffuse septal thickening was noted in the mice, but there were few inflammatory cells, no focal fibrosis, little epithelial hyperplasia, and no epithelial metaplasia, as was observed in rats. Heinrich et al. (1986a) reported that wet lung weight of hamsters increased only 1.8-fold following chronic exposure to DE, compared with an increase of 3.4-fold in rats. Smaller increases in neutrophils, lactic acid dehydrogenase, collagen, and protein supported the conclusion of a lesser inflammatory response

in Syrian hamsters. The histopathologic changes in the lungs of Chinese hamsters after 6 mo exposure to DE, on the other hand, was similar to that of rats (Pepelko and Peirano, 1983). Guinea pigs respond to chronic DE exposure with a well-defined epithelial proliferation, but it is based on an eosinophilic response in contrast to the neutrophil-based responses in other species. Epithelial hyperplasia and metaplasia were quite striking in the terminal and respiratory bronchioles of cats exposed for 27 mo to DE (Plopper et al., 1983). This study is of particular interest because the terminal airways of cats are more similar to those of humans than rodent species are. It should be noted, however, that exposure concentrations were very high (12 mg/m^3) for most of the period. Lewis et al. (1989) exposed rats and cynomolgus monkeys 8 h per day, 5 days per week for 2 years to DE at a particle concentration of 2 mg/m^3. Unfortunately, this exposure rate was sufficiently low that few effects were noted in either species other than focal accumulations of particles, primarily in the alveolar macrophages, interstitium, and lymphoid tissue. It is apparent that species do vary in their pulmonary responses to DE exposure, despite the difficulty in making direct comparisons because of differences in exposure regimes, lifespans, and pulmonary anatomy. Most species do respond, however, suggesting that humans are likely to be susceptible to induction of pulmonary pathology during chronic exposure to DE at some level.

5.5. DOSE-RATE AND PARTICULATE CAUSATIVE ISSUES

The purpose of animal toxicological experimentation is to elucidate mechanisms of action and identify the hazards and dose-response effects posed by a chemical substance or complex mixture and to extrapolate these effects to humans for subsequent health assessments. The cardinal principle in such a process is that the intensity and character of the toxic action are a function of the dose of the toxic agent(s) that reaches the critical site of action. The considerable body of evidence reviewed clearly denotes that major noncancerous health hazards may be presented to the lung following the inhalation of DE. Based on pulmonary function and histopathological and histochemical effects, a determination can be made concerning which dose/exposure rates of DE (expressed in terms of the DPM concentration) result in injury to the lung and which appear to elicit no effect. The inhalation of poorly soluble particles, such as those found in DE, increases the pulmonary particulate burden. When the dosing rate exceeds the ability of the pulmonary defense mechanisms to achieve a steady-state lung burden of particles, there is a slowing of clearance and the progressive retention of particles in the lung that can ultimately approach a complete cessation of lung clearance (Morrow, 1988). This phenomenon, which is reviewed in Chapter 3, has practical significance both for the interpretation of experimental inhalation data and for the prevention of disease in humans exposed to airborne particles.

The data for exposure intensities that cause adverse pulmonary effects demonstrate that they are less than the exposure intensities reported to be necessary to induce lung tumors. Using the most widely studied laboratory animal species and the one reported to be the most sensitive to tumor induction, the laboratory rat, the no-adverse-effect exposure intensity for adverse pulmonary effects was 56 $mg \cdot h \cdot m^{-3}$/week (Brightwell et al., 1986). The lowest-observed-effect level for adverse pulmonary effects (noncancer) in rats was 70 $mg \cdot h \cdot m^{-3}$/week (Lewis et al., 1989), and for pulmonary tumors, 122.5 $mg \cdot h \cdot m^{-3}$/week (Mauderly et al., 1987a). The results clearly show that noncancerous pulmonary effects are produced at lower exposure intensities than are pulmonary tumors. Such data support the position that inflammatory and proliferative changes in the lung may play a key role in the etiology of pulmonary tumors in exposed rats (Mauderly et al., 1990b).

The effects of DE on the developing lung and on a model of a preexisting disease state have been studied in rats (Mauderly et al., 1990a, 1987b). Mauderly et al. (1987b) showed that diesel did not affect the developing lung more severely than the adult rat lung, and in fact, that clearance was faster in the younger lung. Mauderly et al. (1990a) compared the pulmonary response to inhalation of DE in rats with elastase-induced emphysema with normal rats. They found that respiratory tract effects were not more severe in emphysematous rats and that the lung burden of particles was less in the compromised rat. These studies provide limited evidence that some factors that are often considered to result in a wider distribution of sensitivity among members of the population may not have this effect with diesel exposure. However, these studies have no counterpart in human studies and extrapolation to humans remains uncertain.

There is also the issue of whether the noncancerous health effects related to exposure to DE are caused by the carbonaceous core of the particle or substances adsorbed onto the core, or both.

Current understanding, derived primarily from studies in rats, suggests that much of the toxicity resulting from the inhalation of DE relates to the carbonaceous core of the particles. Several studies on inhaled aerosols demonstrate that lung reactions characterized by an appearance of particle-laden AMs and their infiltration into the alveolar ducts, adjoining alveoli, and tracheobronchial lymph nodes; hyperplasia of Type II cells; and the impairment of pulmonary clearance mechanisms are not limited to exposure to diesel particles. Such responses have also been observed in rats following the inhalation of coal dust (Lewis et al., 1989; Karagianes et al., 1981), titanium dioxide (Heinrich et al., 1995; Lee et al., 1985), CB (Nikula et al., 1995; Heinrich et al., 1995), titanium tetrachloride hydrolysis products (Lee et al., 1986), quartz (Klosterkötter and Bünemann, 1961), volcanic ash (Wehner et al., 1986), amosite (Bolton et al., 1983), and manmade mineral fibers (Lee et al., 1988) among others. In more recent studies, animals have been exposed to CB that is similar to the carbon core of the DE particle. Nikula et al. (1995) exposed rats for 24 mo to CB or DE at target exposure concentrations of 2.5

and 6 mg/m^3 (exposure rates of 200 or 520 mg·h·m^{-3}/week). Both concentrations induced AM accumulation, epithelial proliferation, inflammation, and fibrosis. They observed essentially no difference in potency of nonneoplastic or in tumor responses based on a regression analysis.

Dungworth et al. (1994) reported moderate to severe inflammation characterized by multifocal bronchoalveolar hyperplasia, alveolar histiocytosis, and focal segmental fibrosis in rats exposed to CB for up to 20 mo at exposure rates of 510 to 540 mg·h·m^{-3}/week. The observed lung pathology reflects notable dose-response relationships and usually evolves in a similar manner. With increasing dose, there is an increased accumulation and aggregation of particle-laden AMs, Type II cell hyperplasia, a foamy (degenerative) macrophage response, alveolar proteinosis, alveolar bronchiolization, cholesterol granulomas, and often squamous cell carcinomas and bronchioalveolar adenomas derived from metaplastic squamous cells in the areas of alveolar bronchiolization.

Heinrich et al. (1995) compared effects of diesel exposure in rats and mice with exposure to titanium dioxide or carbon black. Exposures to TiO_2 and carbon black were adjusted during the exposure to result in a similar lung burden for the three types of particles. At similar lung burdens in the rat, DPM, TiO_2, and CB had nearly identical effects on lung weights and on the incidence of lesions, both noncancer and cancer. Also, a similar effect on clearance of a labeled test aerosol was measured for the different particles. A comparison of the effect of DPM, TiO_2, and carbon black exposures in mice also showed a similar effect on lung weight, but noncancer effects were not reported and no significant increase in tumors was observed.

Murphy et al. (1998) compared the toxicological effects of DPM with three other particles chosen for their differing morphology and surface chemistry. One mg each of well-characterized crystalline quartz, amorphous silica, CB, and DPM was administered to laboratory rats by a single intratracheal instillation. The laboratory rats were sacrificed at 48 h, and 1, 6, and 12 weeks after instillation. Crystalline quartz produced significant increases in lung permeability, persistent surface inflammation, progressive increases in pulmonary surfactant and activities of epithelial marker enzymes up to 12 wk after primary exposure. Amorphous silica did not cause progressive effects but did produce initial epithelial damage with permeability changes that regressed with time after exposure. By contrast, CB had little if any effect on lung permeability, epithelial markers, or inflammation. Similarly, DPM produced only minimal changes, although the individual particles were smaller and differed in surface chemistry from CB. The authors concluded that DPM is less damaging to the respiratory epithelium than is silicon dioxide, and that the surface chemistry of the particle is more important than ultrafine size in explaining biological activity.

These experiments provide strong support for the idea that DE toxicity results from a mechanism that is analogous to that of other relatively inert particles in the lung. This

qualitative similarity exists along with some apparent quantitative differences in the potency of various particles for producing effects on the lung or on particle clearance.

The exact relationship between toxicity and particle size within the ultrafine particle mode, including DPM (BéruBé et al., 1999), remains unresolved. Studies reviewed in the PM CD (U.S. EPA, 1996) suggest a greater inherent potential toxicity of inhaled ultrafine particles. Exposure to ultrafine particles may increase the release of proinflammatory mediators that could be involved in lung disease. For example, Driscoll and Maurer (1991) compared the effects of fine (0.3 μm) and ultrafine (0.02 μm) TiO_2 particles instilled into the lungs of laboratory rats. Although both size modes caused an increase in the numbers of AMs and PMNs in the lungs, and release of TNF and fibronectin by AMs, the responses were greater and more persistent with the ultrafine particles. While fine particle exposure resulted in a minimally increased prominence of particle-laden macrophages associated with alveolar ducts, ultrafine particle exposure produced a somewhat greater prominence of macrophages, some necrosis of macrophages, and slight interstitial inflammation of the alveolar duct region. Moreover, collagen increased only with exposure to ultrafine particles.

Oberdörster et al. (1992) compared the effects of fine (0.25 μm) and ultrafine (0.02 μm) TiO_2 particles instilled into the lungs of laboratory rats on various indicators of inflammation. Instillation of ultrafine particles increased the number of total cells recovered by lavage, decreased the percentage of AMs, and increased the percentage of PMNs and protein. Instillation with fine particles did not cause statistically significant effects. Thus, the ultrafine particles had greater pulmonary inflammatory potency than did larger sizes of this material. The investigators attributed the enhanced toxicity to greater interaction of the ultrafine particles with their large surface area, with alveolar and interstitial macrophages, which resulted in enhanced release of inflammatory mediators. They suggested that ultrafine particles of low in vitro solubility appear to enter the interstitium more readily than do larger sizes of the same material, which accounted for the increased contact with macrophages in this compartment of the lung. Driscoll and Maurer (1991) noted that the pulmonary retention of ultrafine TiO_2 particles instilled into rat lungs was greater than for the same mass of fine-mode TiO_2 particles. Thus, the available evidence tends to suggest a potentially greater toxicity for inhaled ultrafine particles.

Particle size, volume, surface area, and composition may be the critical elements in the overload phenomenon following exposure to particles, which could explain those quantitative differences. The overloaded AMs secrete a variety of cytokines, oxidants, and proteolytic enzymes that are responsible for inducing particle aggregation and damaging adjacent epithelial tissue (Oberdörster, 1994). For a more detailed discussion of mechanism, see Chapter 3.

On the basis of currently available laboratory animal data, the principal noncancerous health hazard to humans posed by exposure to DE is a structural or functional injury to the lung. Such effects are demonstrable at dose rates or cumulative doses of DPM lower than those

reported to be necessary to induce lung tumors in rats. An emerging human health issue concerning short-term exposure to ambient DE/DPM is the potential for allergenic responses in several studies. Heightened allergenic responses including increased cytokine production as well as increased numbers of inflammatory cells have been detected in nasal lavage from humans exposed to inhaled or instilled DE/DPM. In individuals already allergic to ragweed, exposure to DE/DPM with the allergen was observed to result in an enhanced allergenic response, particularly IgE production. Current knowledge indicates that the carbonaceous core of diesel particles is the major causative factor in the injury to the lung and that other factors such as the cytotoxicity of adsorbed substances on the particles also may play a role. The lung injury appears to be mediated through effects on pulmonary AMs. Because noncancerous pulmonary effects occur at lower doses than tumor induction does in the rat, and because these effects may be cofactors in the etiology of DE-induced tumors, noncancerous pulmonary effects must be considered in the total evaluation of DE, notably the particulate component.

5.6. SUMMARY AND DISCUSSION

5.6.1. Effects of Diesel Exhaust on Humans

The most readily identified acute noncancer health effect of DE on humans is its ability to elicit subjective complaints of eye, throat, and bronchial irritation and neurophysiological symptoms such as headache, lightheadedness, nausea, vomiting, and numbness and tingling of the extremities. Studies of the perception and offensiveness of the odor of DE and a human volunteer study in an exposure chamber have demonstrated that the time of onset of the human subjective symptoms is inversely related to increasing concentrations of DE and the severity is directly related to increasing concentrations of DE. In one study in which a diesel engine was operated under varying load conditions, a dilution factor of 140 to 475 was needed to reduce the exhaust level to an odor-detection threshold level.

A public health issue is whether short-term exposure to DE might result in an acute decrement in ventilatory function and whether the frequent repetition of such acute respiratory effects could result in chronic lung function impairment. One convenient means of studying acute decrements in ventilatory function is to monitor differences in pulmonary function in occupationally exposed workers at the beginning and end of a workshift. In studies of underground miners, bus garage workers, dockworkers, and locomotive repairmen, increases in respiratory symptoms (cough, phlegm, and dyspnea) and decreases in lung function (FVC, FEV_1, PEFR, and FEF_{25-75}) over the course of a workshift were generally found to be minimal and not statistically significant. In a study of acute respiratory responses in diesel bus garage workers, there was an increased reporting of cough, labored breathing, chest tightness, and wheezing, but no reductions in pulmonary function were associated with exposure to DE. Pulmonary function was affected in stevedores over a workshift exposure to DE but normalized

after a few days without exposure to DE fumes. In a third study, there was a trend toward greater ventilatory function changes during a workshift among coal miners, but the decrements were similar in miners exposed and not exposed to DE.

Smokers appeared to demonstrate larger workshift respiratory function decrements and increased incidence of respiratory symptoms. Acute sensory and respiratory symptoms were earlier and more sensitive indicators of potential health risks from diesel exposure than were decrements in pulmonary function. Studies on the acute health effects of exposure to DE in humans, experimental and epidemiologic, have failed to demonstrate a consistent pattern of adverse effects on respiratory morbidity; the majority of studies offer, at best, equivocal evidence for an exposure-response relationship. The environmental contaminants have frequently been below permissible workplace exposure limits; in those few cases where health effects have been reported, the authors have failed to identify conclusively the individual or collective causative agents in the DE.

Chronic effects of DE exposure have been evaluated in epidemiologic studies of occupationally exposed workers (metal and nonmetal miners, railroad yard workers, stevedores, and bus garage mechanics). Most of the epidemiologic data indicate an absence of an excess risk of chronic respiratory disease associated with exposure to DE. In a few studies, a higher prevalence of respiratory symptoms, primarily cough, phlegm, or chronic bronchitis, was observed among the exposed. These increased symptoms, however, were usually not accompanied by significant changes in pulmonary function. Reductions in FEV_1 and FVC and, to a lesser extent, FEF_{50} and FEF_{75}, also have been reported. Two studies detected statistically significant decrements in baseline pulmonary function consistent with obstructive airway disease. One study of stevedores had a limited sample size of 17 exposed and 11 controls. The second study in coal miners showed that both underground and surface workers at diesel-use mines had somewhat lower pulmonary performance than their matched controls. The proportion of workers in or at diesel-use mines, however, showed equivalent evidence of obstructive airway disease, and for this reason the authors of the second paper felt that factors other than diesel exposure might have been responsible. A doubling of the prevalence of minor restrictive airway disease was also observed in workers in or at diesel-use mines. These two studies, coupled with other reported nonsignificant trends in respiratory flow-volume measurements, suggest that exposure to DE may impair pulmonary function among occupational populations.
Epidemiologic studies of the effects of DE on organ systems other than the pulmonary system are scant. Whereas a preliminary study of the association of cardiovascular mortality and exposure to DE found a fourfold higher risk ratio, a more comprehensive epidemiologic study by the same investigators found no significant difference between the observed and expected number of deaths caused by cardiovascular disease.

Caution is warranted in the interpretation of results from the epidemiologic studies that have addressed noncarcinogenic health effects from exposure to DE. These investigations suffer from myriad methodological problems, including (1) incomplete information on the extent of exposure to DE, necessitating in some studies estimations of exposures from job titles and resultant misclassification; (2) the presence of confounding variables such as smoking or occupational exposures to other toxic substances (e.g., mine dusts); and (3) the short duration and low intensity of exposures. These limitations restrict drawing definitive conclusions as to the cause of any noncarcinogenic DE effect, observed or reported.

It is also apparent that at some level of exposure DE as measured by DPM appears to have the potential to induce airway inflammation in humans without disease. Also, in one other study peripheral blood changes were noted. An emerging area of concern is the immunological changes that have been documented in response to DE exposure and the potential relationship of these changes to the explosive growth of asthma in human populations.

5.6.2. Effects of Diesel Exhaust on Laboratory Animals

Laboratory animal studies of the toxic effects of DE have involved acute, subchronic, and chronic exposure regimens. In acute exposure studies, toxic effects appear to have been associated primarily with high concentrations of carbon monoxide, nitrogen dioxide, and aliphatic aldehydes. In short- and long-term studies, toxic effects have been associated with exposure to the complex exhaust mixture. Effects of DE in various animal species are summarized in Tables 5-2 to 5-15. In short-term studies, health effects related to function, when found, are mild and result from extremely high DPM concentrations of about 6 mg/m^3 and extensive durations of exposure approximating 20 h/day. There is ample evidence, however, that other pathophysiological effects such as accumulation of DPM in pulmonary tissues, evidence of inflammatory response, AM aggregation and accumulation near the terminal bronchioles, Type II cell proliferation, and the thickening of alveolar walls adjacent to AM aggregation do occur under short-term exposures at lower levels of DE. Little evidence exists, however, from short-term studies that exposure to DE impairs lung function. Chronic exposures cause lung pathology that results in altered pulmonary function and increased DPM retention in the lung. Exposures to DE have also been associated with increased susceptibility to respiratory tract infection, neurological or behavioral changes, an increase in banded neutrophils, and morphological alterations in the liver.

5.6.2.1. *Effects on Survival and Growth*

The data presented in Table 5-3 show limited effects on survival in mice and rats and some evidence of reduced body weight in rats following chronic exposures to concentrations of 1.5 mg/m^3 DPM or higher and exposure durations of 16 to 20 h/day, 5 days/week for 104 to

130 weeks. Increased lung weights and lung to body-weight ratios in rats, mice, and hamsters; an increased heart to body weight ratio in rats; and decreased lung and kidney weights in cats have been reported following chronic exposure to DE. No evidence was found of an effect of DE on other body organs (Table 5-4). The lowest-observed-effect level in rats approximated 1 to 2 mg/m^3 DPM for 7 h/day, 5 days/week for 104 weeks.

5.6.2.2. *Effects on Pulmonary Function*

Pulmonary function impairment has been reported in rats, hamsters, cats, and monkeys exposed to DE and included lung mechanical properties (compliance and resistance), diffusing capacity, lung volumes, and ventilatory performance (Table 5-5). The effects generally appeared only after prolonged exposures. The lowest exposure levels (expressed in terms of DPM concentrations) that resulted in impairment of pulmonary function occurred at 2 mg/m^3 in cynomolgus monkeys (the only level tested), 1.5 and 3.5 mg/m^3 in rats, 4.24 and 6 mg/m^3 in hamsters, and 11.7 mg/m^3 in cats. Exposures in monkeys, cats, and rats (3.5 mg/m^3) were for 7 to 8 h/day, 5 days/week for 104 to 130 weeks. While this duration is considered to constitute a lifetime study in rodents, it is a small part of the lifetime of a monkey or cat. Exposures in hamsters and rats (1.5 mg/m^3) varied in hours per day (8 to 20) and weeks of exposure (26 to 130). In all species but the monkey, the testing results were consistent with restrictive lung disease; alteration in expiratory flow rates indicated that 1.5 mg/m^3 DPM was a LOAEL for a chronic exposure (Gross, 1981). Monkeys demonstrated evidence of obstructive airway disease. The nature of the pulmonary impairment is dependent on the dose of toxicants delivered to and retained in the lung, the site of deposition and effective clearance or repair, and the anatomy and physiology of the affected species; these variables appear to be factors in the disparity of the airway disease in monkey versus the other species tested.

5.6.2.3. *Histopathological and Histochemical Effects*

Histological studies have demonstrated that chronic exposure to DE can result in effects on respiratory tract tissue (Table 5-6). Typical findings include alveolar histiocytosis, AM aggregation, tissue inflammation, increase in PMNs, hyperplasia of bronchiolar and alveolar Type II cells, thickened alveolar septa, edema, fibrosis, and emphysema. Lesions in the trachea and bronchi were observed in some studies. Associated with these histopathological findings were various histochemical changes in the lung, including increases in lung DNA, total protein, alkaline and acid phosphatase, glucose-6-phosphate dehydrogenase; increased synthesis of collagen; and release of inflammatory mediators such as leukotriene LTB and prostaglandin $PGF_{2\alpha}$. Although the overall laboratory evidence is that prolonged exposure to DPM results in histopathological and histochemical changes in the lungs of exposed animals, some studies have also demonstrated that there may be a threshold of exposure to DPM below which pathologic

changes do not occur. These no-observed-adverse-effect levels for histopathological effects were reported to be 2 mg/m^3 for cynomolgus monkeys (the only concentration tested), 0.11 to 0.35 mg/m^3 for rats, and 0.25 mg/m^3 DPM for guinea pigs exposed for 7 to 20 h/day, 5 to 5.5 days/week for 104 to 130 weeks.

5.6.2.4. *Effects on Airway Clearance*

The pathological effects of DPM appear to be strongly dependent on the relative rates of pulmonary deposition and clearance (Table 5-7). Clearance of particles from the alveolar region of the lungs is a multiphasic process involving phagocytosis by AMs. Chronic exposure to DPM concentrations of about 1 mg/m^3 or above, under varying exposure durations, causes pulmonary clearance to be reduced, with concomitant focal aggregations of particle-laden AMs, particularly in the peribronchiolar and alveolar regions, as well as in the hilar and mediastinal lymph nodes. The exposure concentration at which focal aggregates of particle-laden AMs occur may vary from species to species, depending on rate of uptake and pulmonary deposition, pulmonary clearance rates, the relative size of the AM population per unit of lung tissue, the rate of recruitment of AMs and leukocytes, and the relative efficiencies for removal of particles by the mucociliary and lymphatic transport system. The principal means by which PM clearance is reduced is through a decrease in the function of pulmonary AMs. Impairment of particle clearance seems to be nonspecific and applies primarily to dusts that are persistently retained in the lungs. Lung dust levels of approximately 0.1 to 1 mg/g lung tissue appear to produce this effect in the Fischer 344 rat (Health Effects Institute, 1995). Morrow (1988) suggested that the inability of particle-laden AMs to translocate to the mucociliary escalator is correlated to an average composite particle volume per AM in the lung. When this particle volume exceeds approximately 60 μm^3 per AM in the Fischer 344 rat, impairment of clearance appears to be initiated. When the particulate volume exceeds approximately 600 μm^3 per cell, evidence suggests that AM-mediated particulate clearance virtually ceases, agglomerated particle-laden macrophages remain in the alveolar region, and increasingly nonphagocytized dust particles translocate to the pulmonary interstitium. Data for other laboratory animal species and humans are, unfortunately, limited.

5.6.2.5. *Neurological and Behavioral Effects*

Behavioral effects have been observed in rats exposed to DE from birth to 28 days of age (Table 5-14). Exposure caused a decreased level of spontaneous locomotor activity and a detrimental effect on learning in adulthood. In agreement with the behavioral changes was physiological evidence for delayed neuronal maturation. Exposures were to 6 mg/m^3 DPM for 8 h/day, 7 days/week from birth to about 7, 14, 21, or 28 days of age.

5.6.2.6. *Effects on Immunity and Allergenicity*

Several laboratory animal studies have indicated that exposure to DPM can reduce an animal's resistance to respiratory infection. This effect, which can occur even after only 2 or 6 h of exposure to DE containing 5 to 8 mg/m^3 DPM, does not appear to be caused by direct impairment of the lymphoid or splenic immune systems; however, in one study of influenza virus infection, interferon levels and hemaglutinin antibody levels were adversely affected in the exposed mice.

As with humans, there are animal data suggesting that DPM is a possible factor in the increasing incidence of allergic hypersensitivity. The effects have been demonstrated primarily in acute human and laboratory animal studies and appear to be associated with both the nonextractable carbon core and the organic fraction of DPM. It also appears that synergies with DPM may increase the potency of known airborne allergens. Both animal and human cell culture studies indicate that DPM also has the potential to act as an adjuvant.

5.6.2.7. *Other Noncancer Effects*

Essentially no effects (based on the weight of evidence of a number of studies) were noted for reproductive and teratogenic effects in mice, rats, rabbits, and monkeys; clinical chemistry and hematology in the rat, cat, hamster, and monkeys; and enzyme induction in the rat and mouse (Tables 5-11 through 5-13 and 5-15).

5.6.3. Comparison of Filtered and Unfiltered Diesel Exhaust

The comparison of the toxic responses in laboratory animals exposed to whole DE or filtered exhaust containing no particles demonstrates across laboratories that diesel particles are the principal etiologic agent of noncancerous health effects in laboratory animals exposed to DE (Table 5-16). Whether the particles act additively or synergistically with the gases cannot be determined from the designs of the studies. Under equivalent exposure regimens, hamsters have lower levels of retained DPM in their lungs than rats and mice do and consequently less pulmonary function impairment and pulmonary pathology. These differences may result from a lower intake rate of DPM, lower deposition rate and/or more rapid clearance rate, or lung tissue that is less susceptible to the cytotoxicity of DPM. Observations of a decreased respiration in hamsters when exposed by inhalation favor lower intake and deposition rates.

5.6.4. Interactive Effects of Diesel Exhaust

There is no direct evidence that DE interacts with other substances in an exposure environment, other than an impaired resistance to respiratory tract infections. Young animals were not more susceptible. In several ways, animals with laboratory-induced emphysema were more resistant. There is experimental evidence that both inorganic and organic compounds can

be adsorbed onto carbonaceous particles. When such substances become affiliated with particles, these substances can be carried deeper into the lungs where they might have a more direct and potent effect on epithelial cells or on AM ingesting the particles. Few specific studies to test interactive effects of DE with atmospheric contaminants, other than coal dust, have been conducted. Coal dust and DPM had an additive effect only.

5.6.5. Conclusions

Conclusions concerning the principal human hazard from exposure to DE are as follows:

- Allergenic inflammatory disorders of the airways to responses typical of asthma have been demonstrated under short-term exposure scenarios to either DE or DPM. The evidence indicates that the immunological changes appear to be due to the DPM component of DE and that the immunological changes are caused by both the nonextractable carbon core and the adsorbed organic fraction of the diesel particle. The toxicological significance of these effects has yet to be resolved.
- Some occupational studies of acute exposure to DE during work shifts suggest that increased acute sensory and respiratory symptoms (cough, phlegm, chest tightness, wheezing) are more sensitive indicators of possible health risks from exposure to DE than pulmonary function decrements (which were consistently found not to be significantly associated with DE exposure)
- Noncancer effects in humans from long-term chronic exposure to DPM are not evident. Noncancer effects from long-term exposure to DPM of several laboratory animal species, conducted to assess the pathophysiologic effects of DPM in humans showed pulmonary histopathology (principally fibrosis) and chronic inflammation.

Although the mode of action of DE is not clearly evident for any of the effects documented in this chapter, the respiratory tract effects observed under acute scenarios are suggestive of an irritant mechanism, while lung effects observed in chronic scenarios indicate an underlying inflammatory response. Current knowledge indicates that the carbonaceous core of the diesel particle is the causative agent of the lung effects, with the extent of the injury being mediated at least in part by a progressive impairment of AMs. It is noted that lung effects occur in response to DE exposure in several species and occur in rats at doses lower than those inducing particle overload and a tumorigenic response (see above); it follows that lung effects such as inflammation and fibrosis are relevant in the development of risk assessments for DE.

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6. ESTIMATING HUMAN NONCANCER HEALTH RISKS OF DIESEL EXHAUST

6.1. INTRODUCTION

As discussed earlier in this document (Chapter 2, Section 2.2.7, 2.2.8), diesel engine exhaust (DE) consists of a complex mixture of gaseous pollutants and particles. In attempting to estimate potential health risks associated with human exposure to DE, researchers have focused attention mostly on the particulate matter (PM) components. They have done so, in part, by comparing the relative toxicity of unfiltered versus filtered DE (with gaseous components removed), as discussed in Chapter 5.

Diesel particulate matter (DPM) consists mainly of: (a) elemental carbon (EC) particles having relatively large surface areas, (b) soluble organic carbon, including 5-ring or higher polycyclic aromatic hydrocarbons (PAHs) such as benzo(*a*)pyrene, and other 3- or 4-ring compounds distributed between gas and particle phases, and (c) metallic compounds. DPM also typically contains small amounts of sulfate/sulfuric acid and nitrates, trace elements, and water, plus some unidentified components. DPM is made up almost entirely of fine particles (i.e., all below 1–3 μm) with a significant subset of ultrafine particles (i.e., those with a mass median diameter below about 0.1 μm).

Health concerns have long focused on DPM. Toxicological data described in Chapter 5 (Section 5.2) indicate DPM to be the prime etiologic agent of noncancer health effects when DE is sufficiently diluted to limit the concentrations of gaseous irritants (NO_2 and SO_2), irritant vapors (aldehydes), CO, or other systemic toxicants. The large surface areas of DPM allow for adsorption of organics from the diesel combustion process and for adsorption of additional compounds during transport in ambient air. The small size of DPM, combined with their large surface area, likely enhance the potential for subcellular interactions with important cellular components of respiratory tissues once the particles are inhaled by humans or other species (Johnston et al., 2000; Oberdörster et al., 2000).

The content of DPM as described above and in Chapter 2 is of clear toxicological significance. The experimental evidence described in Chapter 5 concerning DPM's association with and etiology of noncancer effects is extensive and compelling. These points, along with the fact that DPM is easily and most frequently measured and reported in toxicological studies of diesel emissions, make DPM a reasonable choice as a measure of diesel emissions. As a surrogate, DPM is as valid as any other component of DE to show what is currently known—and probably what is not yet known—about diesel emissions. Therefore, DPM is the quantitative focus of this chapter.

The usual agency approach to evaluating noncancer risks from inhaled exposures to toxic air pollutants such as ambient DE has been documented by EPA in the methods for derivation of an inhalation reference concentration (RfC) (U.S. EPA, 1994). For DPM exposures, this means combining key elements derived from evaluations of specific DPM noncancer effects in animals and humans (described in Chapter 5) with the use of quantitative dosimetry models (described in Chapter 3). The goal is to estimate DPM concentrations to which humans might be exposed throughout their lives (i.e., chronically) without experiencing any untoward or adverse effects. Such an effort can be accomplished through analysis of dose-response relationships where the adverse response is considered as a function of a corresponding measure of dose. Chapter 5 is replete with dose-response information on adverse (but nonlethal) noncancer health effects observed in long-term (chronic/lifetime) exposure studies to DE in general and to DPM in particular, albeit mostly in animals. Chapter 3 analyzes available methods to convert external exposure concentrations of DPM in animal studies to estimates of a human-equivalent concentration (HEC). The following sections of this chapter (Sections 6.2, 6.3, and 6.5) assess and integrate this information to derive a chronic RfC, using the above-cited methodology in developing dose-response assessments of the noncancer effects of toxic air pollutants.

Yet another approach to consider in deriving quantitative estimates of potential human health risks associated with ambient (nonoccupational) DPM exposures is the extent to which DPM could contribute to the adverse health effects that have been associated with exposure to ambient fine PM, $PM_{2.5}$. Such associations with adverse health effects are based primarily on epidemiologic studies evaluated in EPA's Air Quality Criteria Document for Particulate Matter (PM CD) (U.S. EPA, 1996a).[1] This PM CD served as the scientific basis for the last periodic review of the national ambient air quality standards (NAAQS) for PM, which resulted in the establishment of revised PM standards in 1997, including standards for $PM_{2.5}$. DPM is a component of ambient fine PM (see Chapter 2) and should be considered as a toxicologically important component of ambient fine PM. Any guidelines established for DPM, then, should be concordant with information on fine PM in general, as presented in the PM CD. To more fully consider the implications of the relationship between ambient DPM and fine PM, the epidemiological evidence on fine PM and the basis for the $PM_{2.5}$ standards are summarized, and the relationship between ambient DPM and fine PM is discussed later in this chapter (Section 6.4). This relationship is of interest with respect to the noncancer assessment of DE. As is noted here , however, and reflected in Sections 6.2–6.4 below, the definitions, procedures, and statutory mandates that apply to criteria pollutants such as PM (regulated through the establishment of

[1]A new PM CD is now being prepared to reflect the latest scientific studies on ambient PM available since the last document was completed.

NAAQS under sections 108 and 109 of the Clean Air Act) are fundamentally different from those that apply to toxic air pollutants such as DE and to the derivation of RfCs for such pollutants. Thus, the ambient $PM_{2.5}$ concentrations that are specified as the levels of the $PM_{2.5}$ NAAQS should not be compared directly with any RfC that may be derived for DPM. It is reasonable to observe, however, that the annual $PM_{2.5}$ standard would be expected to provide a measure of protection from DPM, reflecting DPM's current approximate proportion to $PM_{2.5}$.

Estimates of DE levels associated with effects occurring under less than lifetime exposure scenarios (such as acute exposure) are not addressed in this chapter. Studies of acute exposure to DE are discussed in Chapter 5, but are accompanied by scant dose-response information, with single-exposure studies for various specialized endpoints (e.g., allergenicity/adjuvancy) and other multiple-exposure-level studies reporting data on mortality only. Based on currently available methodologies, these studies do not yet appear to provide a sufficient basis from which to derive a dose-response assessment for an acute DE exposure scenario.

6.2. THE INHALATION REFERENCE CONCENTRATION APPROACH

Historically, approaches such as the Acceptable Daily Intake (ADI) were developed whereby effect levels, such as no-observed-adverse-effect levels (NOAELs) or lowest-observed-adverse-effect levels (LOAELs) from human or animal data, were combined with certain "safety factors" to accommodate areas of uncertainty to make quantitative estimates of a safe dose, i.e., a level at which no adverse effect would be likely to occur. In response to the National Academy of Sciences (NAS) report entitled "Risk Assessment in the Federal Government: Managing the Process" (National Research Council, 1983), EPA developed two approaches similar to the ADI, i.e., the oral reference dose (RfD) (Barnes and Dourson, 1988) and the parallel inhalation reference concentration, the RfC, with its formal methodology (U.S. EPA, 1994). Similar to the ADI in intent, the RfD/C approach is used for dose-response assessment of noncancer effects, using an explicitly delineated, rigorous methodology that adheres to the principles set forth in the 1983 NRC report. The RfC methodology includes comprehensive guidance on a number of complex issues, including consistent application to effect levels of uncertainty factors (UFs) rather than the ADI safety factors for consideration of uncertainty. Basically, these approaches attempt to estimate a likely subthreshold concentration in the human population. Use of the RfD/C approach is one of the principal current agency methods for deriving dose-response assessments.

A chronic RfC is currently defined as:

An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious noncancer effects during a lifetime.

The RfC approach involves the following general steps:

- Identification of a critical effect relevant to humans, i.e., an adverse effect that occurs at the lowest exposure/dose in human or animal studies and whose prevention avoids the occurrence of all other adverse effects;
- Selection of appropriate dose-response data to derive a point of departure (POD) for extrapolation of a key study (or studies) that provides a NOAEL, LOAEL, or benchmark concentration ($BMCL_x$)[2];
- Estimation of HECs when animal exposure-response data are used (via use of PBPK/dosimetry models);
- Application of UFs to the point of departure (e.g., NOAEL, LOAEL, $BMCL_x$) to address extrapolation uncertainties (e.g., interindividual variability, interspecies differences, adequacy of database); and
- Characterization of the "confidence" in the dose-response assessment and resultant RfC.

The basic quantitative formula for derivation of an RfC, given in Equation 6-1, has as its basic components an effect level, here a NOAEL, expressed as an HEC, and UFs. The units of an RfC are typically mg/m^3 or $\mu g/m^3$.

Alternatively, the numerator in Equation 6-1 may be a LOAEL or $BMCL_x$. The

$$RfC = \frac{NOAEL_{HEC}}{UF} \tag{6-1}$$

benchmark concentration (BMC) approach and its application in this assessment are documented in Appendix B and described further below. Also, a modifying factor (MF) may be used in the denominator of this equation to account for scientific uncertainties, usually relating to the study chosen as the basis for the RfC. Further specifics of RfC derivation procedures are discussed as

[2]$BMCL_x$ is defined as the lower 95% confidence limit of the dose that will result in a level of "x" response (e.g., $BMCL_{10}$ is the lower 95% confidence limit of a dose for a 10% increase in a particular response). See Appendix B for further specifics.

they are used in the following sections. All such procedures are described in detail in the RfC Methodology (U.S. EPA, 1994).

6.3. CHRONIC REFERENCE CONCENTRATION FOR DIESEL EXHAUST

As concluded in Chapter 5, chronic respiratory effects are the principal noncancer hazard to humans from long-term environmental exposure to DE. Other effects (e.g., neurological, liver-related) are observed in animal studies at higher exposures than those producing the respiratory effects. The human and animal data for the immunological effects of DE are currently considered inadequate for dose-response evaluation. Thus, the respiratory effects are considered the "critical effect" for the derivation of a chronic RfC for DE.

The evidence for chronic respiratory effects is based mainly on animal studies showing consistent findings of inflammatory, histopathological (including fibrosis), and functional changes in the pulmonary and tracheobronchial regions of laboratory animals, including the rat, mouse, hamster, guinea pig, and monkey. Occupational studies of DE provide some corroborative evidence of possible respiratory effects (e.g., respiratory symptoms and possible lung function changes), although those studies are generally deficient in exposure information.

Mode-of-action information about respiratory effects from DE exposure indicates that, at least in rats, the pathogenic sequence following the inhalation of DPM begins with the phagocytosis of diesel particles by alveolar macrophages (AMs). These activated AMs release chemotactic factors that attract neutrophils and additional AMs. As the lung burden of DPM increases, there are aggregations of particle-laden AMs in alveoli adjacent to terminal bronchioles, increases in the number of Type II cells lining particle-laden alveoli, and the presence of particles within alveolar and peribronchial interstitial tissues and associated lymph nodes. The neutrophils and AMs release mediators of inflammation and oxygen radicals, and particle-laden macrophages are functionally altered, resulting in decreased viability and impaired phagocytosis and clearance of particles. This series of events may result in pulmonary inflammation, fibrosis, and eventually lesions like those described in the studies reviewed in Chapter 5. Although information describing the possible pathogenesis of respiratory effects in humans is not available, the effects reported in studies of humans exposed to DE are not inconsistent with the findings in controlled laboratory animal studies.

Several reasons explain why the dose-response data from rats are considered especially appropriate for use in characterizing noncancer health effects in humans and deriving a chronic RfC for DE. First, similar noncancer respiratory effects are seen in other species (mouse, hamster, guinea pig, and monkey). Second, rats and humans exhibit similar noncancer responses (macrophage response and interstitial fibrosis) to other particles such as coal mine dust, silica, and beryllium (Haschek and Witschi, 1991; Oberdörster, 1994). Third, relative to other species

there exists a plethora of long-term, specialized, and mechanistic studies in rats. Fourth, an expert panel convened by the International Life Sciences Institute (ILSI) recommended that response data on persistent, inflammatory processes may be used to assess nonneoplastic responses of poorly soluble particles (PSP) such as DPM (ILSI, 2000).

6.3.1. Principal Studies for Dose-Response Analysis: Chronic, Multiple-Dose Level Rat Studies

The experimental protocols and results from the long-term, repeated-exposure chronic studies demonstrating and characterizing the critical effects of pulmonary fibrotic changes and inflammation are discussed in Chapter 5. Salient points of these studies, including species/sex of the test species, the exposure regime and concentrations reported in mg DPM/m^3, and effect levels, are abstracted in Table 6-1 for further consideration. The effect levels are designated as N for no-observed-adverse-effect level, A for adverse-effect level, and $BMCL_{10}$.

The purpose of many of the chronic studies listed in this table was not the elucidation of the concentration-response character of DPM. The studies of Heinrich et al. (1982, 1986) in hamsters, mice, and rats; of Iwai et al. (1986) in rats; of Lewis et al. (1989) in monkeys; and of Pepelko (1982a) in rats are all single-dose-level analyses that have as their genesis mechanistic or species-comparative purposes. As discussed in Chapter 5, many of these studies do provide valuable supporting information for designation of the critical effect of pulmonary histopathology. The lack of any clear dose-response data, however, precludes consideration of these studies as a basis for RfC derivation.

Likewise, studies of chronic, multiple-level exposure involving species other than rats, i.e., hamsters (Pepelko, 1982b), cats (Plopper et al., 1983), and guinea pigs (Barnhart et al., 1981, 1982), provide cross-species corroboration of the critical effects of pulmonary histopathology and inflammatory alteration.

The remaining studies showing exposure-response relationships in rats for the critical effects include those of Ishinishi et al. (1986, 1988), Mauderly et al. (1987a), Heinrich et al. (1995), and Nikula et al. (1995). As described in Chapter 5, all of these studies were conducted and reported in a thorough, exhaustive manner on the critical effects and little, if any, basis exists for choosing one over another for purposes of RfC derivation. One way of taking advantage of this high degree of methodological and scientific merit would be to array data from all these studies and their effect levels (NOAEL, LOAEL, $BMCL_x$) subsequent to normalization of the exposure conditions, i.e., conversion of the exposure regimes to yield an HEC. This exercise would result in an interstudy concentration-response continuum normalized to a continuous human exposure to DPM that would facilitate the choice of a concentration to use as a point of departure in deriving an RfC.

Table 6-1. Histopathological effects of diesel exhaust in the lungs of laboratory animals

Study	Species/sex	Exposure period	Particles (mg/m^3)	Effect level[a]	Effects[b]
Lewis et al. (1989)	Monkey, Cynomolgus, M	7 h/day 5 days/wk 104 wks	2.0	N	AM aggregation; no fibrosis, inflammation, or emphysema
Bhatnagar et al. (1980) Pepelko (1982a)	Rat, F344, M, F	7 h/day 5 days/wk 104 wks	2.0		Multifocal histiocytosis; inflammatory changes; Type II cell proliferation; fibrosis
Pepelko (1982b)	Hamster, Chinese, M	8 h/day 5 days/wk 26 wks	6.0 12.0	A	Inflammatory changes; AM accumulation; thickened alveolar lining; Type II cell hyperplasia; edema; increase in collagen
Heinrich et al. (1982)	Hamster, Syrian, M, F	7-8 h/day 5 days/wk 120 wks	3.9	A	Inflammatory changes, 60% adenomatous cell proliferation
Iwai et al. (1986)	Rat, F344, F	8 h/day 7 days/wk 104 wks	4.9	A	Type II cell proliferation; inflammatory changes; bronchial hyperplasia; fibrosis
Mauderly et al. (1987a) Henderson et al. (1988)	Rat, F344, M, F; Mouse, CD-1, M, F	7 h/day 5 days/wk 130 wks	0.35 3.5 7.1	N A A	Alveolar and bronchiolar epithelial metaplasia in rats at 3.5 and 7.0 mg/m^3; fibrosis at 7.0 mg/m^3 in rats and mice; inflammatory changes; few quantitative data given
Heinrich et al. (1995)	Rat, Wistar, F; Mouse, NMRI, F (7 mg/m^3 only)	18 h/day 5 days/wk 24 mo	0.8 2.5 7.0	A A A	Bronchioalveolar hyperplasia, interstitial fibrosis in all groups; severity and incidence increase with exposure concentration; text given only
	Mouse, NMRI, F; C57BL/6N, F	18 h/day 5 days/wk 13.5 mo (NMRI) 24 mo (C57BL/N)	7.0	A	No increase in tumors; noncancer effects not discussed

Table 6-1. Histopathological effects of diesel exhaust in the lungs of laboratory animals (continued)

Study	Species/sex	Exposure period	Particles (mg/m^3)	Effect level[a]	Effects[b]
Ishnishi et al. (1986, 1988)	Rat, M, F, F344, /Jcl.	16 h/day 6 days/wk 130 wks	0.11[c] 0.41[c] 1.08[c] 2.32[c] 0.46[d] 0.96[d] 1.84[d] 3.72[d]	N N A A N A A A	Inflammatory changes; Type II cell hyperplasia and lung tumors seen at >0.4 mg/m^3; shortening and loss of cilia in trachea and bronchi; data given in text only
Heinrich et al. (1986)	Hamster, Syrian, M, F; Mouse, NMRI, F; Rat, Wistar, F	19 h/day 5 days/wk 120 wks	4.24	A	Inflammatory changes; thickened alveolar septa; bronchioloalveolar hyperplasia; alveolar lipo-proteinosis; emphysema (diagnostic methodology not described); hyperplasia; lung tumors
Barnhart et al. (1981, 1982); Vostal et al. (1981)	Guinea pig, Hartley, M	20 h/day 5.5 days/wk 104 wks	0.25 0.75 1.5 6.0	N A A A	Minimal response at 0.25 and ultrastructural changes at 0.75 mg/m^3; thickened alveolar membranes; cell proliferation; fibrosis at 6.0 mg/m^3; increase in PMN at 0.75 mg/m^3 and 1.5 mg/m^3
Plopper et al. (1983) Hyde et al. (1985)	Cat, inbred, M	8 h/day 7 days/wk 124 wks	6.0[e] 12.0[d]	A A	Inflammatory changes; AM aggregation; bronchiolar epithelial metaplasia; Type II cell hyperplasia; peribronchiolar fibrosis
Nikula et al. (1995)	Rat, F344, M	16 h/day 5 days/wk 23 mo	2.44 6.33	A, A $BMCL_{10}$	AM hyperplasia, epithelial hyperplasia, inflammation, septal fibrosis, bronchoalveolar metaplasia

[a]N= no-observed-adverse-effect level; A = adverse-effect level; $BMCL_{10}$ = benchmark concentration, lower limit, at a 10% response level (for incidence); see Appendix A for further specifics.
[b]AM = Alveolar macrophage; PMN = Polymorphonuclear leukocyte
[c]Light-duty engine.
[d]Heavy-duty engine.
[e]1 to 61 weeks exposure.
[d]62 to 124 weeks of exposure.
[e]See Appendix A.

6.3.2. Derivation of Human Continuous Equivalent Concentrations, HECs

Pharmacokinetic, or PK, models can be used to estimate across species the external concentrations of a toxicant that would result in equivalent internal doses. When used for these purposes, PK models may be termed comparative dosimetric models. Chapter 3 reviewed and evaluated a number of dosimetric models applicable to DPM. This analysis indicated that outputs from the human component of the model developed by Yu et al. (1991) specifically for DPM, such as deposition and estimated lung burden, were not substantially different from other available models. The analysis also demonstrated that the Yu model accounted for several diesel-specific phenomena, including particle overload lung clearance rates and interspecies kinetics of desorption of organics from the carbonaceous core of DPM, both slow- and fast-cleared. Of importance, the Yu model was parameterized for deposition and clearance in both animals and humans. Also, the animal component of the model was based on data from rats actually exposed to DPM, whereas other models analyzed used data based only on generic particles in the size range of DPM. It was concluded from this analysis that the Yu model could be used to estimate disposition of DPM both in animals and in humans and would therefore be an acceptable choice in performing animal-to-human extrapolation in deriving a continuous human-equivalent concentration. Note, however, that use of this or any other available PK model would address species differences in dose (i.e., pharmacokinetics, PK), and not necessarily pharmacodynamics (PD), the other component of uncertainty in animal-to-human or interspecies extrapolation (U.S. EPA, 1994).

Guidance on choosing measures of exposure for poorly soluble particles such as DPM (ILSI, 2000) states that some measures of external dose (e.g., the aerosol exposure parameters of MMAD, σ_g, particle surface area, and density) should be characterized. Likewise, some indication of internal dose resulting from the external exposure (e.g., lung burden) should be measured so that differences in dose metrics may be considered as new mechanistic insights are developed. The whole particle, as characterized in this assessment and used in the model of Yu et al. (1991), meets this recommended guidance, and DPM, in $\mu g/m^3$, is used as the measure of external exposure. Internal measures of exposure or dose were also considered in Chapter 3 (Section 3.3.1.1) with the conclusion that the dose metric of lung burden of DPM in terms of surface area (mg/cm^2) at the termination of the exposure period appears to be the most defensible and appropriate measure of internal dose, especially where clearance is involved. More detailed specifics are available in Chapter 3 and in Appendix A.

The logical and operational sequence of deriving a HEC using the Yu model and these metrics, i.e. external air concentration (in $\mu g/m^3$) and lung burden (in mg/cm^2), is demonstrated in Figure 6-1. First, the experimental animal exposures, including external concentration and

Figure 6-1. Flow diagram of procedure for calculating HECs.

daily and weekly duration, are entered into the animal component of the Yu model to estimate the animal lung burden, in mg DPM/cm^2, for the specific exposure scenario. The human component of the Yu model is then used by setting desired exposure conditions (continuous for 70 years) and running the model to find an external exposure DPM concentration that would result in this same lung burden. The human external DPM concentration matching this lung burden is the human-equivalent concentration. The step-by-step specifics and results of this procedure as applied to the various studies in Table 6-1 are shown in Table A-4 and fully explained in Appendix A.

The foregoing discussion does not address the variability in outcomes that may be estimated from the Yu et al. (1991) model from deposition of DPM. The model comparison exercises in Chapter 3 showed relatively minor differences among the various human models for one measure, deposition, and indicated that human lung burdens estimated by the human component of the Yu and ICRP66 models were nearly identical at low-exposure concentrations. Variability in output of their model (lung burden) was also examined by Yu and Yoon (1990), who studied dependency on tidal volume, respiration rate, and clearance (in terms of the overall particle transport rate from the alveolar region, λ_A). Analysis indicated that the model output is sensitive, but not overly so, for these determinative parameters. A ± 20% change in values for λ_A, for example, was estimated to result in a 16%–26% change in soot burden at a 0.1 mg/m^3 continuous diesel exposure for 10 years. For a ± 10% change in tidal volume, the model projected changes in soot burden ranging from 14% to 22% for this same exposure scenario. The fact that the changes in the model outcome were comparable to changes in the input parameters, such as tidal volume, indicates that the variability of the model when applied to the human population would reflect the variability of these physiological parameters across that population. In sum, at low concentrations of DPM (< 0.5 mg/m^3), relatively minor differences exist among the models currently available, and the input parameters in the human population may be a major source of variability. As discussed below, variability within the human population often is addressed by applying safety or uncertainty factors, usually in the range of 10 (Renwick and Lazarus, 1998; U.S. EPA, 1994).

6.3.3. Dose-Response Analysis—Choice of an Effect Level

HECs were obtained for the dose levels and exposure scenarios presented in the studies of Mauderly et al. (1987b), Ishinishi et al. (1986, 1988), Nikula et al. (1995), and Heinrich et al. (1995), the specifics of which are presented in Appendix A, specifically Table A-4. The HECs, along with the corresponding specific lung burdens in terms of $\mu g/cm^2$, were transcribed from Table A-4 and, along with the accompanying effect level (NOAEL, LOAEL or $BMCL_{10}$), are arrayed ordinally in Table 6-2. It is acknowledged that Table 6-2 is by no means a full portrayal of the dose-response relationship that may exist for DPM and health effects.

As indicated by the $BMCL_{10}$ values listed for the Nikula et al. (1995) study in Table 6-2, the BMC analysis was carried out on the DPM database and is documented in Appendix B. The chronic rat studies identified in this chapter were analyzed for information suitable for BMC analysis. Results yielded only a few datasets of pulmonary toxicity data from a single study, that of Nikula et al. (1995), that could be used for BMC analysis. These pulmonary data (histopathology incidence data) were extracted, HEC concentrations were calculated using the model of Yu, and the BMCs were generated. The results yielded a complex array of $BMCL_{10}$s from three different effects in two sexes (both separate and combined) with nine different models that were evaluated based on the nature of the dataset, on the goodness-of-fit parameters, and on visual inspection of the graphical outputs. From among all the benchmark data generated, the $BMCL_{10}$ of 0.37 mg/m^3 calculated from combined male and female rat pulmonary histopathology was judged as the most defensible choice. However, further characterization of this same benchmark value indicates that it is not a suitable candidate for use as a point of departure for development of a dose-response assessment such as the RfC. Limitations included the excessive extent of extrapolation from the observed experimental range (see Figure B-1 in Appendix B) and the paucity of data points (there were only two exposure groups) overall. Another serious limitation is that the high experimental concentrations used (and their $C \times t$ product) are well in the range where the problematic phenomenon of pulmonary overload in rats occurs (Section 5.1.3.3.4).

Inspection of Table 6-2 shows that calculating and ordering the HECs created a partial concentration-response continuum reflected in the estimated internal lung burden also given in this table. The continuum extends from HECs with no observed adverse effects at concentrations as low as 0.032 mg/m^3 to as high as 0.144 mg/m^3 to HECs with an adverse effect level that first appears definitively in the continuum probably at 0.33 mg/m^3 and extends out to 1.95 mg/m^3.

It should be noted that the relationship between HEC and lung burden is not consistently proportional. For example, at the lowest HEC listed, 0.032 mg/m^3, a lifetime (70 years) of continuous exposure to this concentration is estimated to result in a specific burden to the lung of 0.0587 $\mu g/cm^2$. At the other end of this spectrum, a lifetime of continuous exposure to 4.4

Table 6-2. Human equivalent continuous concentrations: 70-year HECs calculated with the model of Yu et al. (1991) from long-term studies of rats repeatedly exposed to DPM[a]

Study	Exposure concentration (mg/m^3)	Effect level[a]	Lung burden (modeled) (μg DPM $/cm^2$)[b]	HEC (mg/m^3)
Ishinishi et al. (1988) (LD[c])	0.11	NOAEL	0.0587	0.032
Mauderly et al. (1987a)	0.35	NOAEL	0.0685	0.038
Ishinishi et al. (1988) (LD[c])	0.41	NOAEL	0.245	0.128
Ishinishi et al. (1988) (HD[c])	0.46	NOAEL	0.281	0.144
Heinrich et al. (1995)	0.84	LOAEL	0.94	0.33
Nikula et al. (1995)	2.44 & 6.3[d]	$BMCL_{10}$ -inflam	1.34	0.37
Ishinishi et al. (1988) (HD[c])	0.96	LOAEL	3.16	0.883
Ishinishi et al. (1988) (LD[c])	1.18	LOAEL	4.50	1.25
Nikula et al. (1995)	2.44 & 6.3[d]	$BMCL_{10}$ - fibrosis	4.70	1.3
Mauderly et al. (1987a)	3.47	LOAEL	4.95	1.375
Nikula et al. (1995)	2.44	LOAEL	7.00	1.95
Ishinishi et al. (1988) (HD[c])	1.84	AEL	7.63	2.15
Heinrich et al. (1995)	2.5	AEL	8.40	2.35
Ishinishi et al. (1988) (LD[c])	2.32	AEL	9.75	2.75
Mauderly et al. (1987a)	7.08	AEL	10.9	3.05
Ishinishi et al. (1988) (HD[c])	3.72	AEL	15.8	4.4

[a]Effect levels are based on the critical effects of pulmonary histopathology and inflammation as reported in the individual studies. NOAEL: no-observed-adverse-effect level; LOAEL: lowest-observed-adverse-effect level; AEL: adverse-effect level; $BMCL_{10}$: lower 95% confidence estimate of the concentration of DPM associated with a 10% incidence of chronic pulmonary inflammation (inflam) or fibrosis (see Appendices A and B for more specifics).

[b]Lung burdens were derived from data generated from the animal portion of the Yu model using the concentration and duration scenario of each study. The human portion of the Yu model was then used to estimate the continuous, 70-year exposures that would result in this same lung burden, i.e., the HEC. See Table A-4 in Appendix A and accompanying text for further specifics on derivation.

[c]LD/HD = light-duty/heavy-duty diesel engine.

[d]These values are the actual exposure levels used in the Nikula study. These values were converted into HEC and entered into BMC equations to obtain the estimate of the $BMCL_{10}$ listed. The lung burdens for the two $BMCL_{10}$s listed here were derived by interpolation.

mg/m^3 is estimated to result in a specific lung burden of 15.8 μg/cm^2. This latter lung burden is disproportionally elevated compared with the burden estimated to result from exposure to the lowest concentration. Applying the absolute ratio of lung burden/HEC at the lowest HEC exposure (i.e., 0.0587/ 0.032 = 1.8) to the highest concentration would result in a lower lung burden, 4.4 × 1.8 = 7.9 μg/cm^2, which is much lower than the 15.8 μg/cm^2 indicated. This disproportionate increase in lung burden as a function of DPM concentration would be predicted from the assumption in the Yu model that the overload phenomena occurs in humans, as is demonstrated in Figure 3-9 in Chapter 3. Inspection of Table 6-2 shows that this disproportion between lung burden and HEC begins to be noticeable around 0.33 mg/m^3, at the HEC derived from the Heinrich et al. (1995) study. HECs below this value are not appreciably influenced by the overload/disproportionate lung burden phenomenon.

Inspection of the combined interstudy dose-response continuum in Table 6-2 to elucidate a point of departure for an RfC entails some interpretation. Exposures at the lower end of this table show that elevated chronic exposures to DPM consistently result in AELs. Conversely, entries in the upper portion of this table show that low-level chronic exposures to DPM have minimal, if any, effects within the capability of these studies to detect them. Intermediate chronic exposures, from 0.128 mg/m^3 to 0.9 mg/m^3, are, however, less clear and effect levels and exposures either have no or few observable effects, or effects that are minimally adverse.
In choosing from among levels (e.g., NOAELs, LOAELs, $BMCL_x$s) as a POD for derivation of an RfC, the methodology (U.S. EPA, 1994) provides guidance for choice of a highest no-effect level below an effect level; the interim guidance for the BMC suggests that for use as a point of departure, a benchmark (e.g., $BMCL_{10}$) should be within the range of the observable response data so as to avoid excessive extrapolation, and take the shape of the dose-response curve into consideration (Barnes et al., 1995; U.S. EPA, 1995). The highest no-effect HECs ($NOAEL_{HEC}$) in this table are 0.128 mg/m^3 and 0.144 mg/m^3 from the Ishinishi et al. (1988) study, nearly fivefold above other no-effect levels of 0.032 and 0.038 mg/m^3. The lower $BMCL_{10}$ (0.37 mg/m^3) is at nearly the same concentration as the lowest LOAEL of 0.33 mg/m^3 and thus may be too high an estimate for use as a POD based on these data. As discussed above, the limitations on this $BMCL_{10}$, including excessive extrapolation out of the observable range (see Appendix B for more specifics), make it a less than optimal candidate for consideration as a POD in the development of dose-response assessments and therefore was not used for this purpose in this assessment. However, this $BMCL_{10}$ (i.e., at a response rate of 0.1 or 10%) was generated directly from a modeled dose-response curve for chronic inflammation and lends credence to the other NOAELs in Table 6-2 as being associated with their respective dose-response curve at incidences of considerably less than 10%. Moreover, the HECs of less than 0.33 mg/m^3 are not appreciably influenced by the overload phenomenon (see above). Based on this analysis, the value of 0.144

mg/m^3 is chosen as the POD for development of the RfC, because it is the highest $NOAEL_{HEC}$ among those available.

6.3.4. Uncertainty Factors (UF) for the RfC—A Composite Factor of 30

Areas of uncertainty designated in the RfC that are relevant to the DPM assessment are interindividual variability and animal-to-human extrapolation. Each shall be addressed in this section.

Considerable qualitative but little, if any, quantitative information exists regarding subgroups that could be sensitive to any respiratory tract effects of DPM. It is acknowledged that exposure to DPM could be additive to many other daily or lifetime exposures to airborne organic compounds and nondiesel ambient PM. It is also likely that individuals who predispose their lungs to increased particle retention through smoking or other high particulate burdens, who have existing respiratory tract inflammation or infections, or who have chronic bronchitis, asthma, or fibrosis could be more susceptible to adverse impacts from DPM exposure (U.S. EPA, 1996a, Chapter 5 of this document). Also, infants and children could have a greater susceptibility to the acute/chronic toxicity of DPM because of their greater breathing frequency and consequent potential for greater particle deposition in the respiratory tract, which has not reached full development. Increased respiratory symptoms and decreased lung function in children versus ambient PM levels, of which DPM is a part, have been observed (U.S. EPA, 1996a). Thus, even though the limited evidence currently available (see Chapter 5) produces no clear evidence that children are especially sensitive to effects from breathing DPM, the possibility that they actually may be more susceptible because of their inherent physiology and anatomy should remain a consideration. Likewise, a number of factors may modify normal lung clearance, including, aging, gender, and disease. It should be noted that the results of Mauderly et al. (1989) discussed in Chapter 5 indicated that rats with diseased lungs (emphysematous) were no more susceptible than rats with normal lungs to the effects of DE exposure. Although the exact role of these factors is not resolved, all would influence the particle dose to the lung tissue from inhalation exposure. Activity patterns related to occupation and habitation in the proximity of major roadways are certain to be contributory for some subgroups in receiving higher DPM exposures (Chapter 2). In the absence of DE-specific data, this assessment relies on a default UF value of 10 to account for possible interindividual human variability (U.S. EPA, 1994; Renwick and Lazarus, 1998).

Application of an animal-to-human extrapolation or interspecies uncertainty factor to an assessment may be modified via a number of circumstances. When the assessment is based on human data, no such UF is necessary. When the assessment is based on animal data, as is the case with DPM, a default UF of 10 typically is applied to the animal effect level. This latter

action implies that the effect observed in the animal study would occur in humans at a 10-fold lower concentration, ostensibly from some combination of pharmacokinetic and pharmacodynamic factors that would reflect greater dose (PK consideration) to the human target or greater sensitivity (PK consideration) of the human tissue.

The circumstances with DPM warrant modification away from application of the default UF for animal-to-human extrapolation. The first circumstance is the extensive effort in this assessment to address the pharmacokinetic component of the UF. The point of employing state-of-the-art lung dosimetry models with specific parameterization for DPM in conversion of animal exposures to human-equivalent exposures is to derive an estimate of interspecies pharmacokinetics; to know this aspect of interspecies difference with some degree of certainty. Having made this informed effort addresses a major portion of the PK component. It is acknowledged, however, that uncertainties about the model employed here (or any other model) persist. Although the model comparison shown in Chapter 3 indicates relatively minor variability in output among the various human models examined (see Table 3-3 and Figure 3-9) other sources of uncertainty and variability remain. These include, but are not limited to, matters such as the estimates if the model were applied to the general population or variability from the animal portion of the model(s). A second circumstance involves the pharmacodynamic or PD component of the interspecies UF, especially the aspect as to whether the experimental animal species used in the assessment is more or less sensitive than humans. In the consensus report of ILSI (2000) a specific recommendation is made concerning the PD aspect of the interspecies uncertainty factor for poorly soluble particles such as DPM. Because the pulmonary responses from DPM in the principal experimental species, the rat, are present under exposure conditions that do not appear to elicit any response in humans, the experimental species is considered more sensitive than humans. Accordingly, the report suggested that no accommodation be made for uncertainty concerning the pharmacodynamic component of the interspecies UF for DPM and presumably for any other PSP, as the rat appeared to be a sensitive species, more so even than the human. However, other information currently available on DPM suggests that, at least with regard to inflammatory effects, humans may indeed be as sensitive or even more so than rats. Section 5.1.1.1.3 discusses several studies where humans were exposed to airborne DPM and either precursors (Salvi et al., 2000; Nordenhall et al., 2000) or markers (Nightingale et al., 2000; Salvi et al.,1999) of inflammation were detected. These indicators of inflammation were in response to DPM levels of only 200–300 $\mu g/m^3$ of 1–2h duration. Note that in Table 6-2, NOAEL concentrations to which rats actually were exposed were only 100–400 $\mu g/m^3$, clearly within the range of the aforementioned human exposure levels. Thus, adverse effects (inflammation) have been shown to occur in humans at equivalent or possibly even lower levels

of DPM than observed in rats, indicating that humans may indeed be at least as sensitive if not more so than rats.

The sum of these considerations on the animal-to-human UF is that, although major portions of uncertainty have been addressed, degrees of uncertainty persist in both the pharmacodynamic and pharmacokinetic components of the factor. In considering both this residual uncertainty and the information discussed above, it would be prudent to acknowledge partial degrees of uncertainty in both these areas with a partial uncertainty factor, i.e., $10^{0.5}$ vice 10^{1}, such that a factor of 3 would be applied for interspecies extrapolation.

In summary, the application of UFs for the two areas discussed above, interhuman and animal to human, would result in a composite uncertainty factor of 30, 10 for interhuman × 3 for animal to human. Use of other UFs, as discussed in the RfC methodology (U.S. EPA, 1994) for deficiencies in database or for duration extrapolation, is not considered necessary. It should be noted that, given the emerging research on DE-induced immunological effects, it may be necessary at a later date to reconsider the basis for selection of the critical effect and UFs and thus the entire derivation of the DE RfC.

6.3.5. Derivation of the RfC for Diesel Exhaust

On the basis of the above analysis, the value of 0.144 mg/m^3 DPM was selected as the point of departure for the RfC evaluation. This value was derived from concentrations in rat chronic studies that were modeled to obtain HECs. The pulmonary effects, histopathology and inflammation, were determined to be the critical noncancer effects. Response data on inflammation also were suggested by a specific scientific working group as a satisfactory surrogate for fibrogenic responses in assessing the pulmonary responses of poorly soluble particles such as DPM (ILSI, 2000). Sufficient documentation from other studies showed no effect in the portal-of-entry tissues, the extrathoracic (nasopharyngeal) region of the respiratory system, or in other organs at the lowest levels that produce pulmonary effects in chronic exposures. Application of the dosimetric model of Yu et al. (1991) to the exposure value from Ishinishi et al. (1988) of 0.46 mg/m^3 16 hr/day, 6 days/wk, a NOAEL, yielded a $NOAEL_{HEC}$ of 0.144 mg/m^3. Application of the composite UF yields the RfC:

$$NOAEL_{HEC} \div UF = RfC$$

$$0.144\ mg/m^3 \div 30 = 0.0048 mg/m^3 = 5\mu g/m^3.$$

6.4. EPIDEMIOLOGICAL EVIDENCE AND NAAQS FOR FINE PM

Historically, EPA has established primary NAAQS to protect sensitive human population groups against adverse health effects associated with ambient exposures to certain widespread air pollutants, including PM, ozone (O_3), carbon monoxide (CO), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and lead (Pb). The U.S. Clean Air Act (the Act) requires that EPA periodically review and revise as appropriate the criteria (scientific bases) and standards for each pollutant or class of pollutants (e.g., PM) for which NAAQS have been established. The primary, health-based NAAQS must be based on the latest scientific information useful in indicating the kind and extent of all effects on public health expected from the presence of the pollutant in the ambient air, which is evaluated in a "Criteria Document" (CD). The NAAQS are then set at levels that, in the judgment of the EPA Administrator, protect public health (as contrasted with the health of any individual) with an adequate margin of safety. In determining the degree of protection that will satisfy this mandate, EPA considers the nature and severity of the effects, the types of health evidence available, the kind and degree of scientific uncertainty that effects would in fact occur at any particular level of pollution, and the size and nature of sensitive populations at risk of experiencing exposures of concern. The EPA develops a staff paper to bridge the gap between the scientific criteria and the public health policy considerations the Administrator must take into account in reaching a final judgment. The EPA also must consider the recommendations of the Clean Air Scientific Advisory Committee (CASAC), an independent committee established by the Act specifically to advise the Administrator on air quality criteria and NAAQS. In contrast to an RfC, the NAAQS are not intended to identify a concentration that is protective against a hypothetical continuous lifetime exposure to a given level, but rather take into account expected actual exposure conditions of U.S. populations.

The original PM NAAQS were set in 1971 in terms of total suspended particulate matter (TSP) and included both inhalable and noninhalable particles, ranging in size up to 25–50 μm. A later periodic review of the PM criteria and NAAQS led to the setting in 1987 of PM_{10} NAAQS (150 μg/m^3, 24-h average; 50 μg/m^3, annual average) aimed at protecting against health effects associated with those inhalable particles capable of penetrating to lower (thoracic) regions of the human respiratory tract and depositing in tracheobronchial and alveolar tissue of the lung ($\leq$10.0 μm) (52 FR 24634, July 1, 1987). The most recently completed PM NAAQS review was based on an assessment of the latest available scientific information characterized in the EPA PM CD (U.S. EPA, 1996a) and additional staff assessments contained in an associated PM Staff Paper (U.S. EPA, 1996b). In 1997, on the basis of this information and taking into account CASAC recommendations and extensive public comments, EPA established new $PM_{2.5}$ NAAQS (15 μg/m^3, annual average; 65 μg/m^3, 24-h average) to protect against adverse health effects associated with exposures to fine PM. At the same time, EPA retained, in modified form, the

PM_{10} NAAQS originally set in 1987 to protect against effects associated with coarse fraction PM (62 FR 38652, July 18, 1997).[3]

The 1997 PM NAAQS decisions were based, in part, on important distinctions already highlighted by information present in the PM CD between the fine and coarse fractions of PM_{10} with regard to size, chemical composition, sources, and transport. Also of key importance were the assessment and interpretation of new epidemiological findings on health effects associated with ambient PM. The epidemiological evidence and basis for the NAAQS for fine PM are summarized below, followed by a discussion of the relevance of this information for noncancer assessment of DE.

6.4.1. Epidemiological Evidence for Fine PM

The PM CD (U.S. EPA, 1996a) and Staff Paper (U.S. EPA, 1996b) highlighted more than 80 newly published community epidemiologic studies, of which more than 60 found significant associations between increased mortality and/or morbidity risks and various ambient PM indicators. The main findings of concern were community epidemiology results showing ambient PM exposures to be statistically associated with increased mortality (especially among people over 65 years of age and those with preexisting cardiopulmonary conditions) and morbidity (indexed by increased hospital admissions, respiratory symptom rates, and decrements in lung function).

Time-series mortality studies reviewed in the 1996 PM CD (U.S. EPA, 1996a) provide strong evidence that ambient PM air pollution is associated with increases in daily human mortality and morbidity (e.g., increased hospital admissions and respiratory symptoms). These studies provided evidence that such effects occur at routine ambient PM levels, extending to 24-h concentrations below the 150 $\mu g/m^3$ level of the PM_{10} NAAQS set in 1987. Overall, as shown in Table 6-3, the PM_{10} effects estimates derived from the recent PM_{10} total mortality studies suggest that an increase of 50 $\mu g/m^3$ in 24-h average PM_{10} is significantly associated with an increase in total mortality, with an RR on the order of 1.025 to 1.05 in the general population. Table 6-3 also shows higher relative risks for increased hospital admissions for the elderly and for those with preexisting respiratory conditions, both of which represent subpopulations at special risk for mortality implications of acute exposures to air pollution, including PM; higher relative risks are also shown for increased respiratory symptoms and decreased lung function in children. Results are very similar over a range of statistical models used in the analyses, and are not artifacts of the methods by which the data were analyzed. Further, these studies suggest a possible linear,

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[3]At present, the 1997 $PM_{2.5}$ standards are the subject of ongoing litigation, although they legally remain in effect, as do the 1987 PM_{10} standards.

Table 6-3. Effect estimates per 50 μg/m³ increase in 24-h PM_{10} concentrations from U.S. and Canadian studies

Study location	RR (± CI) only PM in model	RR (± CI) other pollutants in model	Reported PM_{10} levels mean (min/max)[†]
Increased total acute mortality			
Six Cities[a]		—	
Portage, WI	1.04 (0.98, 1.09)	—	18 (±11.7)
Boston, MA	1.06 (1.04, 1.09)	—	24 (±12.8)
Topeka, KS	0.98 (0.90, 1.05)	—	27 (±16.1)
St. Louis, MO	1.03 (1.00, 1.05)	—	31 (±16.2)
Kingston/Knoxville, TN	1.05 (1.00, 1.09)	—	32 (±14.5)
Steubenville, OH	1.05 (1.00, 1.08)	—	46 (±32.3)
St. Louis, MO[c]	1.08 (1.01, 1.12)	1.06 (0.98, 1.15)	28 (1/97)
Kingston, TN[c]	1.09 (0.94, 1.25)	1.09 (0.94, 1.26	30 (4/67)
Chicago, IL[h]	1.04 (1.00, 1.08)	—	37 (4/365)
Chicago, IL[g]	1.03 (1.02, 1.04)	1.02 (1.01, 1.04)	38 (NR/128)
Utah Valley, UT[h]	1.08 (1.05, 1.11)	1.19 (0.96, 1.47)	47 (11/297)
Birmingham, AL[d]	1.05 (1.01, 1.10)	—	48 (21, 80)
Los Angeles, CA[f]	1.03 (1.00, 1.055)	1.02 (0.99, 1.036)	58(15/177)
Increased hospital admissions (for elderly > 65 yrs.)			
Respiratory Disease			
Toronto, CAN[i]	1.23 (1.02, 1.43)[‡]	1.12 (0.88, 1.36)[‡]	30-39[*]
Tacoma, WA[j]	1.10 (1.03, 1.17)	1.11 (1.02, 1.20)	37 (14, 67)
New Haven, CT[j]	1.06 (1.00, 1.13)	1.07 (1.01, 1.14)	41 (19, 67)
Cleveland, OH[k]	1.06 (1.00, 1.11)	—	43 (19, 72)
Spokane, WA[l]	1.08 (1.04, 1.14)	—	46 (16, 83)
COPD			
Minneapolis, MN[n]	1.25 (1.10, 1.44)	—	36 (18, 58)
Birmingham, AL[m]	1.13 (1.04, 1.22)	—	45 (19, 77)
Spokane, WA[l]	1.17 (1.08, 1.27)	—	46 (16, 83)
Detroit, MI[o]	1.10 (1.02, 1.17)	—	48 (22, 82)
Pneumonia			
Minneapolis, MN[n]	1.08 (1.01, 1.15)	—	36 (18,58)
Birmingham, AL[m]	1.09 (1.03, 1.15)	—	45 (19, 77)

Table 6-3. Effect estimates per 50 μg/m³ increase in 24-h PM_{10} concentrations from U.S. and Canadian studies (continued)

Study location	RR (± CI) only PM in model	RR (± CI) other pollutants in model	Reported PM_{10} levels mean (min/max)[†]
Spokane, WA[l]	1.06 (0.98, 1.13)	—	46 (16, 83)
Detroit, MI[o]	—	1.06 (1.02, 1.10)	48 (22, 82)
Ischemic HD			
Detroit, MI[p]	1.02 (1.01, 1.03)	1.02 (1.00, 1.03)	48 (22, 82)
Increased respiratory symptoms			
Lower Respiratory			
Six Cities[q]	2.03 (1.36, 3.04)	Similar RR	30 (13,53)
Utah Valley, UT[r]	1.28 (1.06, 1.56)[ε]	—	46 (11/195)
	1.01 (0.81, 1.27)[π]		
Utah Valley, UT[s]	1.27 (1.08, 1.49)	—	76 (7/251)
Cough			
Denver, CO[x]	1.09 (0.57, 2.10)	—	22 (0.5/73)
Six Cities[q]	1.51 (1.12, 2.05)	Similar RR	30 (13, 53)
Utah Valley, UT[s]	1.29 (1.12, 1.48)	—	76 (7/251)
Decrease in Lung Function			
Utah Valley, UT[r]	55 (24, 86)[**]	—	46 (11/195)
Utah Valley, UT[s]	30 (10, 50)[**]	—	76 (7/251)
Utah Valley, UT[w]	29 (7,51)[***]	—	55 (1,181)

References:

[a]Schwartz et al. (1996a).
[b]Pope et al. (1992, 1994)/O_3.
[c]Dockery et al. (1992)/O_3.
[d]Schwartz (1993).
[f]Kinney et al. (1995)/O_3, CO.
[g]Ito and Thurston (1996)/O_3.
[h]Styer et al. (1995).
[i]Thurston et al. (1994)/O_3.
[j]Schwartz (1995)/SO_2.
[k]Schwartz et al. (1996b).
[l]Schwartz (1996).
[m]Schwartz (1994e).
[n]Schwartz (1994f).
[o]Schwartz (1994d).
[p]Schwartz and Morris (1995)/O_3, CO, SO_2.
[q]Schwartz et al. (1994).
[r]Pope et al. (1991).
[s]Pope and Dockery (1992).
[t]Schwartz (1994g)
[u]Pope and Kanner (1993).
[v]Ostro et al. (1991)
[†]Min/Max 24-h PM_{10} in parentheses unless noted otherwise as standard deviation (± S.D), 10 and 90 percentile (10, 90). NR = not reported.
[ε]Children.
[π]Asthmatic children and adults.
[*]Means of several cities.
[**]PEFR decrease in ml/sec.
[***]FEV_1 decrease.
[‡]RR refers to total population, not just>65 years.

Source: Adapted from U.S. EPA, 1996b, Tables V-3, V-6, and V-7. See U.S. EPA (1996a,b) for all reference citations.

non-threshold PM/mortality relationship, but the data do not rule out the existence of an underlying nonlinear, threshold relationship (U.S. EPA, 1996a, 12-310-311; 1996b, VI-16). Figure 6-2 illustrates the consistency and coherence of the PM_{10} epidemiology findings for increased total and cause-specific mortality and morbidity risks in adults and children. In addition, Table 6-4 summarizes results from a wide array of U.S. and Canadian studies that showed increased risks of mortality and morbidity to be related to changes in short-term (24-h) fine PM (indexed by $PM_{2.5}$ and other fine particle indicators).

As summarized below, long-term exposure studies reviewed in the 1996 PM CD (U.S. EPA, 1996a) also provide evidence of associations between indicators of PM, including fine particle indicators, and chronic mortality and morbidity. Table 6-5 shows the direct comparisons of two key prospective studies of long-term PM mortality: the Harvard Six Cities Study (Dockery et al., 1993) and the American Cancer Society (ACS) Study (Pope et al., 1995). These two studies agree in their findings of strong associations between fine particles and increased mortality. The RR estimates for total mortality are large and highly significant in the Six Cities study. With their 95% confidence intervals, the RR estimate for a 50 $\mu g/m^3$ increase in $PM_{15/10}$ is 1.42 (1.16, 2.01), the RR estimate for a 25 $\mu g/m^3$ increase in $PM_{2.5}$ is 1.31 (1.11, 1.68), and the RR estimate for a 15 $\mu g/m^3$ increase in SO_4 is 1.46 (1.16, 2.16). The ACS study estimates for total mortality are smaller, but also more precise: RR = 1.17 (1.09, 1.26) for a 25 $\mu g/m^3$ increase in $PM_{2.5}$, and RR = 1.10 (1.06, 1.16) for a 15 $\mu g/m^3$ increase in SO_4. Both studies used Cox regression models and were adjusted for similar sets of individual covariates. In each case, however, caution must be applied in use of the stated quantitative risk estimates, given that the lifelong cumulative exposures of the study cohorts (especially in the dirtiest cities) included distinctly higher past PM exposures than those indexed by the more current PM measurements used to estimate long-term PM exposures in the study. Thus, somewhat lower relative risk estimates than the published ones may well apply. A third study by Abbey et al. (1991, 1995) reported no association between long-term PM exposure (indexed by TSP and other estimated PM indices) after 10 years, although the PM CD (U.S. EPA, 1996a) noted TSP may have been an inadequate index for exposure to inhalable particles and that additional follow-up might still reveal chronic effects.

An additional line of evidence concerning long-term effects may be seen in comparing cause-specific deaths in the Six Cities and ACS studies. The relative risks for the most versus the least polluted cities in the two studies are very similar for mortality from cardiopulmonary causes (U.S. EPA, 1996b, V-17). These two long-term exposure studies, taken together, suggest that there may be increases in mortality for specific disease categories that are consistent with long-term exposure to ambient fine particles. Moreover, at least some fraction of these deaths is

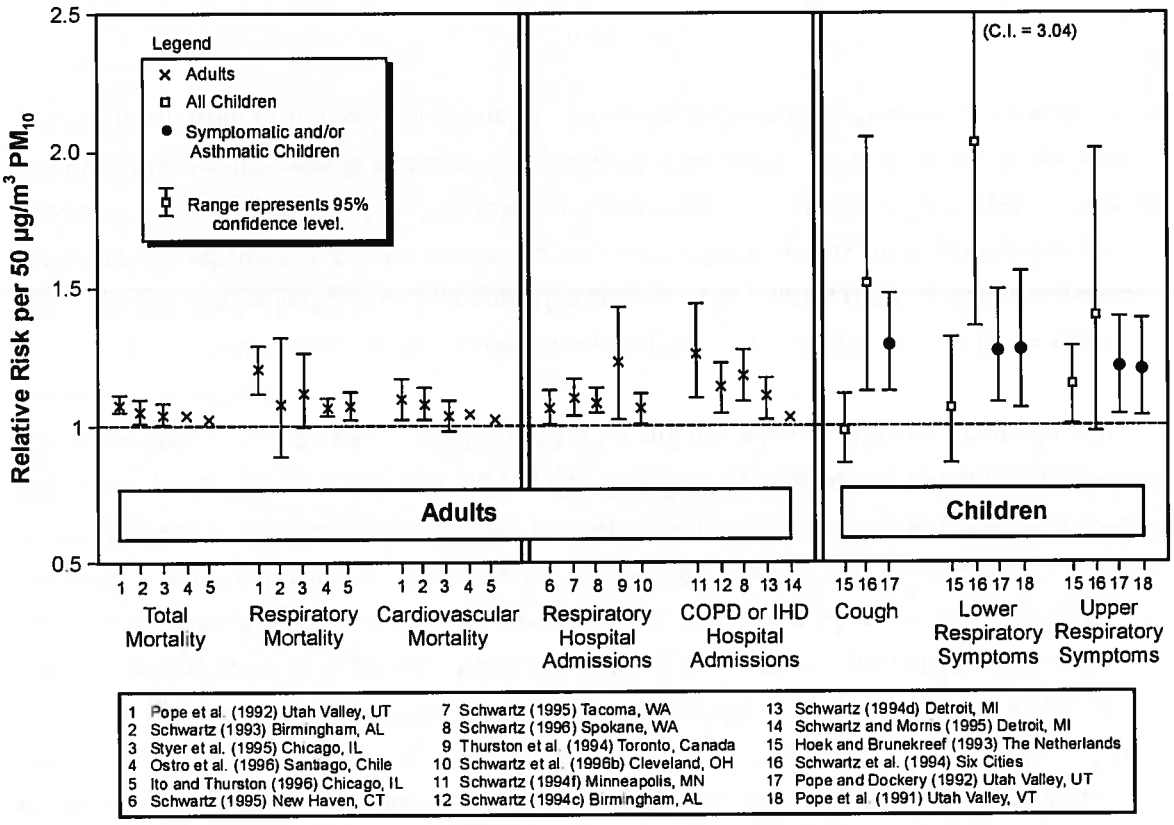

Figure 6-2. Relative risk (RR) estimates for increased mortality and morbidity endpoints associated with 50 µg/m³ increments in PM_{10} concentrations as derived from studies cited by numbers listed above each given type of health endpoint.

Note: Notice the consistency of RR elevations across studies for given endpoint and coherence of RR estimates across endpoints, e.g., higher RR values for symptoms versus hospital admissions and cause-specific mortality.

Source: PM Staff Paper (see U.S. EPA, 1996b for full reference citations for each study identified in figure.)

Table 6-4. Effect estimates per variable increments in 24-h concentrations of fine particle indicators ($PM_{2.5}$, $SO_4^=$, H^+) from U.S. and Canadian studies

Acute mortality	Indicator	RR (± CI) per 25 μg/m³ PM increase	Reported PM levels mean (min/max)†
Six Cities[a]			
Portage, WI	$PM_{2.5}$	1.030 (0.993, 1.071)	11.2 (±7.8)
Topeka, KS	$PM_{2.5}$	1.020 (0.951, 1.092)	12.2 (±7.4)
Boston, MA	$PM_{2.5}$	1.056 (1.038, 1.0711)	15.7 (±9.2)
St. Louis, MO	$PM_{2.5}$	1.028 (1.010, 1.043)	18.7 (±10.5)
Kingston/Knoxville, TN	$PM_{2.5}$	1.035 (1.005, 1.066)	20.8 (±9.6)
Steubenville, OH	$PM_{2.5}$	1.025 (0.998, 1.053)	29.6 (±21.9)
Increased hospitalization			
Ontario, CAN[b]	$SO_4^=$	1.03 (1.02, 1.04)	R = 3.1-8.2
Ontario, CAN[c]	$SO_4^=$ O_3	1.03 (1.02, 1.04) 1.03 (1.02, 1.05)	R = 2.0-7.7
NYC/Buffalo, NY[d]	$SO_4^=$	1.05 (1.01, 1.10)	NR
Toronto[d]	H^+ (Nmol/m³) $SO_4^=$ $PM_{2.5}$	1.16 (1.03, 1.30)* 1.12 (1.00, 1.24) 1.15 (1.02, 1.78)	28.8 (NR/391) 7.6 (NR, 48.7) 18.6 (NR, 66.0)
Increased respiratory symptoms			
Southern California[e]	$SO_4^=$	1.48 (1.14, 1.91)	R = 2-37
Six Cities[f] (Cough)	$PM_{2.5}$ $PM_{2.5}$ Sulfur H^+	1.19 (1.01, 1.42)** 1.23 (0.95, 1.59)** 1.06 (0.87, 1.29)**	18.0 (7.2, 37)*** 2.5 (3.1, 61)*** 18.1 (0.8, 5.9)***
Six Cities[f] (Lower Resp. Symp.)	$PM_{2.5}$ $PM_{2.5}$ Sulfur H^+	1.44 (1.15-1.82)** 1.82 (1.28-2.59)** 1.05 (0.25-1.30)**	18.0 (7.2, 37)*** 2.5 (0.8, 5.9)*** 18.1 (3.1, 61)***
Decreased lung function			
Uniontown, PA[g]	$PM_{2.5}$	PEFR 23.1 (-0.3, 36.9) (per 25 μg/m³)	25/88 (NR/88)

References:
[a]Schwartz et al. (1996a)
[b]Burnett et al. (1994)
[c]Burnett et al. (1995) O_3
[d]Thurston et al. (1992, 1994)
[e]Ostro et al (1993)
[f]Schwartz et al. (1994)
[g]Neas et al. (1995)

†Min/Max 24-h PM indicator level shown in parentheses unless otherwise noted as (± S.D.), 10 and 90 percentile (10,90) or R = range of values from min-max, no mean value reported.
*Change per 100 nmoles/m³.
**Change per 20 μg/m³ for $PM_{2.5}$; per 5 μg/m³ for $PM_{2.5}$ sulfur; per 25 nmoles/m³ for H^+.
***50th percentile value (10,90 percentile).

Source: Adapted from U.S. EPA, 1996b, Table V-12. See U.S. EPA (1996a,b) for all reference citations.

Table 6-5. Effect estimates per increments[a] in annual average levels of fine particle indicators from U.S. and Canadian studies

Type of health effect and location	Indicator	Change in health indicator per increment in PM[a]	Range of city PM levels mean ($\mu g/m^3$)
Increased total chronic mortality in adults		**Relative risk (95% CI)**	
Six City[b]	$PM_{15/10}$	1.42 (1.16-2.01)	18-47
	$PM_{2.5}$	1.31 (1.11-1.68)	11-30
	$SO_4^=$	1.46 (1.16-2.16)	5-13
ACS Study[c] (151 U.S. SMSA)	$PM_{2.5}$	1.17 (1.09-1.26)	9-34*
	$SO_4^=$	1.10 (1.06-1.16)	4-24
Increased bronchitis in children		**Odds ratio (95% CI)**	
Six City[d]	$PM_{15/10}$	3.26 (1.13, 10.28)	20-59
Six City[e]	TSP	2.80 (1.17, 7.03)	39-114
24 City[f]	H^+	2.65 (1.22, 5.74)	6.2-41.0
24 City[f]	$SO_4^=$	3.02 (1.28, 7.03)	18.1-67.3
24 City[f]	$PM_{2.1}$	1.97 (0.85, 4.51)	9.1-17.3
24 City[f]	PM_{10}	3.29 (0.81, 13.62)	22.0-28.6
Southern California[g]	$SO_4^=$	1.39 (0.99, 1.92)	—
Decreased lung function in children			
Six City[d,h]	$PM_{15/10}$	NS Changes	20-59
Six City[e]	TSP	NS Changes	39-114
24 City[i,j]	H^+ (52 nmoles/m^3)	-3.45% (-4.87, -2.01) FVC	—
24 City[i]	$PM_{2.1}$ (15 $\mu g/m^3$)	-3.21% (-4.98, -1.41) FVC	—
24 City[i]	$SO_4^=$ (7 $\mu g/m^3$)	-3.06% (-4.50, -1.60) FVC	—
24 City[i]	PM_{10} (17 $\mu g/m^3$)	-2.42% (-4.30, -.0.51) FVC	—

[a]Estimates calculated annual-average PM increments assume: a 100 $\mu g/m^3$ increase for TSP; a 50 $\mu g/m^3$ increase for PM_{10} and PM_{15}; a 25 $\mu g/m^3$ increase for $PM_{2.5}$; and a 15 $\mu g/m^3$ increase for $SO_4^=$, except where noted otherwise; a 100 nmole/m^3 increase for H^+.

[b]Dockery et al. (1993).
[c]Pope et al. (1995).
[d]Dockery et al. (1989).
[e]Ware et al. (1986).
[f]Dockery et al. (1996).
[g]Abbey et al. (1995a,b,c).
[h]NS Changes = No significant changes.
[i]Raizenne et al. (1996).
[j]Pollutant data same as for Dockery et al. (1996).
*Range of annual median values for subset of 50 cities.

Source: Adapted from U.S. EPA, 1996a, Table 12-6 and U.S. EPA, 1996b, Table V-8. See U.S. EPA (1996a,b) for all reference citations.

likely to be a consequence of cumulative, long-term exposure effects. These effects extend beyond the additive impacts of short-term exposure episodes, in terms of producing marked increases above the expected number of daily deaths among especially susceptible groups, such as the elderly and those with pulmonary disease.

The PM CD (U.S. EPA, 1996a) also highlighted a growing body of evidence directly comparing fine and coarse fraction PM effects that suggests that fine particles are more strongly related than coarse fraction particles to increased mortality and morbidity in both short- and long-term exposure studies. Such evidence notably includes the results of analyses of the type illustrated in Figure 6-3 through 6-5. More specifically, Figure 6-3 shows a stronger relationship between changes in short-term (24-h) concentrations of fine particles (indexed by $PM_{2.5}$) and increased mortality risks than for changes in short-term concentrations of coarse fraction particles (indexed by $PM_{15-2.5}$). Similarly, a stronger relationship is seen between chronic mortality and long-term exposure to fine particles (including both the sulfate and nonsulfate components) than exposure to coarse fraction particles (Figure 6-4), and a much stronger relationship between lung function decrements and long-term exposure to fine particles than to coarse fraction particles (Figure 6-5).

6.4.2. NAAQS for Fine PM

The health effects evidence discussed above is relevant to this current HAD, as both this document (Chapter 2) and the PM CD present information that clearly shows DPM to be a constituent of ambient fine particles. Therefore, it is reasonable to conclude that DPM is associated, but to an undetermined degree, with the health effects described above. Whereas broader public health factors are taken into account in setting NAAQS than are relevant for this noncancer assessment of lifetime exposure for DPM, the annual $PM_{2.5}$ NAAQS based primarily on this evidence is of interest in considering the extent to which the RfC for DE (as derived above in Section 6.3) is concordant with the information on fine particles.

As presented in the Federal Register final rule notice (62 FR 38652, July 18, 1997), EPA drew upon the quantitative epidemiology information concisely summarized above to derive a rationale for selection of an annual-average $PM_{2.5}$ standard.[4] First, to appropriately reflect the

[4]As an initial matter, EPA concluded that the existing PM_{10} standards were not adequate to protect public health, that fine and coarse fraction particles should be considered separately, that $PM_{2.5}$ was the appropriate indicator to use for fine particles, and that an annual $PM_{2.5}$ standard could provide the requisite reduction in risk associated with both annual and 24-h averaging times in most areas of the United States. This annual standard, together with a 24-h standard, could provide supplemental protection against extreme peak fine particle levels that

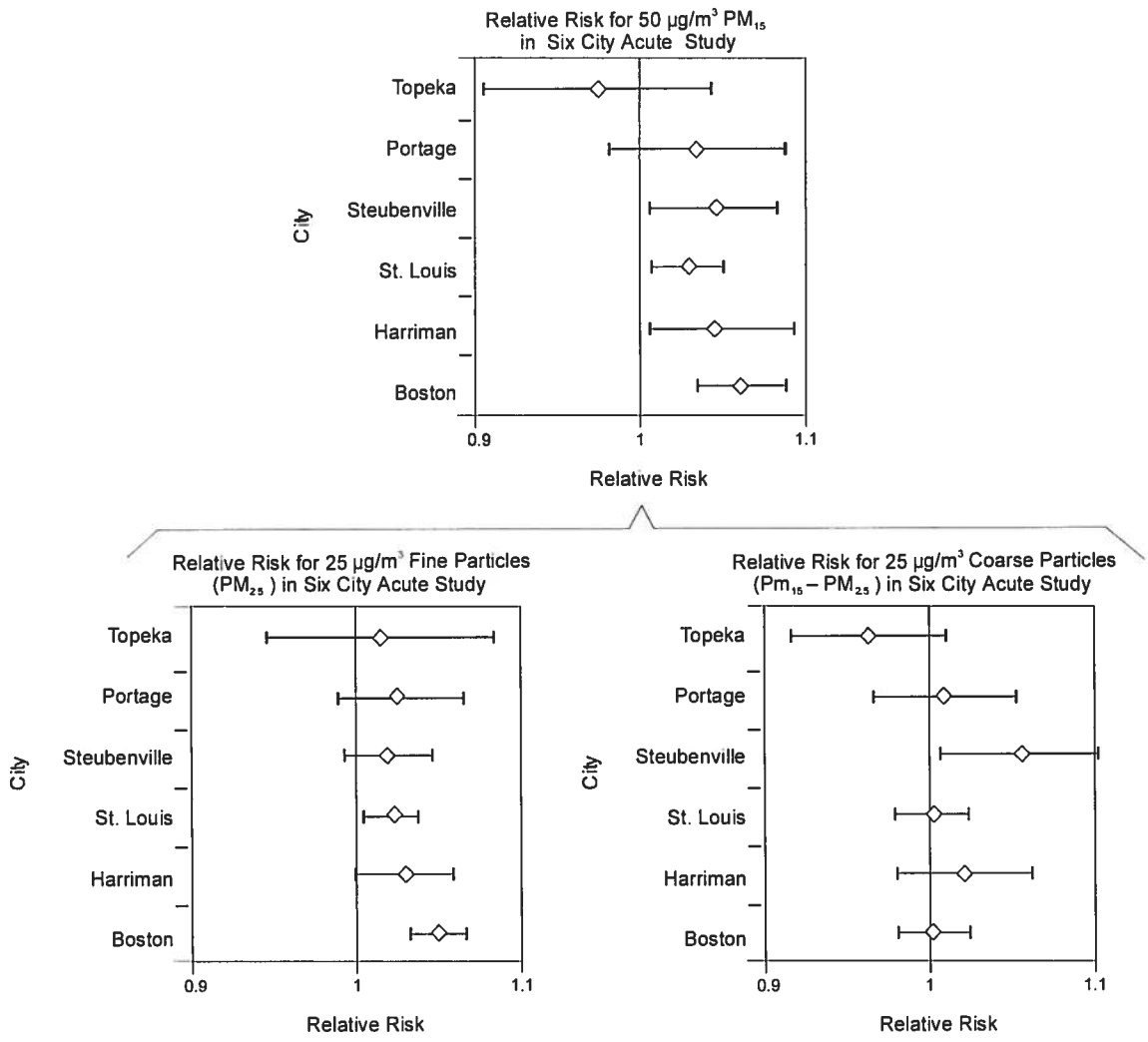

Figure 6-3. Relative risks of acute mortality in Harvard Six Cities Study, for inhalable thoracic particles (PM_{15}/PM_{10}), fine particles ($PM_{2.5}$), and coarse fraction particles (PM_{15}-$PM_{2.5}$).

Note: The coarse fraction effects are smaller and statistically nonsignificant (i.e., lower 95% confidence intervals do not exceed relative risk of 1.0), except in Steubenville where there is high correlation between fine and coarse particles ($R^2 = 0.69$).

Source: PM CD (U.S. EPA, 1996a) graphical depiction of results from Schwartz et al. (1996).

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might occur in some localized situations or in areas with distinct variations in seasonal fine particle levels (62 FR 38652).

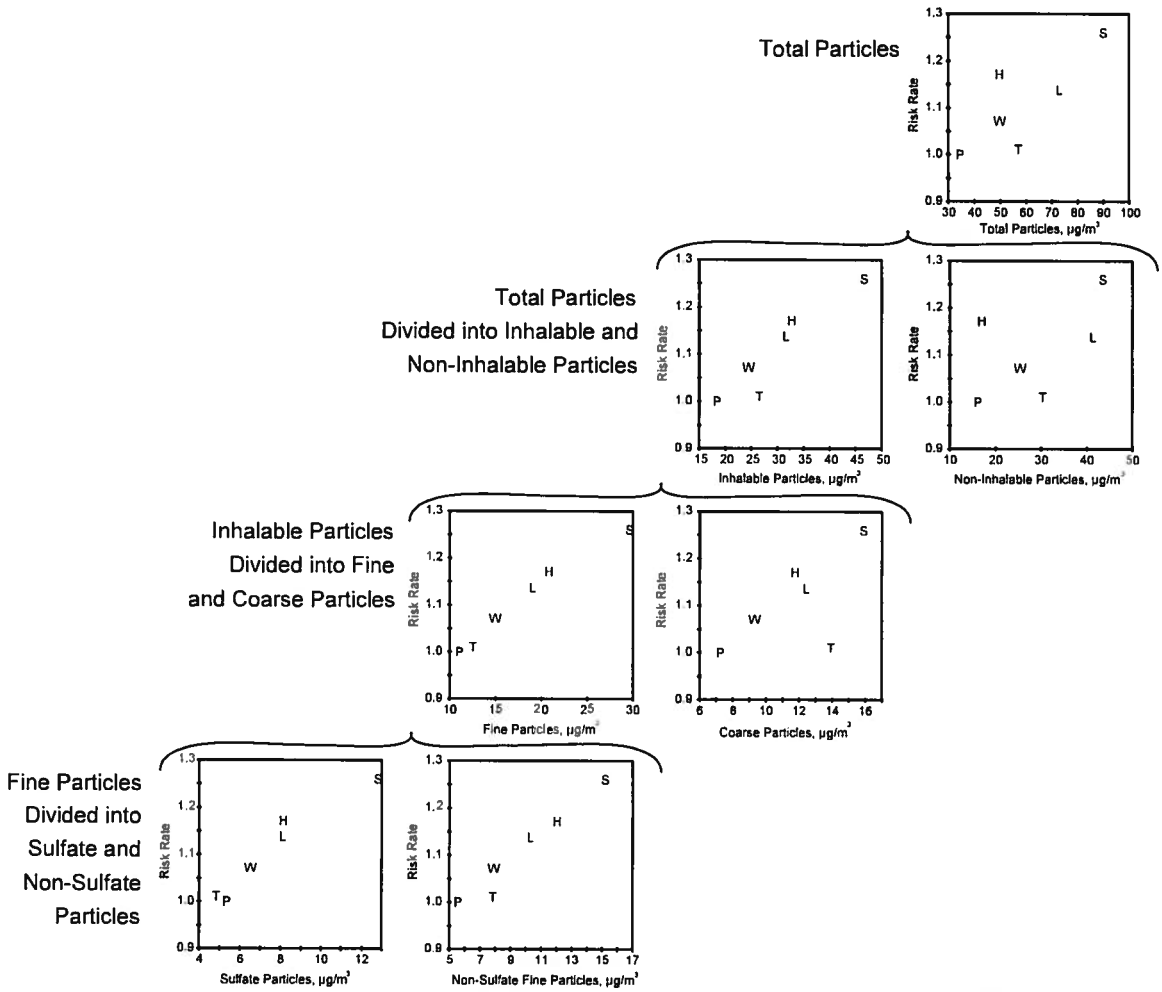

Figure 6-4. Adjusted relative risks for mortality are plotted against each of seven long-term average particle indices in the Harvard Six Cities Study, from largest range (total suspended particles, upper right) through sulfate and nonsulfate fine particle concentrations (lower left).

Note: A relatively strong linear relationship is seen for fine particles, and for sulfate and nonsulfate components. Topeka, which has a substantial coarse particle component of inhalable (thoracic) particle mass, stands apart from the linear relationship between relative risk and inhalable particle concentration.
Source: U.S. EPA (1996a) replotting of results from Dockery et al. (1993).

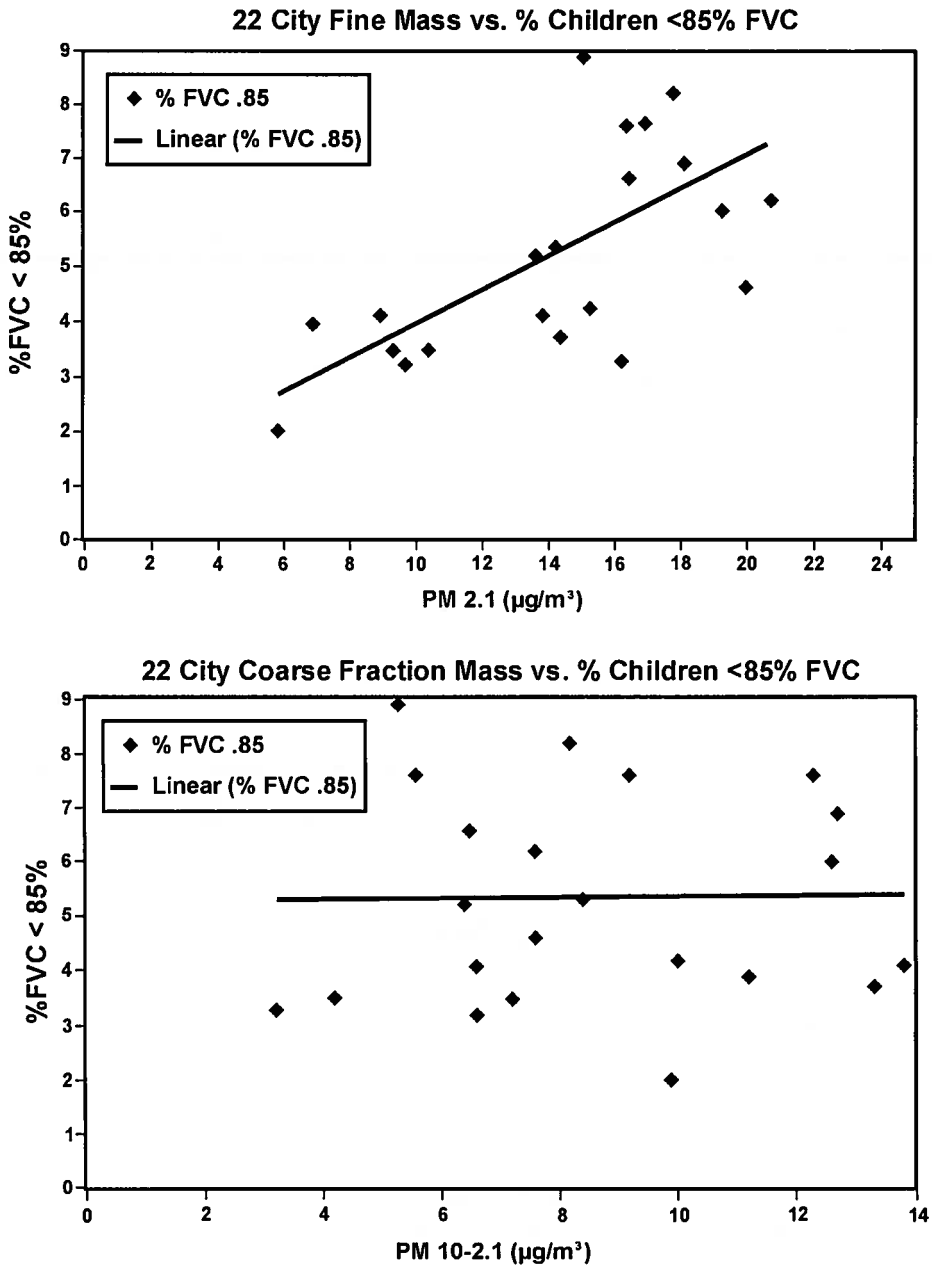

Figure 6-5. Percent of children with <85% normal FVC versus annual-average fine ($PM_{2.1}$) particle concentrations and coarse fraction ($PM_{10-2.1}$) levels for 22 North American cities.

Note: A much stronger connection appears between fine particles and lung function decrements (top panel) than for coarse fraction particles (bottom panel).
Source: PM Staff Paper (1996b) graphical depiction of results from Razienne et al. (1996).

weight of evidence as a whole, EPA concluded that it was appropriate to limit annual $PM_{2.5}$ concentrations to somewhat below those where the body of epidemiological evidence is most consistent and coherent, recognizing both the strengths and limitations of the full range of information on the health effects of PM, as well as associated uncertainties. In accordance with EPA staff and CASAC views on the relative strengths of the epidemiologic studies, major reliance was placed on several short-term (24-h) exposure studies showing significantly increased risks of daily mortality (Schwartz et al., 1996) and morbidity indexed by hospital admissions (Thurston et al., 1994) and respiratory symptoms/lung function decrements in children (Schwartz et al., 1994; Neas et al., 1995) in relationship to increased fine particle ($PM_{2.5}$) concentrations. Whereas it was recognized that health effects may occur over the full range of concentrations observed in these studies, it was concluded that the strongest evidence for short-term $PM_{2.5}$ effects occurs at concentrations near the long-term (e.g., annual) average. More specifically, the strength of the evidence of effects increases for concentrations of $PM_{2.5}$ that are at or above the long-term mean levels reported for these studies. Given the serious nature of the potential effects, EPA judged that it was both prudent and appropriate to select a level for an annual standard at or below such concentrations. More specifically, statistically significant increases in relative risks for daily mortality or morbidity were most clearly observed in these studies to be associated with 24-h fine particle concentrations in cities with long-term mean fine particle concentrations ranging from about 16 to about 21 $\mu g/m^3$, leading to the judgment that an annual standard level of 15 $\mu g/m^3$ would be appropriate.

Before reaching a final conclusion, the epidemiologic studies of long-term exposures to fine particles were also considered, which may reflect the accumulation of daily effects over time as well as potential effects uniquely associated with long-term exposures. Even subject to additional uncertainties, these studies were judged to provide important insights with respect to the overall protection afforded by an annual standard. In particular, the annual mean $PM_{2.5}$ concentrations for the multiple cities included in the two key long-term exposure mortality studies (Dockery et al., 1993; Pope et al., 1995) were 18 $\mu g/m^3$ and about 21–22 $\mu g/m^3$, respectively, with most of the 50 cities in the Pope, et al. (1995) having mean $PM_{2.5}$ concentrations above 15 $\mu g/m^3$. Taken together with other long-term exposure studies and considering other factors discussed in the final rule (62 FR 38676, July 18, 1997), EPA concluded that the concordance of evidence for PM effects and associated levels provides clear support for an annual standard set at 15 $\mu g/m^3$.

6.4.3. DPM as a Component of Fine PM

Chapter 2 of this document, as well as the PM CD (U.S. EPA, 1996a), report the extent to which DPM may contribute to ambient $PM_{2.5}$ concentrations. In some urban situations, the annual average fraction of $PM_{2.5}$ attributable to DPM (according to mass concentrations) is about 35% on the high end, although the proportion appears to be more typically in the range of about 10% (see Chapter 2, Table 2-23 and Section 2.4.2.1).

An approach to considering the relationship of toxicity between DPM and $PM_{2.5}$ would be simply to assume that, as DPM is contributory to the content of ambient $PM_{2.5}$, so too would it be contributory to toxicity of $PM_{2.5}$. This approach is qualitative only because no firm basis currently exists for apportioning toxicity among the various components of $PM_{2.5}$. Nevertheless, some qualitative information from laboratory animal studies does exist, showing that DPM is no more potent at eliciting pulmonary pathology than other poorly soluble particles such as talc, titanium dioxide, or carbon black in rats, or talc or titanium dioxide in mice. No data suggest that DPM is any more potent in eliciting pulmonary pathology than any other poorly soluble particle that typically may be present in ambient $PM_{2.5}$. It may be reasonable to suggest, then, that DPM is no more likely to be toxicologically potent than any other fine particle constituents that typically make up ambient $PM_{2.5}$.

Based on the foregoing aspects of such an approach, a conclusion could be drawn that as long as DPM constituted its current approximate proportion to $PM_{2.5}$, the annual $PM_{2.5}$ standard would also be expected to provide a measure of protection for DPM. Even if a basis did exist to apportion toxicity among the various components of ambient $PM_{2.5}$, such as DPM, use of such information in an approach to derive a safe air level for DPM would result in only a generalized, nonspecific estimate limited by a variety of factors including the accuracy of the apportionment of DPM from $PM_{2.5}$. The RfC derived in Section 6.3 was based on an approach that utilized toxicological information from actual DPM exposures, a more direct approach that would result in a more specific estimate not limited by any apportionment scheme.

6.5. CHARACTERIZATION OF THE NONCANCER ASSESSMENT FOR DIESEL EXHAUST

Adverse health effects from short-term acute (high-level) exposures to DE such as occupational reports of decreases in lung function, wheezing, chest tightness, increases in airway resistance, and reports in laboratory animals of inflammatory airway changes and lung function changes are acknowledged but are not assessed quantitatively. The focus of this dose-response assessment is on the adverse noncancer health consequences of a lifetime, low-level, continuous air exposure by humans to DE.

This assessment uses the whole particle, termed DPM, as the key index or measure of DE dose. DPM includes any and all adsorbed organics, among which are a large number of PAHs, heterocyclic compounds, and their derivatives (Chapter 2), as well as the carbon core. It is not possible to separate the carbon core of DPM from the adsorbed organics to compare the toxicity in exposures other than with limited in-vitro-type scenarios. The dosimetric model used in the derivation of the RfC (Yu et al., 1991) is consistent with this designation, as it considers DPM as well as the adsorbed organics as two types, slow-cleared and fast-cleared. Studies with diesel do occasionally report levels of accompanying gaseous components of DE (e.g., NO_x, CO), but nearly all report particle concentration and characteristics.

Adverse responses occurring in the rat lung have been used in this assessment as the basis for characterizing nonneoplastic human lung responses, yet use of these data in hazard evaluation for cancer is not considered relevant to humans. The basis for this use of these noncancer pulmonary effects in rats for derivation of an RfC includes the fact that humans and rats exhibit similar responses to other poorly soluble particles and also that similar noncancer effects are seen in other species (ILSI, 2000; Freedman and Robinson, 1988). Thus, when viewed across species (including humans), the nonneoplastic pulmonary effects of inflammation and fibrosis used in this assessment are dissociable from the cancer response and are of likely relevance to humans.

As a part of the RfC methodology (U.S. EPA, 1994), dose-response assessments are assigned levels of confidence that are intended to reflect the strengths and limitations of an assessment as well as to indicate the likelihood of the assessment changing with any additional information. Confidence levels of either low, medium, or high are assigned both to the study (or studies) used in the assessment to characterize the critical effects and to the overall toxicological database of the substance. An overall confidence level also is assigned to the entire assessment. Usually, it is the same, or in any case no higher than the level assigned to the database.

Compared with the databases of most other toxicants, the basic toxicological database for DE is substantial. The critical effects are characterized using not one but multiple long-term chronic studies conducted independently of one another (Tables 6-1 and 6-2). The exhaustive manner in which these studies were conducted and reported also imparts a high degree of confidence. Both developmental and reproductive areas are addressed. Also, ancillary studies that address mechanistic aspects of DE toxicity, either as the whole particle with adsorbed organics, or segregated as a poorly soluble particle and extracted organics, are available and used in this assessment. Although only limited human data are available, extensive consideration has been given to the relevancy of the animal studies to the human condition. On the other hand, data from related toxicants such as general ambient PM indicate effects in endpoints (e.g., cardiovascular measures) that have not been addressed in the DPM database. A major point to

consider in assigning confidence in this assessment, and a reason that the value of the RfC may change in the future, is the emerging issue of allergenicity caused or exacerbated by DE. Although information to evaluate allergenicity in parallel to the present effects (pulmonary inflammation and histopathology) is currently lacking, future efforts to elucidate and characterize this effect may well be a driver to make a reevaluation of the noncancer RfC derivation for DE appropriate. With respect to the current RfC for DE, the confidence level is medium, both for the database and overall. The level reflects the relevance of (and information lacking on) allergenicity effects associated with DE in humans, and the possibility that the current RfC could change as a consequence of this information becoming available from the scientific community.

In the introductory portion of this chapter, DPM is acknowledged as a constituent of ambient PM (U.S. EPA, 1996a,b). A discussion of the quantitative epidemiology, particularly regarding fine PM, indicated that public health effects, including premature mortality, increased hospital admissions, respiratory symptoms, and decreased lung function, were observed in populations living in areas with long-term mean $PM_{2.5}$ levels generally ranging above 15 $\mu g/m^3$. Application of the RfC method, which involved critical consideration of the entirety of the disparate DE database with many chronic studies from several different species, evaluation of a myriad of possible DE-specific toxicological endpoints, and use of extrapolation models, produced a value of 5 $\mu g/m^3$. As the accuracy of the RfC is stated in the definition (*"...within an order of magnitude ..."*), this dose-response estimate could be considered to be not different from the level of 15 $\mu g/m^3$, the lower end of the range identified for $PM_{2.5}$. It is acknowledged here again that the levels of the $PM_{2.5}$ NAAQS should not be considered as indicative of the same degree of health protection for DE as intended by the RfC. Nevertheless, the congruence of these estimates tends to enhance the overall confidence that this range of levels is near or inclusive of those that would be expected to be protective of the human population against the health effects of DE.

6.6. SUMMARY

Table 6-6 summarizes the key data and factors used in the dose-response analysis leading to the derivation of the RfC for DE. The DE RfC of 5 μg DPM/m^3 is a chronic exposure likely to be without an appreciable risk of adverse human health effects.

The link between ambient fine PM and DPM with respect to origin, content, and possible health effects has been presented and discussed in this chapter, and the general congruence between the DE RfC and the level of the annual NAAQS for fine particles has been noted. Although these values should not be compared directly, it is reasonable to observe that the annual $PM_{2.5}$ standard would be expected to provide a measure of protection for DPM, reflecting DPM's

Table 6-6. Decision summary for the quantitative noncancer RfC assessment for continuous exposure to diesel particulate matter (DPM)

Quantitative assessment for noncancer effects from lifetime exposure to DPM	5 μg/m³
Critical effect	Pulmonary inflammation and histopathology in rats
Principal study	Array of four chronic rat studies
Designated basis for quantitation (exposures in rats)	0.46 mg DPM /m³, 16 hr/day, 6 d/wk, 130 wks; a NOAEL
$NOAEL_{HEC}$ (HEC)	0.144 mg DPM / m³
Adjustments for uncertainty factors (interspecies variability and intraspecies extrapolation)	30
$NOAEL_{HEC}$/UF = RfC	0.144 mg/m³ / 30 = 5 μg/m³

current approximate proportion to $PM_{2.5}$.

The estimated air concentration of 5 μg/m³ (the RfC, a lifetime exposure to DE measured as DPM) is above the ambient air levels reported in most rural areas but could be below those levels reported under short-term conditions in some urban scenarios, such as at busy intersections or bus stops (see Chapter 2, Table 2-23). The RfC is intended to address lifetime chronic exposures and aspects of time-averaging for less than lifetime scenarios, such as, for example, acute exposures at busy intersections or bus stops, which are not addressed in this particular assessment.

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7. CARCINOGENICITY OF DIESEL EXHAUST

7.1. INTRODUCTION

Initial health hazard concerns regarding the potential carcinogenicity of diesel engine exhaust (DE) were based on the reported induction of skin papillomas by diesel particle extracts (Kotin et al., 1955), evidence for mutagenicity of extracts (Huisingh et al., 1978), evidence that components of diesel extract act as weak tumor promoters (Zamora et al., 1983), and the knowledge that diesel particles and their associated organics are respirable. During the 1980s, both human epidemiologic studies and long-term animal cancer bioassays were initiated. In 1981, Waller published the first epidemiologic investigation, a retrospective mortality study of London transport workers. Since then a large number of retrospective cohort and case-control studies have been carried out with railroad workers, dockworkers, truck drivers, construction workers, miners, and bus garage employees. During 1986 and 1987, several chronic animal cancer bioassays were published. These studies and numerous laboratory investigations carried out since then have been directed toward assessing the carcinogenic potential of whole exhaust, evaluating the importance of various exhaust components in the induction of cancer, and understanding the mode of action and implications of deposition, retention, and clearance of DE particles.

7.1.1. Overview

This chapter evaluates the carcinogenic potential of DE in both humans (Section 7.2) and animals (Section 7.3), discusses mode(s) of action (Section 7.4), and provides an overall weight-of-evidence evaluation (Section 7.5) for carcinogenicity in humans. This chapter also summarizes evaluations of DE conducted by other organizations (Section 7.6) and the final conclusions (Section 7.7) identify major uncertainties for which additional research is needed. This assessment focuses on DE, although it should be noted that diesel particles make up a portion of ambient particulate matter (PM) (Chapter 2, Section 2.2.3; Chapter 6, Section 6.4.3), and thus, the ambient PM data may have some relevance.

7.1.2. Ambient PM-Lung Cancer Relationships

A brief overview of the data regarding exposure to ambient PM and lung cancer is provided as background information and is based on analyses contained in the 1996 Air Quality Criteria for PM (PM CD) (U.S. EPA, 1996a).[1] With DE being part of ambient PM, the question

[1]As noted in Chapter 6, a new PM CD is now being prepared to reflect the latest scientific studies on ambient PM available since the last document was completed.

of what is seen in the ambient PM data is of interest, as epidemiologic evidence for an effect of ambient PM on lung cancer mortality or incidence could possibly contribute to evaluation of DE-specific epidemiologic data.

Chapters 2 and 5 noted that DPM, consisting mostly of fine particles (<1.0 mm diameter), represents a toxicologically important component of typical ambient fine particle mixes. As discussed in Chapter 6, several large-scale prospective studies (Harvard Six Cities Study; American Cancer Society (ACS) Study; Adventist Health Study of Smog (AHSMOG) provide important evidence regarding associations between chronic exposures to ambient fine particles and increased risks of noncancer mortality/morbidity effects (e.g., cardiorespiratory-related deaths or hospital admissions) (U.S. EPA, 1996a). As summarized below, these same studies also evaluated relationships between chronic PM exposures and lung cancer mortality and/or incidence.

As an initial matter, both the Harvard Six Cities Study (Dockery et al., 1993), of approximately 8,000 adults in six cities comprising a transect across the northcentral and northeastern United States, and the ACS Study (Pope et al., 1995), of 550,000 adults in 151 cities across all U.S. geographic regions, found markedly increased relative risks (RR) of lung cancer mortality associated with smoking. More specifically, the Six City Study reported increased risks of smoking for current (RR = 8.00, 95% CI = 2.97-21.6) and former (RR = 2.54, CI = 0.90-7.18) smokers, with the ACS Study reporting striking similar increased risks for current smokers (RR = 9.73, 95% CI = 5.96-15.9).

After controlling for smoking and other risk factors, both the Six Cities Study and the ACS Study (using a subset of 50 of the 151 cities) evaluated relationships between long-term exposure to fine PM (indexed by $PM_{2.5}$), from the least to the most polluted of the cities in each study, and lung cancer mortality. In both studies, lung cancer mortality risks were not statistically significantly associated with ambient $PM_{2.5}$ concentrations in combined analyses of data for both males and females (RR = 1.37, 95% CI = 0.81-2.31, in the Six Cities Study; RR = 1.03, 95% CI = 0.80-1.33, in the ACS Study). Also, lung cancer mortality risks were not statistically significantly associated with ambient $PM_{2.5}$ concentrations in the ACS Study for smaller sample size subgroups broken out by sex and smoking status. In addition, analyses of data from the AHSMOG series of studies, of 6,338 nonsmoking long-term California adult residents, found no statistically significant associations between $PM_{2.5}$ (estimated from visibility data) and lung cancer mortality or total mortality (Abbey et al., 1995); further, no such associations were reported for PM_{10} (estimated from total suspended particulate matter [TSP] data) in the same study. Earlier AHSMOG analyses (Abbey et al., 1991) reported no statistically significant associations between TSP (which includes not only fine PM but also larger coarse-

mode particles ranging up to 25-50 μm) and respiratory cancer for either sex (only respiratory symptoms and any-site female cancers were reported to be associated with TSP in this study).

The ACS Study and the later AHSMOG analyses (Abbey et al., 1995) also evaluated relationships between long-term exposures to sulfates (SO_4) (which are predominantly but not exclusively found in fine-mode particles, and can be considered an index for ambient fine particles) and lung cancer mortality. The ACS Study reported somewhat elevated and statistically significant lung cancer risk (RR = 1.36, 95% CI = 1.11-1.66) across 151 cities in combined analyses of data for both males and females. However, in further analyses of subgroups broken out by sex and smoking status (and thus having smaller sample sizes in each than for the above overall combined analyses), only the lung cancer mortality risks for male "ever-smokers" (RR = 1.44, 95% CI = 1.14-1.83) were statistically significant; no statistically significant relationships were reported for male "never-smokers" (RR = 1.36, 95% CI = 0.40 - 4.66), for female "ever-smokers" (RR = 1.10, 95% CI = 0.72-1.68), or for female "never-smokers" (RR = 1.61; 95% CI = 0.66 -3.92). In the later AHSMOG analyses, Abbey et al. (1995) found no statistically significant associations between sulfates and lung cancer or total mortality.

In summary, the three key prospective cohort studies summarized above, and discussed in more detail in the 1996 PM CD (U.S. EPA, 1996a), provide an equivocal array of results with regard to possible associations between chronic exposures to ambient PM and lung cancer mortality and/or incidence. None of the analyses of fine particles (as indexed by $PM_{2.5}$) in these three studies reported statistically significant relationships between long-term $PM_{2.5}$ concentrations and lung cancer mortality. Only the ACS Study found a statistically significant association of increased risk of lung cancer with one indicator of ambient fine particles (sulfates). Overall, then, these studies support a conclusion that there continues to be little epidemiologic evidence for an effect of ambient PM on lung cancer mortality or incidence. It is recognized, however, that subsequent AHSMOG analyses and other studies, published since completion of the 1996 PM CD, have further analyzed relationships between ambient PM and lung cancer. Results from these more recent studies are now being evaluated as part of the integrated assessment of ambient PM that will be part of the new PM CD targeted for completion in 2002.

7.2. EPIDEMIOLOGIC STUDIES OF THE CARCINOGENICITY OF EXPOSURE TO DIESEL EXHAUST

An increased risk from malignancies of the lung, bladder, and lymphatic tissue has been reported in populations potentially exposed to higher levels of DE than typically seen in the environment. A few authors have reported other malignancies, including testicular cancer

(Garland et al., 1988), gastrointestinal cancer (Balarajan and McDowall, 1988; Guberan et al., 1992), and prostate cancer (Aronsen et al., 1996). A detailed review of 22 lung cancer studies is presented in this section; a few more studies exist, but these 22 are judged to be the key ones. A detailed review of other health effect studies is not presented because findings are equivocal.

Excess risk of bladder cancer has been reported in several studies (Howe et al., 1980; Wynder et al., 1985; Hoar and Hoover et al., 1985; Silverman et al., 1983; Vineis and Magnani 1985; Silverman et al., 1986; Jensen et al., 1987; Steenland et al., 1987; Isocovich et al., 1987; Risch et al., 1988; Iyer et al., 1990; Steineck et al., 1990; Cordier et al., 1993; Notani et al., 1993). Very few studies found significant excesses after adjustment for cigarette smoking. Most studies failed to show any association between exposure to DE and occurrence of bladder cancer. Some authors have reported excess mortality from lymphohematopoietic system cancers in people potentially exposed to diesel fumes. Rushton and Alderson (1983) and Howe and Lindsay (1983) found increased mortality from lymphatic neoplasms. Balarajan and McDowall (1983) found raised mortality for malignant lymphomas. Flodin et al. (1987) observed increased risk for multiple myeloma, and Bender et al. (1989) reported excess mortality from leukemia. Because evidence for bladder cancer and lymphohematopoietic cancer was found to be equivocal, detailed reviews of these studies are not presented here.

The potential for elevated DE exposure in the occupational setting generally includes miners, railroad workers, truckers, bus and taxi drivers, heavy equipment operators, farm tractor drivers, and those involved with heavy duty marine engines. Regarding the mining industry some assert that excess lung cancer should be observed in the miners if exposure to DE is causally associated with the occurrence of lung cancer since DE is allegedly present in the mines. Our review of the mining industry data dose not support this assertion for the following reasons. In the United States, the introduction of diesel engines into metal mines dates from the early to the mid 1960s. Currently, there are approximately 265 underground metal/nonmetal mines in the United States. Virtually all of these mines use diesel powered equipment for various tasks, such as haulage, roof bolting etc. (Department of Labor, Mine Safety and Health Administration, 2001). Introduction of diesel equipment into coal mines was even later. Of 910 existing underground coal mines in the United States, only 145 currently use diesel-powered equipment. Of these 145 mines, 32 mines are currently using diesel equipment for face coal haulage. The remaining mines use diesel equipment for transportation, materials handling, and other support operations (Department of Labor, Mine Safety and Health Administration, 2001). It should be noted that there is a paucity of epidemiologic studies in miners where exposure to DE and health effects are explored. Furthermore, the majority of epidemiologic studies in miners do not mention exposure to diesel equipment use. Thus, it is impossible to know how many miners were exposed to DE and for how long and at what concentrations in a given study,

if any. Hence the studies in miners (coal, metal, and nonmetal with the exception of potash miners) are not reviewed in this chapter, because the available studies are uninformative relative to DE.

In this section, various mortality and morbidity studies of lung cancer from potential exposure to diesel engine emissions are reviewed. Although an attempt was made to cover all the relevant studies, a number of studies are not included for several reasons. In the United States the change from steam to diesel engines in locomotives began after World War II. By 1946 about 10% of the locomotives in service were diesel, by 1952 55% were diesel, and dieselization was about 95% complete by 1959 (Garshick et al., 1988). Therefore, exposure to DE was less common, and the follow-up period for studies conducted prior to 1960 (Raffle, 1957; Commins et al., 1957; Kaplan, 1959) was not long enough to cover the long latency period of lung cancer. The usefulness of these studies in evaluating the carcinogenicity of DE is greatly reduced; thus, they are not considered here.

On the other hand, the trucking industry changed to diesel trucks by the 1960s. In the 1960s sales of diesel-powered Class 8 trucks (long-haul trucks) were 48% of the market, and by the 1970s sales had risen to 85%. Thus, studies conducted among truck drivers prior to the 1970s may reflect exposures to gasoline exhaust as well as DE. Hence, studies with ambiguous exposures or studies that examined several occupational risk factors were excluded because they would have contributed little to the evaluation of the carcinogenicity of DE (Waxweiler et al., 1973; Williams et al., 1977; Ahlberg et al., 1981; Stern et al., 1981; Buiatti et al., 1985; Gustafsson et al., 1986; Siemiatycki et al., 1988). A study by Coggon et al. (1984) was excluded because occupational information abstracted from death certificates had not been validated; this would have resulted in limited information.

Several types of studies of the health effects of exposure to diesel engine emissions are reviewed in this chapter, such as cohort studies, case-control studies, and studies that conducted meta-analysis. In the cohort studies, cohorts of heavy construction equipment operators, railroad and locomotive workers, bus garage employees, and miners were studied retrospectively to determine increased mortality and morbidity resulting from exposures to varying levels of diesel emissions in the workplace. The evaluation of each study presents the study population, methodology used for the study, i.e., data collection and verification, analysis, results, and a critique of the study. There are some methodologic limitations that are common to studies with similar design. The total evidence, including limitations, is discussed at the end of the chapter in the summary and discussion section.

7.2.1. Cohort Studies

7.2.1.1. *Waller (1981): Trends in Lung Cancer in London in Relation to Exposure to Diesel Fumes*

A retrospective mortality study of a cohort of London transport workers was conducted to determine if there was an excess of deaths from lung cancer that could be attributed to DE exposure. From nearly 20,000 male employees in the early years, those aged 45 to 64 were followed for the 25-year period between 1950 and 1974 (the actual number of employees is not given in the paper), constituting a total of 420,700 man-years at risk. These workers were distributed among five job categories: drivers, garage engineers, conductors, motormen or guards, and engineers (works). Lung cancer were ascertained from death certificates of individuals who died while still employed, or if retired, following diagnosis. Expected death rates were calculated by applying greater London death rates to the population at risk within each job category. Data were calculated in 5-year periods and 5-year age ranges, and the results were combined to obtain the total expected deaths in the required age range for the calendar period. A total of 667 cases of lung cancer was reported, compared with 849 expected, to give a cancer mortality ratio of 79%. In each of the five job categories, the observed numbers were below those expected. Engineers in garages had the highest mortality ratio, 90%, motormen and guards had a mortality ratio of 87%, and both the bus drivers and conductors had mortality ratios of 75%. The engineers in the central works had a mortality ratio of 66%. These mortality ratios did not differ significantly from each other. Environmental sampling was done at one garage, on one day in 1979, for benzo[*a*]pyrene (B[*a*]P) concentrations and was compared with corresponding values recorded in 1957. Concentrations of B[*a*]P recorded in 1957 were at least 10 times greater than those measured in 1979.

This study failed to find any association between DE and occurrence of lung cancer, which may be due to several methodologic limitations. The lung cancer deaths were ascertained while the workers were employed (the worker either died of lung cancer or retired after lung cancer was diagnosed). Although man-years at risk were based on the entire cohort, no attempt was made to trace or evaluate the individuals who had resigned from the London transport company for any other reason. Hence, information on resignees who may have had significant exposure to DE, and on lung cancer deaths among them, was not available for analysis. This may have led to a dilution effect, resulting in underascertainment of observed lung cancer deaths and underestimation of mortality ratios. Eligibility criteria for inclusion in the cohort, such as starting date and length of service with the company, were not specified. Therefore, there may not have been sufficient latency for the development of lung cancer. Use of greater London population death rates to obtain expected number of deaths may have resulted in a deficit in mortality ratios reflecting the "healthy worker effect." Investigators did not categorize the five

job categories either by qualitative or quantitative levels of DE exposure; neither did they use an internal comparison group to derive risk estimates.

The age range considered for this study was limited (45 to 64 years of age) for the period between 1950 and 1974. It is not clear whether this age range was applied to calendar year 1950 or 1974, or at the midpoint of the 25-year follow-up period. No analyses were presented either by latency or by duration of employment (surrogate for exposure). The environmental survey based on B[*a*]P concentrations suggests that the cohort in its earlier years was exposed to much higher concentrations of environmental contaminants than currently exist. It is not clear when the reduction in B[*a*]P concentration occurred, because there are no environmental readings available between 1957 and 1979. It is also important to note that the concentrations of B[*a*]P inside the garage in 1957 were not very different from those outside the garage, thus indicating that exposure for garage workers was not much different from that of the general population. Thus, this study fails to provide either positive or negative association between the DE exposure and the occurrence of lung cancer.

7.2.1.2. *Howe et al. (1983): Cancer Mortality (1965 to 1977) in Relation to Diesel Fumes and Coal Exposure in a Cohort of Retired Railroad Workers*

This is a retrospective cohort study of the mortality experience of 43,826 male pensioners of the Canadian National Railroad (CNR) between 1965 and 1977. Members of this cohort consisted of male CNR pensioners who had retired before 1965 and who were known to be alive at the start of that year, as well as those who retired between 1965 and 1977. The records were obtained from a computer file that is regularly updated and used by the company for payment of pensions. To receive a pension, each pensioner must provide, on a yearly basis, evidence that he is alive. Specific cause of death among members of this cohort was ascertained by linking these records to the Canadian Mortality Data Base, which contains records of all deaths registered in Canada since 1950. Of the 17,838 deaths among members of the cohort between 1965 and 1977, 16,812 (94.4%) were successfully linked to a record in the mortality file. A random sample manual check on unlinked data revealed that failure to link was due mainly to some missing information on the death records.

Occupation at time of retirement was used by the Department of Industrial Relations to classify workers into three diesel fume and coal dust exposure categories: (1) nonexposed, (2) possibly exposed, and (3) probably exposed. Person-years of observation were calculated and classified by age at observation in 5-year age groups (35 to 39, 40 to 44, . . . , 80 to 84, and ≥85 years). The observed deaths were classified by age at death for different cancers, for all cancers combined, and for all causes of death combined. Standard mortality ratios (SMRs) were then calculated using rates of the Canadian population for the period between 1965 and 1977. The

relative risks were calculated using the three exposure categories: nonexposed, possibly exposed, and probably exposed.

Both total mortality (SMR = 95, $p<0.001$) and all cancer deaths (SMR = 99, $p>0.05$) were close to that expected for the entire cohort. Analysis by exposure to diesel fume levels in the three categories (nonexposed, possibly exposed, and probably exposed) revealed an increased relative risk for lung cancer among workers with increasing exposure to diesel fumes. The relative risk for nonexposed workers was presumed to be 1.0; for those possibly exposed, the relative risk was significantly elevated to 1.2 (p=0.013); and for those probably exposed, it was significantly elevated to 1.35 (p=0.001). The corresponding rates for exposure to varying levels of coal dust were very similar at 1.00, 1.21 (p=0.012), and 1.35 (p=0.001), respectively. The trend tests were highly significant for both exposures ($p<0.001$). Analysis performed after the exclusion of individuals who worked in the maintenance of steam engines, and hence were exposed to high levels of asbestos, yielded a risk of lung cancer of 1.00, 1.21, and 1.33 for those nonexposed, possibly exposed, and probably exposed to DE, respectively, with a highly significant trend ($p<0.001$).

An analysis done on individuals who retired prior to 1950 showed the relative risk of lung cancer among nonexposed, possibly exposed, and probably exposed to be 1.00, 0.70, and 0.44, respectively, based on fewer than 15 deaths in each category. A similar analysis of individuals who retired after 1950 found the results in the same categories to be 1.00, 1.23, and 1.40, respectively. Although retirement prior to 1950 indicated exposure to coal combustion fumes alone, retirement after 1950 shows the results of mixed exposure to coal combustion fumes and diesel fumes. As there was considerable overlap between occupations involving probable exposure to diesel fumes and probable exposure to coal, and as most members of the cohort were employed during the years in which the transition from coal to diesel occurred, it was difficult to distinguish whether lung cancer was associated with exposure to coal combustion fumes or diesel fumes or a mixture of both.

Although this study showed a highly significant dose-response relationship between diesel fumes and lung cancer, it has some methodological limitations. There were concurrent exposures to both diesel fumes and coal combustion fumes during the transition period; therefore, misclassification of exposure may have occurred, because only occupation at retirement was available for analysis. It is possible that the elevated response observed for lung cancer was due to the combined effects of exposure to both coal dust/coal combustion products and diesel fumes and not just one or the other. However, deaths due to lung cancer were not elevated among workers who retired prior to the 1950s and thus would have been primarily exposed to coal dust/coal combustion products. Furthermore, it should be noted that so far coal dust has not been demonstrated to be a pulmonary carcinogen in studies of coal miners. This

study was restricted to deaths among retired workers; therefore, it is unclear if a worker who developed lung cancer when actively employed and filed for a disability claim instead of retirement claim would be included in the study or not. Thus, it is possible that workers with heavy exposure might have been excluded from the study. Neither information on duration of employment in diesel work, nor coal dust-related jobs other than those held at retirement, nor details of how the exposure categories were created was provided. Therefore, it was not possible to evaluate whether this omission would have led to an under- or overestimate of the true relative risk. Although information on potential confounders such as smoking is lacking, the use of an internal comparison group to compute the relative risks minimizes the potential for confounding by smoking, as there is no reason to assume different smoking patterns among individuals exposed to DE versus those not exposed. Despite these limitations, this study provides suggestive evidence toward a causal association between exposure to DE and excess lung cancer.

7.2.1.3. *Rushton et al. (1983): Epidemiological Survey of Maintenance Workers in the London Transport Executive Bus Garages and Chiswick Works*

This is a retrospective mortality cohort study of male maintenance workers employed for at least 1 continuous year between January 1, 1967, and December 31, 1975, at 71 London transport bus (also known as rolling stock) garages and at Chiswick Works. The following information was obtained from computer listings: surname with initials, date of birth, date of joining company, last or present job, and location of work. For those individuals who left their job, date of and reason for leaving were also obtained. For those who died in service or after retirement, and for men who had resigned, full name and last known address were obtained from an alphabetical card index in the personnel department. Additional tracing of individuals who had left was carried out through social security records. The area of residence was assumed to be close to their work; therefore place of work was coded as residence. One hundred different job titles were coded into 20 broader groups. These 20 groups were not ranked for DE exposure, however. The reason for leaving was coded as died in service, retired, or other. The underlying cause of death was coded using the eighth revision of the International Classification of Diseases (ICD). Person-years were calculated from date of birth and dates of entry to and exit from the study using the man-years computer language program. The workers were then subdivided into 5-year age and calendar period groups. The expected number of deaths was calculated by applying the 5-year age and calendar period death rates of the comparison population with the person-years of corresponding groups. The mortality experience of the male population in England and Wales was used as the comparison population. Significance values were calculated for the difference between the observed and expected deaths, assuming a Poisson distribution.

The person-years of observation totaled 50,008 and were contributed by 8,490 individuals in the study, with a mean follow-up of 5.9 years. Only 2.2% (194) of the men were not traced. Observed deaths from all causes were significantly lower than expected (O = 495, $p<0.001$). Observed deaths from all neoplasms and cancer of the lung were approximately the same as those expected. The only significant excess observed, for cancer of the liver and gall bladder at Chiswick Works, was based on four deaths ($p<0.05$). A few job groups showed a significant excess of risks for various cancers. All the excess deaths observed for the various job groups, except for the general hand category, were based on very small numbers (usually fewer than five) and merited cautious interpretation. Only a notable excess in the general hand category for lung cancer was based on as many as 48 cases (SMR = 133, $p<0.03$).

This mortality study did not demonstrate any cancer excess. Details of work history were not obtained to permit any analysis by DE exposure. The study's limitations, including small sample size, short duration of follow-up (average of only 6 years), and lack of sufficient latency period, make it inadequate to draw any conclusions.

7.2.1.4. *Wong et al. (1985): Mortality Among Members of a Heavy Construction Equipment Operators Union With Potential Exposure to DE Emissions*

This retrospective mortality study was conducted on a cohort of 34,156 male members of a heavy construction equipment operators union with potential exposure to DE emissions. Study cohort members were identified from records maintained at Operating Engineers' Local Union No. 3-3A in San Francisco, CA. This union has maintained both work and death records on all its members since 1964. Individuals with at least 1 year of membership in this union between January 1, 1964, and December 31, 1978, were included in the study. Work histories of the cohort were obtained from job dispatch computer tapes. The study follow-up period was January 1964 to December 1978. Death information was obtained from a trust fund, which provided information on retirement dates, vital status, and date of death for those who were entitled to retirement and death benefits. Approximately 50% of the cohort had been union members for less than 15 years, whereas the other 50% had been union members for 15 years or more. The average duration of membership was 15 years. As of December 31, 1978, 29,046 (85%) cohort members were alive, 3,345 (9.8%) were dead, and 1,765 (5.2%) remained untraced. Vital status of 10,505 members who had left the union as of December 31, 1978, was ascertained from the Social Security Administration. Death certificates were obtained from appropriate State health departments. Altogether, 3,243 deaths (for whom death certificates were available) in the cohort were coded using the seventh revision of the ICD. For 102 individuals, death certificates could not be obtained, only the date of death; these individuals were included in the calculation of the SMR for all causes of death but were deleted from the

cause-specific SMR analyses. Expected deaths and SMRs were calculated using the U.S. national age-sex-race cause-specific mortality rates for 5-year time periods between 1964 and 1978. The entire cohort population contributed to 372,525.6 person-years in this 15-year study period.

A total of 3,345 deaths was observed, compared with 4,109 expected. The corresponding SMR for all causes was 81 (p=0.01), which is consistent with the "healthy worker effect." A total of 817 deaths was attributed to malignant neoplasms, slightly fewer than the 878 expected based on U.S. white male cancer mortality rates (SMR = 93, p=0.05). Mostly there were SMR deficits for cause-specific cancers, including lung cancer for the entire cohort (SMR = 99, O = 309). The only significant excess SMR was observed for cancer of the liver (SMR = 167, O = 23, p<0.05).

Analysis by length of union membership as a surrogate of duration for potential exposure showed statistically significant increases in SMRs of cancer of the liver (SMR = 424, p<0.01) in the 10- to 14-year membership group and of the stomach (SMR = 248, p<0.05) in the 5- to 9-year membership group. No cancer excesses were observed in the 15- to 19-year and 20+-year membership groups. Although the SMR for cancer of the lung had a statistically significant deficit in the less-than-5-year duration group, it showed a positive trend with increasing length of membership, which leveled off after 10 to 14 years.

Cause-specific mortality analysis by latency period showed a positive trend for SMRs of all causes of death, although all of them were statistically significant deficits, reflecting the diminishing "healthy worker effect." This analysis also demonstrated a statistically significant SMR excess for cancer of the liver (10- to 19-year group, SMR = 258). The SMR for cancer of the lung showed a statistically significant deficit for a <10-year latency but showed a definite positive trend with increasing latency.

In addition to these analyses of the entire cohort, similar analyses were carried out in various subcohorts. Analyses of retirees, 6,678 individuals contributing to 32,670 person-years, showed statistically significant increases (p<0.01) in SMRs for all cancers; all causes of death; cancers of the digestive system, large intestine, respiratory system, and lung; emphysema; and cirrhosis of the liver. The other two significant excesses (p<0.01) were for lymphosarcoma and reticulosarcoma and nonmalignant respiratory diseases. Further analysis of the 4,075 retirees (18,678 person-years) who retired at age 65 or who retired earlier but had reached the age of 65 revealed statistically significant SMR increases (p<0.05) for all cancers, cancer of the lung, and lymphosarcoma and reticulosarcoma.

To analyze cause-specific mortality by job held (potential exposure to DE emissions), 20 functional job titles were used, which were further grouped into three potential categories: high exposure, low exposure, and unknown exposure. A person was classified in a job title if he ever

worked on that job. Based on this classification system, if a person had ever worked in a high-exposure job title he was included in that group, even though he may have worked for a longer time in a low-exposure group or in an unknown exposure group. Information on length of work in any particular job, hence indirect information on potential length of exposure, was not available either.

For the high-exposure group a statistically significant excess was observed for cancer of the lung among bulldozer operators who had 15 to 19 years of membership and 20+ years of follow-up (SMR = 343, $p<0.05$). This excess was based on 5 out of 495 deaths observed in this group of 6,712 individuals, who contributed 80,328 person-years of observation.

The cause-specific mortality analysis in the low-exposure group revealed statistically significant SMR excesses in individuals who had ever worked as engineers. These excesses were for cancer of the large intestine (SMR = 807, O = 3, $p<0.05$) among those with 15 to 19 years of membership and length of follow-up of at least 20 years, and cancer of the liver (SMR = 872, O = 3, $p<0.05$) among those with 10 to 14 years of membership and length of follow-up of 10 to 19 years. There were 7,032 individuals who contributed to 78,403 person-years of observation in the low-exposure group.

For the unknown exposure group, a statistically significant SMR was observed for motor vehicle accidents only (SMR = 174, O = 21, $p<0.05$). There were 3,656 individuals who contributed to 33,388 person-years of observation in this category.

No work histories were available for those who started their jobs before 1967 and for those who held the same job prior to and after 1967. This group comprised 9,707 individuals (28% of the cohort) contributing to 104,448 person-years. Statistically significant SMR excesses were observed for all cancers (SMR = 112, O = 339, $p<0.05$) and cancer of the lung (SMR = 119, O = 141, $p<0.01$). A significant SMR elevation was also observed for cancer of the stomach (SMR = 199, O = 30, $p<0.01$).

This study demonstrates a statistically significant excess for cancer of the liver but also shows statistically significant deficits in cancers of the large intestine and rectum. It may be, as the authors suggested, that the liver cancer cases actually resulted from metastases from the large intestine and/or rectum, as tumors of these sites will frequently metastasize to the liver. The excess in liver cancer mortality and the deficits in mortality that are due to cancer of the large intestine and rectum could also, as the authors indicate, be due to misclassification. Both possibilities have been considered by the investigators in their discussion.

Cancer of the lung showed a positive trend with length of membership as well as with latency, although none of the SMRs were statistically significant except for workers without any work histories. The individuals without any work histories may have been the ones who were in their jobs for the longest period of time, because workers without job histories included those

who had the same job before and after 1967 and thus may have worked 12 to 14 years or longer. If they had belonged to the category in which heavy exposure to DE emissions was very common for this prolonged time, then the increase in lung cancer, as well as stomach cancer, might be linked to DE. Further information on those without work histories should be obtained if possible, because such information may be quite informative with regard to the evaluation of the carcinogenicity of DE.

The study design is adequate, covers about a 15-year observation period, has a large enough population, and is appropriately analyzed; however, it has too many limitations to permit any conclusions. First, no exposure histories are available; one has to make do with job histories, which provide limited information on exposure level. Any person who ever worked at the job, or any person working at the same job over any period of time, is included in the same category; this would have a dilution effect, because extremely variable exposures were considered in the study. Second, the length of time worked in any particular job is not available. Third, work histories were not available for 9,707 individuals, who contributed 104,448 person-years, a large proportion of the study cohort (28%). These individuals happen to show the most evidence of a carcinogenic effect. Confounding by alcohol consumption for cancer of the liver and smoking for emphysema and cancer of the lung was not ruled out. Fourth, 15 years' follow-up may not provide sufficient latency to observe excess lung cancer. Last, although 34,156 members were eligible for the study, the vital status of 1,765 individuals was unknown. Nevertheless, they were still considered in the denominator of all the analyses. The investigators fail to mention how the person-year calculation for these individuals was handled. Also, some of the person-years might have been overestimated, as people may have paid the dues for a particular year and then left work. These two causes of overestimation of the denominator may have resulted in some or all the SMRs being underestimated.

7.2.1.5. *Edling et al. (1987): Mortality Among Personnel Exposed to DE*

This retrospective cohort mortality study of bus company employees investigated a possible increased mortality of cardiovascular diseases and cancers from DE exposure. The cohort comprised all males employed at five different bus companies in southeastern Sweden between 1950 and 1959. Based on information from personnel registers, individuals were classified into one or more categories and could have contributed person-years at risk in more than one exposure category. The study period was from 1951 to 1983; information was collected from the National Death Registry, and copies of death certificates were obtained from the National Bureau of Statistics. Workers who died after age 79 were excluded from the study because diagnostic procedures were likely to be more uncertain at higher ages (according to investigators). The cause-, sex-, and age-specific national death rates in Sweden were applied to

the 5-year age categories of person-years of observation to determine expected deaths for all causes, malignant diseases, and cardiovascular diseases. A Poisson distribution was used to calculate *p*-values and confidence limits for the ratio of observed to expected deaths. The total cohort of 694 men (after loss of 5 men to follow-up) was divided into three exposure categories: (1) clerks with lowest exposure, (2) bus drivers with moderate exposure, and (3) bus garage workers with highest exposure.

The 694 men provided 20,304 person-years of observation, with 195 deaths compared with 237 expected. A deficit in cancer deaths largely accounted for this lower-than-expected mortality in the total cohort. Among subcohorts, no difference between observed and expected deaths for total mortality, total cancers, or cardiovascular causes was observed for clerks (lowest diesel exposure), bus drivers (moderate diesel exposure), and garage workers (high diesel exposure). The risk ratios for all three categories were less than 1 except for cardiovascular diseases among bus drivers, which was 1.1.

When the analysis was restricted to members who had at least a 10-year latency period and either any exposure or an exposure exceeding 10 years, similar results were obtained, with fewer neoplasms than expected, whereas cardiovascular diseases showed risk around or slightly above unity.

Five lung cancer deaths were observed among bus drivers who had moderate DE exposure, whereas seven were expected. The only other lung cancer death was observed among bus garage workers who had the highest DE exposure. This study's major limitations, including small size and poor data on DE exposure, make it inadequate to draw any conclusions.

7.2.1.6. *Boffetta and Stellman (1988): DE Exposure and Mortality Among Males in the American Cancer Society Prospective Study*

Boffetta and Stellman conducted a mortality analysis of 461,981 males with known smoking history and vital status at the end of the first 2 years of follow-up. The analysis was restricted to males aged 40 to 79 years in 1982 who enrolled in the American Cancer Society's prospective mortality study of cancer. Mortality was analyzed in relation to exposure to DE and to employment in selected occupations related to DE exposure. In 1982, more than 77,000 American Cancer Society volunteers enrolled more than 1.2 million men and women from all 50 States, the District of Columbia, and Puerto Rico in a long-term cohort study, the Cancer Prevention Study II (CPS-II). Enrollees were usually friends, neighbors, or relatives of the volunteers; enrollment was by family groups, with at least one person in the household 45 years of age or older. Subjects were asked to fill out a four-page confidential questionnaire and return it in a sealed envelope. The questionnaire included history of cancer and other diseases; use of medications and vitamins; menstrual and reproductive history; occupational history; and

information on diet, drinking, smoking, and other habits. The questionnaire also included three questions on occupation: (1) current occupation, (2) last occupation, if retired, and (3) job held for the longest period of time, if different from the other two. Occupations were coded to an ad hoc two-digit classification in 70 categories. Exposures at work or in daily life to any of the 12 groups of substances were also ascertained. These included diesel engine exhausts, asbestos, chemicals/acids/solvents, dyes, formaldehyde, coal or stone dusts, and gasoline exhausts. Volunteers checked whether their enrollees were alive or dead and recorded the date and place of all deaths every other year during the study. Death certificates were then obtained from State health departments and coded by a trained nosologist according to a system based on the ninth revision of the ICD.

The data were analyzed to determine the mortality for all causes and lung cancer in relation to DE exposure, mortality for all causes and lung cancer in relation to employment in selected occupations with high DE exposure, and mortality from other causes in relation to DE exposure. The incidence-density ratio was used as a measure of association, and test-based confidence limits were calculated by the Miettinen method. For stratified analysis, the Mantel-Haenszel method was used for testing linear trends. Although data on 476,648 subjects comprising 939,817 person-years of risk were available for analysis, 3% of the subjects (14,667) had not given any smoking history, and 20% (98,026) did not give information on DE exposure and were therefore excluded from the main DE analysis. Among individuals who had provided DE exposure history, 62,800 were exposed and 307,143 were not exposed. Comparison of the population with known information on DE exposure with the excluded population with no information on DE exposure showed that the mean ages were 54.7 and 57.7 years, the nonsmokers were 72.4% and 73.2%, and the total mortality rates per 1,000 per year were 23.0% and 28.8%, respectively.

All-cause mortality was elevated among railroad workers (relative risk [RR] = 1.43, 95% confidence interval [CI] = 1.2, 1.72), heavy equipment operators (RR = 1.7, 95% CI = 1.19, 2.44), miners (RR = 1.34, 95% CI = 1.06, 1.68), and truck drivers (RR = 1.19, 95% CI = 1.07, 1.31). The age-adjusted lung cancer relative risk was elevated significantly (RR = 1.41, 95% CI = 1.19,1.66), which was slightly decreased to 1.31 (95% CI = 1.10, 1.54). For lung cancer mortality the age- and smoking-adjusted risks were significantly elevated for miners (RR = 2.67, 95% CI = 1.63, 4.37) and heavy equipment operators (RR = 2.60, 95% CI = 1.12, 6.06). Risks were also elevated, but not significantly, for railroad workers (RR = 1.59, 95% CI = 0.94, 2.69) and truck drivers (RR = 1.24, 95% CI = 0.93, 1.66). These risks were calculated with the Mantel-Haenszel method, controlling for age and smoking. Although the relative risk was nonsignificant for truck drivers, a small dose-response effect was observed when duration of DE exposure was examined. For drivers who worked for 1 to 15 years, the relative risk was 0.87,

whereas for drivers who worked for more than 16 years, the relative risk was 1.33 (95% CI = 0.64, 2.75). Relative risks for lung cancer were not presented for other occupations. Mortality analysis for other causes and DE exposure showed a significant excess of deaths ($p<0.05$) in the following categories: cerebrovascular disease, arteriosclerosis, pneumonia, influenza, cirrhosis of the liver, and accidents.

The main strength of this study is detailed information on smoking. The two main methodologic concerns are the representativeness of the study population and the quality of information on exposure. The sample, though very large, was composed of volunteers. Thus, the cohort was healthier and less frequently exposed to important risk factors such as smoking and alcohol. Self-administered questionnaires were used to obtain data on occupation and DE exposure. None of this information was validated. Nearly 20% of the individuals had an unknown exposure status to DE, and they experienced a higher mortality for all causes and lung cancer than both the DE exposed and unexposed groups. This could have introduced a substantial bias in the estimate of the association. Given that all DE exposure occupations, such as heavy equipment operators, truck drivers, and railroad workers, showed elevated lung cancer risk, this study is suggestive of a causal association. It should be noted that after adjusting for smoking, the RR reduced slightly from 1.41 to 1.31 and remained significant, indicating that observed excess of lung cancer was associated mainly with DE exposure.

7.2.1.7. *Garshick et al. (1988): A Retrospective Cohort Study of Lung Cancer and DE Exposure in Railroad Workers*

An earlier case-control study of lung cancer and DE exposure in U.S. railroad workers by these investigators had demonstrated a relative odds of 1.41 (95% CI = 1.06, 1.88) for lung cancer with 20 years of work in jobs with DE exposure. To confirm these results, a large retrospective cohort mortality study was conducted by the same investigators. Data sources for the study were the work records of the U.S. Railroad Retirement Board (RRB). The cohort was selected based on job titles in 1959, which was the year by which 95% of the locomotives in the United States were diesel powered. DE exposure was considered to be a dichotomous variable depending on yearly job codes between 1959 and death or retirement through 1980. Industrial hygiene evaluations and descriptions of job activities were used to classify jobs as exposed or unexposed to diesel emissions. A questionnaire survey of 534 workers at one of the railroads where workers were asked to indicate the amount of time spent in railroad locations, either near or away from sources of DE, was used to validate this classification. Workers selected for this survey were actively employed at the time of the survey, 40 to 64 years of age, started work between 1939 and 1949 in the job codes sampled in 1959, and eligible for railroad benefits. To qualify for benefits, a worker must have had 10 years or more of service with the railroad and

should not have worked for more than 2 years in a nonrailroad job after leaving railroad work. Workers with recognized asbestos exposure, such as repair of asbestos-insulated steam locomotive boilers, passenger cars, and steam pipes, or railroad building construction and repairs, were excluded from the job categories selected for study. However, a few jobs with some potential for asbestos exposure were included in the cohort, and the analysis was done both ways, with and without them.

The death certificates for all subjects identified in 1959 and reported by the RRB to have died through 1980 were searched. Twenty-five percent of them were obtained from the RRB and the remainder from the appropriate State departments of health. Coding of cause of death was done without knowledge of exposure history, according to the eighth revision of the ICD. If the underlying cause of death was not lung cancer, but was mentioned on the death certificate, it was assigned as a secondary cause of death, so that the ascertainment of all cases was complete. Workers not reported by the RRB to have died by December 31, 1980, were considered to be alive. Deceased workers for whom death certificates had not been obtained or, if obtained, did not indicate cause of death, were assumed to have died of unknown causes.

Proportional hazard models were fitted that provided estimates of relative risk for death caused by lung cancer using the partial likelihood method described by Cox, using the time dimension being the time since first entry into the cohort. The model also controlled for the birth year and the calendar time. The 95% confidence intervals were constructed using the asymptotic normality of the estimated regression coefficients of the proportional hazards model. Exposure was analyzed by DE-exposed jobs in 1959 and by cumulative number of years of DE exposure through 1980. Directly standardized rate ratios for deaths from lung cancer were calculated for DE exposed compared with unexposed for each 5-year age group in 1959. The standardized rates were based on the overall 5-year person-year time distribution of individuals in each age group starting in 1959. The only exception to this was between 1979 and 1980, when a 2-year person-year distribution was used. The Mantel-Haenszel analogue for person-year data was used to calculate 95% confidence intervals for the standardized rate ratios.

The cohort consisted of 55,407 workers, 19,396 of whom had died by the end of 1980. Death certificates were not available for 11.7% of all deaths. Of the 17,120 deaths for whom death certificates were obtained, 48.4% were attributable to diseases of the circulatory system, whereas 21% were attributable to all neoplasms. Of all neoplasms, 8.7% (1,694 deaths) were due to lung cancer. A higher proportion of workers in the younger age groups, mainly brakemen and conductors, were exposed to DE, while a higher proportion of workers in the older age groups were potentially exposed to asbestos. In a proportional hazards model, analyses by age in 1959 found a relative risk of 1.45 (95% CI = 1.11, 1.89) among the age group 40 to 44 years and a relative risk of 1.33 (95% CI = 1.03, 1.73) for the age group 45 to 49 years. Risk estimates in

the older age groups 50 to 54, 55 to 59, and 60 to 64 years were 1.2, 1.18, and 0.99, respectively, and were not statistically significant. The two youngest age groups in 1959 had workers with the highest prevalence and longest duration of DE exposure and lowest exposure to asbestos. When potential asbestos exposure was considered as a confounding variable in a proportional hazards model, the estimates of relative risk for asbestos exposure were all near null value and not significant. Analysis of workers exposed to DE in 1959 (n = 42,535), excluding workers with potential past exposure to asbestos, yielded relative risks of 1.57 (95% CI = 1.19, 2.06) and 1.34 (95% CI = 1.02, 1.76) in the 1959 age groups 40 to 44 years and 45 to 49 years. Directly standardized rate ratios were also calculated for each 1959 age group based on DE exposure in 1959. The results confirmed those obtained by using the proportional hazards model.

Relative risk estimates were then obtained using duration of DE exposure as a surrogate for dose. In a model that used years of exposure up to and including exposure in the year of death, no exposure duration-response relationship was obtained. When analysis was done by disregarding exposure in the year of death and 4 years prior to death, the risk of dying from lung cancer increased with the number of years worked in a diesel-exhaust-exposed job. In this analysis, exposure to DE was analyzed by exposure duration groups and in a model entering age in 1959 as a continuous variable. The workers with greater than 15 years of exposure had a relative risk of lung cancer of 1.72 (95% CI = 1.27, 2.33). The risk for 1 to 4 years of cumulative exposure was 1.20 (95% CI = 1.01, 1.44); for 5 to 9 years of cumulative exposure, it was 1.24 (95% CI = 1.06, 1.44); and for 10 to 14 years of cumulative exposure, it was 1.32 (95% CI = 1.13, 1.56).

The results of this study, demonstrating a positive association between DE exposure and increased lung cancer, are consistent with the results of the case-control study conducted by the same investigators in railroad workers dying of lung cancer from March 1981 through February 1982. This cohort study has addressed many of the weaknesses of the other epidemiologic studies. The large sample size (55,400) allowed sufficient power to detect small risks and also permitted the exclusion of workers with potential past exposure to asbestos. The stability of job career paths in the cohort ensured that of the workers 40 to 44 years of age in 1959 classified as DE-exposed, 94% of the cases were still in DE-exposed jobs 20 years later.

The main limitation of the study is the lack of quantitative data on exposure to DE in either individual workers or overall job categories. This is one of the few studies in which industrial hygiene measurements of DE were done. These measurements were correlated with job titles to divide the cohort in dichotomous exposure groups of exposed and nonexposed. This may have led to an underestimation of the risk of lung cancer because exposed groups included individuals with low to high exposure. The number of years exposed to DE was used as a surrogate for dose. The dose, based on duration of employment, was inaccurate because

individuals were working on steam and diesel locomotives during the transition period. It should be noted that the investigators only included exposures after 1959; the duration of exposure prior to 1959 was not known. If the categories of exposure to DE had been set up as no, low, moderate, and high exposure, the results would have been more meaningful, as would the dose-response relationship. Another limitation of this study was its inability to examine the effect of years of exposure prior to 1959 and latency. No adjustment for smoking was made in this study. However, an earlier case-control study done in the same cohort (Garshick et al., 1987) showed no significant difference in the risk estimate after adjusting for smoking. Despite these limitations, the results of this study indicate that occupational exposure to DE is associated with a modest risk (1.5) of lung cancer.

The data of this study were used by Crump et al. (1991) to explore the development of dose-response-based quantitative estimates of lung cancer associated with DE exposure by using diesel exposure estimate data from the industrial hygiene (IH) studies conducted by Hammond (1998) and Woskie et al. (1988a,b). These studies were conducted in conjunction with the Garshick et al. (1988) study. The Woskie et al. (1988a,b) IH studies were conducted in four small northern railroads where the workers were exposed to DE in the early 1980s, prior to the Garshick et al. (1988) epidemiologic study. A total of 39 job titles were identified by Woskie et al. (1988a,b), which were subsequently combined into 13 job groups and finally merged into 5 career exposure job codes as follows: brakers, conductors, and hostlers; clerks; engineers and firers; signal maintainers; and shop workers. The average exposure estimates were assigned to the cohort members by Crump et al. (1991) based on the job codes in 1959. Cumulative exposures were calculated using these average exposures for each job code. The exposures in the IH study by Hammond (1998) were defined as the concentrations of respirable-sized particles (RSP), the adjusted respirable particles (ARP) concentrations, and the adjusted extractable mass (AEM). The concentrations of ARP were estimated in the IH study by removing the particle contribution of environmental tobacco smoke (ETS). Crump et al. (1991) also used another index called total extractable material (TEX), which was the extractable RSP including the particle contribution of ETS. Using these four exposure indices and the regional climates for the United States, Crump et al. (1991) constructed various exposure metrics. They conducted more than 50 analyses based on calendar year, age in 1959, attained age, and five job codes identified in 1959: brakers, conductors, and hostlers; clerks; engineers and firers; signal maintainers; and shop workers; using the exposure metrics. Crump et al. (1991) used the U.S. general population age- and year-specific death rates for comparison and found that the relative risk can be positively or negatively related to the duration of exposure depending on how age was controlled in a model. Their use of the U.S. general population rates instead of the internal unexposed group of railroad workers that was used by Garshick et al. (1988) identified that the

death ascertainment between 1977 and 1980 as incomplete. The Crump et al. (1991) analysis, limited to 1959 through 1976, found an excess lung cancer risk similar to the subsequent Garshick analysis (letter from Garshick, Harvard Medical School, to Chao Chen, U.S. EPA, dated August 15, 1991).

Garshick conducted some additional analyses after confirming the underascertainment of deaths by RRB identified by Crump et al. (1991). He reported that the relationship between years of exposure, when adjusted for attained age and calendar year, was flat to negative depending upon which model was used. He also found that in the years 1977-1980 the death ascertainment was incomplete; approximately 20% to 70% of deaths were missing depending upon the calendar year. Garshick's analysis, based on job titles in 1959 and limited to deaths occurring through 1976, showed that even though the relative risk for all exposure groups was elevated, the youngest workers still had the highest risk of dying of lung cancer.

Crump (1999), on the other hand, reported that the negative dose-response continued to be upheld in his latest analysis when age was controlled more carefully and years of exposure quantified more accurately. Crump (1999) asserted that the negative dose-response trends for lung cancer observed either with the cumulative exposure or with duration of exposure may be due to underascertainment of deaths in the last 4 years of follow-up of the Garshick et al. (1988) study as well as incomplete follow-up in earlier years.

California EPA's (Cal EPA, 1998) Office of Environmental Health Hazard Assessment (OEHHA) used the same railroad worker data for its quantitative risk assessment. The five job categories defined by Woskie et al. (1988a,b) and used by Crump et al. (1991) were combined into three exposure categories: exposed (engineers and firers; brakers, conductors, and hostlers; collectively known as "train workers"), unexposed (clerks and signalmen), and uncertain exposure (shop workers). In its analysis, OEHHA found a positive dose-response and a steadily increasing risk of lung cancer with increasing duration of exposure by using age in 1959 but allowing for an interaction term of age and calendar year in the model. This positive dose-response finding was contradictory to the negative to flat dose-response findings of both Crump et al. (1991) and Garshick (letter from Garshick, Harvard Medical School, to Chao Chen, U.S. EPA, dated August 15, 1991).

The Health Effects Institute (HEI, 1999) convened an expert panel specifically to evaluate strengths and limitations of two epidemiologic studies that had some exposure data, for quantitative risk estimation and to resolve the discrepancies in the dose-response results reported by Garshick et al. (1988), Crump et al. (1991), and OEHHA (Cal EPA, 1998). In their evaluation of the epidemiologic study of railroad worker data for quantitative risk assessment, the panel conducted their own analysis of the Garshick et al. (1988) data. They excluded the last 4 years of follow-up (1977-1980) because of underascertainment of deaths during these years.

The panel categorized the duration of exposure in 12 categories that were basically the duration of employment. The exposure was assumed to be linearly increasing for 15 years prior to 1959. Lags of 5 and 10 years were also considered in the analysis. The job categories based on job held in 1959 were classified as clerks, signalmen, engineers and firers, conductors and brakers, hostlers, and shop workers. For final analysis these were collapsed into three groups: clerks and signalmen, train workers (engineers and firers, conductors and brakers, and hostlers), and shop workers. Seven different models were used. The panel's analysis revealed consistently elevated lung cancer risk for train workers compared with clerks for each duration of employment (1-4, 5-9, 10-14, 15-17, 18+) in years and that shop workers had an intermediate risk of lung cancer. Their analysis also revealed decreasing risk of lung cancer with increasing duration of employment in all three job categories. These findings were similar to those of Garshick (letter from Garshick, Harvard Medical School, to Chao Chen, U.S. EPA, dated August 15, 1991) and Crump et al. (1991).

In addition to differences in adjusting the age (age in 1959 versus attained age) in their respective analyses, these three investigators made different assumptions in estimating exposure patterns in these railroad workers. Garshick et al. (1988) assumed that there was no exposure to DE prior to 1959 and that the exposure to DE was constant throughout the period of follow-up, i. e., 1959 to 1980 (block exposure pattern). Crump et al. (1991) assumed that the exposure to DE increased steadily from 1945 to 1959 to the same level as assumed in the block exposure pattern by Garshick et al. (1988) and then remained constant from 1959 through 1980 (ramp exposure pattern). OEHHA assumed that the exposure increased steeply from 1945 to 1959. The peak exposure attained in 1959 according to OEHHA was twice as high as assumed in the block and ramp exposure patterns by Garshick et al. (1988) and Crump et al. (1991), respectively. The exposures then declined steeply from 1959 to reach the levels assumed in the block and ramp exposure patterns in 1980 (roof exposure pattern). The roof exposure pattern was constructed on the assumption that diesel engines were "smokier" in the past. A detailed discussion of divergent results observed by Crump and Cal EPA can be found in Chapter 8.

The panel discussed various possibilities for the negative dose-response found among train workers and to a lesser extent among shop workers. They asserted that several types of biases could affect the data, alone or in combination, and mask a true positive association. The biases enumerated by the panel were: unmeasured confounding by smoking, exposure to other sources of pollution, previous occupational exposures, exposure misclassification, use of "duration of employment" as a surrogate measure for exposure, healthy worker survivor effect, and differential or incomplete ascertainment of lung cancer deaths (for detailed discussion of how an individual bias affects the results, please see HEI, 1999). The panel concluded, "However, despite the reason or reasons why the relative risks in these data decrease with

duration of employment, the lack of a positive exposure-response association in the railroad worker cohort substantially weakens that study's potential to provide a reliable quantitative estimate of risk of exposure to diesel engine emissions." Thus, the panel recommended against using the current railroad worker data as the basis for quantitative risk assessment in ambient settings.

The panel also reported that the Garshick et al. study (1987, 1988) had several strengths, such as a large number of study subjects (55,407 subjects, including 1,694 lung cancer deaths in the cohort study and 1,256 lung cancer cases for the case-control study). The workers were employed in an industry where many of them were exposed to DE. Confounding by asbestos was handled by either excluding certain job categories from the analyses or controlling for it in the analyses. Confounding by smoking was controlled in the analyses of case-control study. The panel concluded that the overall results of the Garshick studies were generally consistent with findings of a weak association between exposure to DE and occurrence of lung cancer.

Thus, it should be noted that although the railroad worker data are unsuitable for quantitative risk assessment, they provide qualitative support for a positive association between exposure to DE and occurrence of lung cancer.

7.2.1.8. *Gustavsson et al. (1990): Lung Cancer and Exposure to DE Among Bus Garage Workers*

A retrospective mortality study (from 1952 to 1986), cancer incidence study (from 1958 to 1984), and nested case-control study were conducted among a cohort of 708 male workers from five bus garages in Stockholm, Sweden, who had worked for at least 6 months between 1945 and 1970. Thirteen individuals were lost to follow-up, reducing the cohort to 695.

Information was available on location of workplace, job type, and beginning and ending of work periods. Workers were traced through a computerized register of the living population, death and burial books, and data from the Stockholm city archives.

For the cohort mortality analyses, death rates of the general population of greater Stockholm were used. Death rates of occupationally active individuals, a subset of the general population of greater Stockholm, were used as a second comparison group to reduce the bias from "healthy worker effect." Mortality analysis was conducted using the "occupational mortality analysis program" (OCMAP-PC). For cancer incidence analysis, the "epidemiology in Linköping" (EPILIN) program was used, with the incidence rates obtained from the cancer registry.

For the nested case-control study, both dead and incident primary lung cancers identified in the register of cause of deaths and the cancer register were selected. Six controls matched on age ± 2 years, selected from the noncases at the time of the diagnosis of cases, were drawn at

random without replacements. Matched analyses were done to calculate odds ratios using conditional logistic regression. The EGRET and Epilog programs were used for these analyses.

DE and asbestos exposure assessments were performed by industrial hygienists based on the intensity of exposure to DE and asbestos, specific for workplace, work task, and calendar time period. A DE exposure assessment was based on (1) amount of emission (number of buses, engine size, running time, and type of fuel), (2) ventilatory equipment and air volume of the garages, and (3) job types and work practices. Based on detailed historical data and very few actual measurements, relative exposures were estimated (these were not absolute exposure levels). The scale was set to 0 for unexposed and 1 for lowest exposure, with each additional unit increase corresponding to a 50% increase in successive intensity (i.e., 1.5, 2.25, 3.38, and 5.06).

Based on personal sampling of asbestos during 1987, exposures were estimated and time-weighted annual mean exposures were classified on a scale of three degrees (0, 1, and 2). Cumulative exposures for both DE and asbestos were calculated by multiplying the level of exposure by the duration of every work period. An exposure index was calculated by adding for every individual contribution from all work periods for both DE and asbestos. Four DE index classes were created: 0 to 10, 10 to 20, 20 to 30, and >30. The four asbestos index classes were 0 to 20, 20 to 40, 40 to 60, and >60. The cumulative exposure indices were used for the nested case-control study.

Excesses were observed for all cancers and some other site-specific cancers using both comparison populations for the cohort mortality study, but none of them was statistically significant. Based on 17 cases, SMRs for lung cancer were 122 and 115 using Stockholm occupationally active and general population, respectively. No dose-response was observed with increasing cumulative exposure in the mortality study. The cancer incidence study reportedly confirmed the mortality results (results not given).

The nested case-control study, on the other hand, showed increasing risk of lung cancer with increasing exposure. Using 0 to 10 DE exposure index as the comparison group yielded RRs of 1.34 (95% CI = 1.09 to 1.64), 1.81 (95% CI = 1.20 to 2.71), and 2.43 (95% CI = 1.32 to 4.47) for the DE indices 10 to 20, 20 to 30, and >30, respectively. The study was based on 17 cases and 6 controls for each case matched on age ± 2 years. Adjustment for asbestos exposure did not change the lung cancer risk for DE.

The main strength of this study is the detailed exposure matrices constructed for both DE and asbestos exposure, although they were based primarily on job tasks and very few actual measurements. There are a few methodological limitations to this study. The cohort is small and there were only 17 lung cancer deaths; thus the power is low. Exposure or outcome may be misclassified, although any resulting bias in the relative risk estimates is likely to be toward

unity, because exposure classification was done independently of the outcome. Although the analysis by dose indices was done, no latency analysis was performed. Although data on smoking were missing, it is unlikely to confound the results because this is a nested case-control study; therefore, smoking is not likely to be different among the individuals irrespective of their exposure status to DE. Overall, this study provides some support to the excess lung cancer results found earlier among populations exposed to DE.

7.2.1.9. *Hansen (1993): A Follow-up Study on the Mortality of Truck Drivers*

This is a retrospective cohort mortality study of unskilled male laborers, ages 15 to 74 years, in Denmark, identified from a nationwide census file of November 9, 1970. The exposed group included all truck drivers employed in the road delivery or long-haul business (14,225). The unexposed group included all laborers in certain selected occupational groups considered to be unexposed to fossil fuel combustion products and to resemble truck drivers in terms of work-related physical demands and various personal background characteristics (43,024).

Through automatic record linkage between the 1970 census register (the Central Population Register 1970 to 1980) and the Death Certificate Register (1970 to 1980), the population was followed for cause-specific mortality or emigration up to November 9, 1980. Expected number of deaths among truck drivers was calculated by using the 5-year age group and 5-year time period death rates of the unexposed group and applying them to the person-years accumulated by truck drivers. ICD Revision 8 was used to code the underlying cause of death. Test-based CIs were calculated using Miettinen's method. A Poisson distribution was assumed for the smaller numbers, and CI was calculated based on exact Poisson distribution (Ciba-Geigy). Total person-years accrued by truck drivers were 138,302, whereas for the unexposed population, they were 407,780. There were 627 deaths among truck drivers and 3,811 deaths in the unexposed group. Statistically significant excesses were observed for all cancer mortality (SMR = 121, 95% CI = 104 to 140); cancer of respiratory organs (SMR = 160, 95% CI = 128 to 198), which was due mainly to cancer of bronchus and lung (SMR = 160, 95% CI = 126 to 200); and multiple myeloma (SMR = 439, 95% CI = 142 to 1,024). When lung cancer mortality was further explored by age groups, excesses were observed in most age groups (30 to 39, 45 to 49, 50 to 54, 55 to 59, 60 to 64, and 65 to 74), but there were small numbers of deaths in each group when stratified by age, and the excesses were statistically significant for the 55 to 59 (SMR = 229, O = 19, 95% CI = 138 to 358) and 60 to 64 (SMR = 227, O = 22, 95% CI = 142 to 344) age groups only.

As acknowledged by the author, the study has quite a few methodologic limitations. The exposure to DE is assumed in truck drivers based on use of diesel-powered trucks, but no validation of qualitative or quantitative exposure is attempted. It is also not known whether any

of these truck drivers or any other laborers had changed jobs after the census of November 9, 1970, thus creating potential misclassification bias in exposure to DE. The truck drivers and the unexposed laborers were from the same socioeconomic class and may have the same smoking habits. Still, the lack of information on smoking data and a 36% rural population (usually consuming less tobacco) in the unexposed group may potentially confound the lung cancer results. However, a population survey carried out in 1988 showed very little difference in smoking habits of residents of rural areas and the total Danish male population. The investigator reports that diesel trucks were introduced in Denmark after World War II, and since the late 1940s the majority of the Danish fleet has been composed of diesel trucks. Consequently, even though the follow-up period is relatively short, the truck drivers may have had exposure to DE for 20 to 30 years. Therefore, the finding of excess lung cancer in this study is consistent with the findings of other truck driver studies.

7.2.1.10. *Saverin et al. (1999): DE and Lung Cancer Mortality in Potash Mining*

This is a cohort mortality study conducted in male potash miners in Germany. The mines began using mobile diesel-powered vehicles in 1969 and 1970. Miners who had worked underground for at least 1 year after 1969 to 1991, when the mines were closed, were followed from 1970 to 1994. A total of 5,981 individuals were identified from the medical records by a team of medical personnel familiar with the mining technology. A total of 5,536 were eligible for follow-up after 5.5% were excluded due to implausible or incomplete work history and 1.9% were lost to follow-up. A subcohort of 3,258 miners who had worked for at least 10 years underground (80% had held a single job) was also identified. The miners' biannual medical examination records were used to extract the information about personal data, smoking data, and pre-mining occupation, and to reconstruct a chronology of workplaces occupied by the worker since hire for each person.

Exposure categories were defined as production, maintenance, and workshop, roughly corresponding to high, medium, and low. Concentrations of total carbon, including elemental and organics, were measured in the airborne fine dust in 1992. A total of 255 samples covering all workplaces was obtained. Most were personal dust samples; some were area dust samples. Cumulative exposure was calculated for each miner, for each year of observation, using the work chronology and the work category. For the workshop category years of employment were considered as exposure time; for production and maintenance years of employment was weighted by a factor of 5/8, since these workers for an 8-hour shift worked for only 5 hours underground. As neither the mining technology nor the type of machinery used had changed substantially from 1970 to 1992, the exposure measurements were considered to represent the exposures throughout the study period. Accrued person-years were classified into cumulative

exposures and were expressed in intervals of 0.5 ymg/m^3. Both the exposure data and the smoking data obtained from the medical files were validated by personal interviews with 1,702 cohort members. Death certificates were obtained from local health centers for 94.4% of deceased members. Autopsy data were available for 13% of the deceased. Internal comparison was done between production and workshop categories. Using East German general male population rates, SMRs were computed for the total cohort as well as the subcohort. Analyses were done using Poisson and Cox regression models.

The concentrations of total carbon for production, maintenance, and workshop categories were 0.39 mg/m^3, 0.23 mg/m^3, and 0.12 mg/m^3, respectively. The cumulative exposure ranged from 0.25 ymg/m^3 to 6.25 ymg/m^3. The regression analysis showed that the cohort's smoking habits were homogenous and that smoking had an even distribution over cumulative exposure.

A total of 424 deaths were observed for the entire cohort (SMR = 54). The all-cancer deaths were 133, of which 38 were from lung cancer (SMR = 78). Analysis for the subcohort using the internal comparison group of low exposure (workshop category, mean cumulative exposure = 2.12 ymg/m^3) RR of 2.17 (95% CI = 0.79, 5.99) was found for the production category (mean cumulative exposure = 4.38 ymg/m^3). The relative risks for lung cancer for 20 years of exposure in the production category (highest exposure = cumulative exposure of 4.9 ymg/m^3) were calculated using Poisson and Cox regression methods. RRs of 1.16 and 1.68 were observed for the total cohort, while RRs of 1.89 and 2.7 were observed for the subcohort by Poisson and Cox regression methods respectively.

The main strengths of the study are the information available on DE exposure and smoking. Although these potash miners were exposed to salt dust and nitric gases, exposures to other confounders such as heavy metals and radon were absent. Smoking does not seem to be a confounder in this study but cannot be completely ruled out. Unfortunately, the age distribution of the cohort is not available. Since there were only 424 deaths in 25 years of follow-up in this cohort of 5,536, it appears that the cohort is young. Although lung cancer risk was elevated by twofold in the production category of the subcohort of miners who had worked for at least 10 years underground at the same job for 80% of their time and did not have more than 3 jobs, it was not statistically significant. The follow-up period for this study was 25 years, but the cohort members could have entered the cohort any time between 1970 and 1990, as long as they worked underground for a year, i.e., they could have worked in the mines for 1 year to 21 years. Thus, the authors may not have had enough follow-up or latency to observe the lung cancer excess. Despite these limitations, the results of this study provide suggestive evidence for the causal association between DE and excess lung cancer.

Table 7-1 summarizes the above cohort studies.

Table 7-1. Epidemiologic studies of the health effects of exposure to DE: cohort mortality studies

Authors	Population studied	DE exposure assessment	Results	Limitations
Waller (1981)	Approximately 20,000 male London transportation workers Aged 45 to 64 years 25 years follow-up (1950-1974)	Five job categories used to define exposure Environmental B[*a*]P concentrations measured in 1957 and 1979	SMR = 79 for lung cancer for the total cohort SMRs for all five job categories were less than 100 for lung cancer	Exposure measurement of B[*a*]P showed very little difference between inside and outside the garage Incomplete information on cohort members No adjustment for confounding such as other exposures, cigarette smoking, etc. No latency analysis
Howe et al. (1983)	43,826 male pensioners of the Canadian National Railway Company Mortality between 1965 and 1977 among these pensioners was compared with mortality of general Canadian population	Exposure groups classified by a group of experts based on occupation at the time of retirement Three exposure groups: Nonexposed Possibly exposed Probably exposed	RR = 1.2 (p=0.013) and RR = 1.3 (p=0.001) for lung cancer for possible and probable exposure, respectively A highly significant dose-response relationship demonstrated by trend test (p<0.001)	Incomplete exposure assessment due to lack of lifetime occupational history Mixed exposures to coal dust/combustion products and DE No validation of method was used to categorize exposure Lack of data on smoking but use of internal comparison group to compute RRs minimizes the potential confounding by smoking No latency analysis

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Table 7-1. Epidemiologic studies of the health effects of exposure to DE: cohort mortality studies (continued)

Authors	Population studied	DE exposure assessment	Results	Limitations
Rushton et al. (1983)	8,490 male London transport maintenance workers Mortality of workers employed for 1 continuous year between January 1, 1967, and December 31, 1975, was compared with mortality of general population of England and Wales	100 different job titles were grouped in 20 broad categories The categories were not ranked for DE exposure	SMR = 133 (p<0.03) for lung cancer in the general hand job group Several other job categories showed SS increased SMRs for several other sites based on fewer than five cases	Ill-defined DE exposure without any ranking Average 6-year follow-up i.e., not enough time for lung cancer latency No adjustment for confounders
Wong et al. (1985)	34,156 male heavy construction equipment operators Members of the local union for at least 1 year between January 1, 1964, and December 1, 1978	20 functional job titles grouped into three job categories for potential exposure Exposure groups (high, low, and unknown) based on job description and proximity to source of DE emissions	SMR = 166 (p<0.05) for liver cancer for total cohort SMR = 343 (observed = 5, p<0.05) for lung cancer for high-exposure bulldozer operators with 15-19 years of membership, 20+ years of follow-up SMR = 119 (observed = 141, p<0.01) for workers with no work histories	No validation of exposure categories, which were based on surrogate information Incomplete employment records Employment history other than from the union not available 15 year follow-up may not provide sufficient time for lung cancer latency No data on confounders such as other exposures, alcohol, smoking, etc.
Edling et al. (1987)	694 male bus garage employees Follow-up from 1951 through 1983 Mortality of these men was compared with mortality of general population of Sweden	Three exposure groups based on job titles: High exposure, bus garage workers Intermediate exposure, bus drivers Low exposure, clerks	No SS differences were observed between observed and expected for any cancers by different exposure groups	Small sample size No validation of exposure No data on confounders such as other exposures, smoking, etc.

Table 7-1. Epidemiologic studies of the health effects of exposure to DE: cohort mortality studies (continued)

Authors	Population studied	DE exposure assessment	Results	Limitations
Boffetta and Stellman (1988)	46,981 male volunteers enrolled in the American Cancer Society's Prospective Mortality Study of Cancer in 1982 Aged 40 to 79 years at enrollment First 2-year follow-up	Self-reported occupations were coded into 70 job categories Employment in high DE exposure jobs were compared with nonexposed jobs	Total mortality (SS) elevated for railroad workers (RR=1.43), heavy equipment operators (RR=1.7), miners (RR=1.34), and truck drivers (RR=1.19) Lung cancer mortality (SS) adjusted for age & smoking, elevated for total cohort (RR=1.31), miners (RR=2.67), and heavy equipment operators (RR=2.6) Lung cancer mortality (SNS) elevated among railroad workers and truck drivers Truck drivers also showed a dose-response	Exposure information based on self-reported occupation for which no validation was done Volunteer population, probably healthy population

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Table 7-1. Epidemiologic studies of the health effects of exposure to DE: cohort mortality studies (continued)

Authors	Population studied	DE exposure assessment	Results	Limitations
Garshick et al. (1988)	55,407 white male railroad workers Aged 40 to 64 years in 1959 Started work 10-20 years earlier than 1959	Industrial hygiene data correlated with job titles to dichotomize the jobs as "exposed" or "not exposed"	RR = 1.45 (40-44 year age group) RR = 1.33 (45-49 year age group) Both SS After exclusion of workers exposed to asbestos RR = 1.57 (40-44 year age group) RR = 1.34 (45-49 year age group) Both SS	Years of exposure used as surrogate for dose Not possible to separate the effect of time since first exposure and duration of exposure Lack of smoking data but case-control study showed very little difference between those exposed to DE versus those who were not
Garshick (ltr to Chao Chen, EPA, dtd 8/15/91			Dose response indicated by increasing lung cancer risk with increasing cumulative exposure Further analysis using attained age, limited through 1976 showed youngest workers still had the highest risk	
Crump et al. (1991) Crump (1999)	Reanalysis of Garshick et al., 1988 data		Dose response found to be positive or negative depending upon how the age was controlled in the model Negative dose-response upheld in the latest analysis	
California EPA (1998)	Reanalysis of Garshick et al., 1988		Positive dose response using age at 1959 and interaction term of age & calendar year	

Table 7-1. Epidemiologic studies of the health effects of exposure to DE: cohort mortality studies (continued)

Authors	Population studied	DE exposure assessment	Results	Limitations
Gustavsson et al. (1990)	695 male workers from 5 bus garages in Stockholm, Sweden, who had worked for 6 months between 1945 and 1970 34 years follow-up (1952-1986) Nested case-control study 17 cases, six controls for each case matched on age ± 2 years	Four DE indices were created: 0 to 10, 10 to 20, 20-30, and >30 based on job tasks and duration of work	SNS SMRs of 122 and 115 (OA and GP), respectively Case-control study results showed dose response: RR = 1.34 (10 to 20) RR = 1.81 (20 to 30) RR = 2.43 (>30) All SS with 0-10 as comparison group	Exposure matrix based on job tasks (not on actual measurements) Small cohort, hence low power Lack of smoking data is unlikely to confound the results since it is a nested case-control study
Hansen (1993)	Cohort of 57,249 unskilled laborers, ages 15 to 74, in Denmark (nationwide census file) November 9, 1970 Follow-up through November 9, 1980	DE exposure assumed based on diesel-powered trucks	SS SMRs for lung cancer : SMR = 160 for total population SMR = 229 for age 55-59 years SMR = 227 for age 60-64 years	No actual exposure data available Lack of smoking data but population survey showed very little difference between rural and urban smoking habits Job changes may have occurred from laborer to driver Short follow-up period
Saverin et al. (1999)	Cohort of 5,536 potash miners who had worked underground for at least 1 year after 1969 Subcohort of 3,258 who had worked for at least 10 years underground Follow-up from 1970 to 1994	DE exposure categories defined as: production (high) maintenance (medium) workshop (low) 225 air samples obtained: for total carbon, organics, & fine dust in 1992	SNS increased RRs adjusted for smoking: 1.68 and 2.7 for total cohort & subcohort, respectively	Small, young cohort Few deaths No latency analysis

Abbreviations: RR = relative risk; SMR = standardized mortality ratio; SNS = statistically nonsignificant; SS = statistically significant; O = occupationally active; GP = general population.

7.2.2. Case-Control Studies of Lung Cancer

7.2.2.1. *Hall and Wynder (1984): A Case-Control Study of DE Exposure and Lung Cancer*

Hall and Wynder (1984) conducted a case-control study of 502 male lung cancer cases and 502 controls without tobacco-related diseases that examined an association between occupational DE exposure and lung cancer. Histologically confirmed primary lung cancer patients who were 20 to 80 years old were ascertained from 18 participating hospitals in 6 U.S. cities 12 months prior to the interview. Eligible controls, patients at the same hospitals without tobacco-related diseases, were matched to cases by age (± 5 years), race, hospital, and hospital room status. The number of male lung cancer cases interviewed totaled 502, which was 64% of those who met the study criteria for eligibility. Of the remaining 36%, 8% refused, 21% were too ill or had died, and 7% were unreliable. Seventy-five percent of eligible controls completed interviews. Of these interviewed controls, 49.9% were from the all-cancers category, whereas 50.1% were from the all-noncancers category. All interviews were obtained in hospitals to gather detailed information on smoking history, coffee consumption, artificial sweetener use, residential history, and abbreviated medical history as well as standard demographic variables. Occupational information was elicited by a question on the usual lifetime occupation and was coded by the abbreviated list of the U.S. Bureau of Census Codes. The odds ratios were calculated to evaluate the association between DE exposure and risk of lung cancer incidence. Summary odds ratios were computed by the Mantel-Haenszel method after adjusting for potential confounding by age, smoking, and socioeconomic class. Two-sided, 95% confidence intervals were computed by Woolf's method. Occupational exposure to DE was defined by two criteria. First, occupational titles were coded "probably high exposure" as defined by the industrial hygiene standards established for the various jobs. The job titles included under this category were warehousemen, bus and truck drivers, railroad workers, and heavy equipment operators and repairmen. The second method used the National Institute for Occupational Safety and Health (NIOSH) criteria to analyze occupations by diesel exposure. In this method, the estimated proportion of exposed workers was computed for each occupational category by using the NIOSH estimates of the exposed population as the numerator and the estimates of individuals employed in each occupational category from the 1970 census as the denominator. Occupations estimated to have at least 20% of their employees exposed to DE were defined as "high exposure," those with 10% to 19% of their employees exposed were defined as "moderate exposure," and those with less than 10% of their employees exposed were defined as "low exposure."

Cases and controls were compared with respect to exposure. The relative risk was 2.0 (95% CI = 1.2, 3.2) for those workers who were exposed to DE versus those who were not. The risk, however, decreased to a nonsignificant 1.4 when the data were adjusted for smoking.

Analysis by NIOSH criteria found a nonsignificant relative risk of 1.7 in the high- exposure group. There were no significantly increased cancer risks by occupation either by the first method or by the NIOSH method. To assess any possible synergism between DE exposure and smoking, the lung cancer risks were calculated for different smoking categories. The relative risks were 1.46 among nonsmokers and ex-smokers, 0.82 among current smokers of <20 cigarettes/day, and 1.3 among current smokers of 20+ cigarettes/day, indicating a lack of synergistic effects.

The major strength of this study is the availability of a detailed smoking history for all the study subjects. However, this is offset by lack of DE exposure measurements, use of a poor surrogate for exposure, and lack of consideration of latency period. Information was collected on only one major lifetime occupation, and it is likely that those workers who had more than one major job may not have reported the occupation with the heaviest DE exposures. Furthermore, the exposure categories based on job titles were broad, and thus would have made a true effect of DE difficult to detect.

7.2.2.2. *Damber and Larsson (1987): Occupation and Male Lung Cancer, a Case-Control Study in Northern Sweden*

A case-control study of lung cancer was conducted in northern Sweden to determine the occupational risk factors that could explain the large geographic variations of lung cancer incidence in that country. The study region comprised the three northernmost counties of Sweden, with a total male population of about 390,000. The rural municipalities, with 15% to 20% of the total population, have forestry and agriculture as dominating industries, and the urban areas have a variety of industrial activities (mines, smelters, steel factories, paper mills, and mechanical workshops). All male cases of lung cancer reported to the Swedish Cancer Registry during the 6-year period between 1972 and 1977 who had died before the start of the study were selected. Of 604 eligible cases, 5 did not have microscopic confirmation, and in another 5 the diagnosis was doubtful, but these cases were included nevertheless. Cases were classified as small-cell carcinomas, squamous cell carcinomas, adenocarcinomas, and other types. For each case a dead control was drawn from the National Death Registry matched by sex, year of death, age, and municipality. Deaths in controls classified as lung cancer and suicides were excluded. A living control matched to the case by sex, year of birth, and municipality was also drawn from the National Population Registry. Postal questionnaires were sent to close relatives of cases and dead controls, and to living controls themselves to collect data on occupation, employment, and smoking habits. Replies were received from 589 cases (98%), 582 surrogates of dead controls (96%), and 453 living controls (97%).

Occupational data were collected on occupations or employment held for at least 1 year and included type of industry, company name, task, and duration of employment. Supplementary telephone interviews were performed if occupational data were lacking for any period between age 20 and time of diagnosis. Data analysis involved calculation of the odds ratios by the exact method based on the hypergeometric distribution and the use of a linear logistic regression model to adjust for the potential confounding effects of smoking. Separate analyses were performed with dead and living controls, and on the whole there was good agreement between the two control groups. A person who had been active for at least 1 year in a specific occupation was in the analysis assigned to that occupation.

Using dead controls, the odds ratios adjusted for smoking were 1.0 (95% CI = 0.7, 1.5) and 2.7 (95% CI = 1.0, 8.1) for professional drivers (≥1 year of employment) and underground miners (≥1 year of employment), respectively. For 20 or more years of employment in those occupations, the odds ratios adjusted for smoking were 1.2 (95% CI = 0.9, 2.6) and 9.8 (95% CI = 1.5, 414). These were the only two occupations listed with potential DE exposure. An excess significant risk was detected for copper smelter workers, plumbers, electricians, and asbestos workers, as well as concrete and asphalt workers. All the odds ratios were calculated by adjusting for age, smoking, and municipality. A comparison with the live controls resulted in the odds ratios being lower than those observed with dead controls, and none were statistically significant in this comparison.

This study did not detect any excess risk of lung cancer for professional drivers, who, among all the occupations listed, had the most potential for exposure to motor vehicle exhaust. However, it is not known whether these drivers were exposed exclusively to gasoline exhaust, DE, or varying degrees of both. An excess risk was detected for underground miners, but it is not known if this was due to diesel emissions from engines or from radon daughters in poorly ventilated mines. Although a high response rate (98%) was obtained by the postal questionnaires, the use of surrogate respondents is known to lead to misclassification errors that can bias the results in either direction.

7.2.2.3. *Lerchen et al. (1987): Lung Cancer and Occupation in New Mexico*

This is a population-based case-control study conducted in New Mexico that examined the association between occupation and occurrence of lung cancer in Hispanic and non-Hispanic whites. Cases involved residents of New Mexico, 25 through 84 years of age, and diagnosed between January 1, 1980, and December 31, 1982, with primary lung cancer, excluding bronchioalveolar carcinoma. Cases were ascertained through the New Mexico Tumor Registry, which is a member of the Surveillance Epidemiology and End Results (SEER) Program of the National Cancer Institute. Controls were chosen by randomly selecting residential telephone

numbers and, for those over 65 years of age, from the Health Care Financing Administration's roster of Medicare participants. They were frequency-matched to cases for sex, ethnicity, and 10-year age category with a ratio of 1.5 controls per case. The 506 cases (333 males and 173 females) and 771 controls (499 males and 272 females) were interviewed, with a nonresponse rate of 11% for cases. Next of kin provided interviews for 50% and 43% of male and female cases, respectively. Among controls, only 2% of the interviews were provided by next of kin for each sex. Data were collected by personal interviews conducted by bilingual interviewers in the participants' homes. A lifetime occupational history and a self-reported history of exposure to specific agents were obtained for each job held for at least 6 months since age 12. Questions were asked about the title of the position, duties performed, location and nature of industry, and time at each job title. A detailed smoking history was also obtained. The variables on occupational exposures were coded according to the Standard Industrial Classification scheme by a single person and reviewed by another. To test the hypothesis about high-risk jobs for lung cancer, the principal investigator created an a priori listing of suspected occupations and industries by a two-step process involving a literature review for implicated industries and occupations. The principal investigator also determined the appropriate Standard Industrial Classification and Standard Occupational Codes associated with job titles. For four agents—asbestos, wood dust, DE, and formaldehyde—the industries and occupations determined to have exposure were identified, and linking of specific industries and occupations was based on literature review and consultation with local industrial hygienists.

The relative odds were calculated for suspect occupations and industries, classifying individuals as ever employed for at least 1 year in an industry or occupation and defining the reference group as those subjects never employed in that particular industry or occupation. Multiple logistic regression models were used to control simultaneously for age, ethnicity, and smoking status. For occupations with potential DE exposure, the analysis showed no excess risks for diesel engine mechanics and auto mechanics. Similarly, when analyzed by exposure to specific agents, the odds ratio (OR) adjusted for age, smoking, and ethnicity was not elevated for DE fumes (OR = 0.6, 95% CI = 0.2, 1.6). Significantly elevated ORs were found for uranium miners (OR = 2.8), underground miners (OR = 2.4), construction workers, and welders (OR = 4.3). No excess risks were detected for the following industries: shipbuilding, petroleum refining, printing, blast furnace, and steel mills. No excess risks were detected for the following occupations: construction workers, painters, plumbers, paving equipment operators, roofers, engineers and firemen, woodworkers, and shipyard workers. Females were excluded from detailed analysis because none of the Hispanic female controls had been employed in high-risk jobs; among the non-Hispanic white controls, employment in a high-risk job was recorded for at

least five controls for only two industries, construction and painting, for which the OR were not significantly elevated. Therefore, the analyses were presented for males only.

Among the many strengths of this study are its population-based design, high participation rate, detailed smoking history, and the separate analysis done for two ethnic groups, southwestern Hispanic and non-Hispanic white males. The major limitations pertain to the occupational exposure data. Job titles obtained from occupational histories were used as proxy for exposure status, but these were not validated. Further, for nearly half the cases, next of kin provided occupational histories. The authors acknowledge the above sources of bias but state without substantiation that these biases would not strongly affect their results. They also did not use a job exposure matrix to link occupations to exposures and did not provide details on the method they used to classify individuals as DE exposed based on reported occupations. The observed absence of an association for exposure to asbestos, a well-established lung carcinogen, may be explained by the misclassification errors in exposure status or by sample size constraints (not enough power). Likewise, the association for DE reported by only 7 cases and 17 controls also may have gone undetected because of low power. In conclusion, there is insufficient evidence from this study to confirm or refute an association between lung cancer and DE exposure.

7.2.2.4. *Garshick et al. (1987): A Case-Control Study of Lung Cancer and DE Exposure in Railroad Workers*

An earlier pilot study of the mortality of railroad workers by the same investigators (Schenker et al., 1984) found a moderately high risk of lung cancer among workers exposed to DE compared with those who were not. Based on these findings the investigators conducted a case-control study of lung cancer in the same population. The population base for this case-control study was approximately 650,000 active and retired male U.S. railroad workers with 10 years or more of railroad service who were born in 1900 or later. The U.S. Railroad Retirement Board (RRB), which operates the retirement system, is separate from the Social Security System, and to qualify for the retirement or survivor benefits the workers had to acquire 10 years or more of service. Information on deaths that occurred between March 1, 1981, and February 28, 1982, was obtained from the RRB. For 75% of the deceased population, death certificates were obtained from the RRB, and, for the remaining 25%, they were obtained from the appropriate State departments of health. Cause of death was coded according to the eighth revision of the ICD. The cases were selected from deaths with primary lung cancer, which was the underlying cause of death in most cases. Each case was matched to two deceased controls whose dates of birth were within 2.5 years of the date of birth of the case and whose dates of death were within 31 days of the date of death noted in the case. Controls were selected randomly from workers

who did not have cancer noted anywhere on their death certificates and who did not die of suicide or of accidental or unknown causes.

Each subject's work history was determined from a yearly job report filed by his employer with the RRB from 1959 until death or retirement. The year 1959 was chosen as the effective start of DE exposure for this study since by this time 95% of the locomotives in the United States were diesel powered. Investigators acknowledge that because the transition to diesel-powered engines took place in the early 1950s, some workers had additional exposure prior to 1959; however, if a worker had died or retired prior to 1959, he was considered unexposed. Exposure to DE was considered to be dichotomous for this study, which was assigned based on an industrial hygiene evaluation of jobs and work areas. Selected jobs with and without regular DE exposure were identified by a review of job title and duties. Personal exposure was assessed in 39 job categories representative of workers with and without DE exposure. Those jobs for which no personal sampling was done were considered exposed or unexposed based on similarities in job activities and work locations and by degree of contact with diesel equipment. Asbestos exposure was categorized based on jobs held in 1959, or on the last job held if the subject retired before 1959. Asbestos exposure in railroads occurred primarily during the steam engine era and was related mostly to the repair of locomotive steam boilers that were insulated with asbestos. Smoking history information was obtained from the next of kin.

Death certificates were obtained for approximately 87% of the 15,059 deaths reported by the RRB, from which 1,374 cases of lung cancer were identified. Fifty-five cases of lung cancer were excluded from the study for either incomplete data (20) or refusal by two States to use information on death certificates to contact the next of kin. Successful matching to at least one control with work histories was achieved for 335 (96%) cases ≤64 years of age at death and 921 (95%) cases ≥65 years of age at death. In both age groups, 90% of the cases were matched with two controls. There were 2,385 controls in the study; 98% were matched within ± 31 days of the date of death, whereas the remaining 2% were matched within 100 days. Deaths from diseases of the circulatory system predominated among controls. Among the younger workers, approximately 60% had exposure to DE, whereas among older workers, only 47% were exposed to DE.

Analysis by a regression model, in which years of DE exposure were the sum total of the number of years in diesel-exposed jobs, used as a continuous exposure variable, yielded an odds ratio of lung cancer of 1.39 (95% CI = 1.05, 1.83) for >20 years of DE exposure in the ≤64 years of age group. After adjustment for asbestos exposure and lifetime smoking (pack-years), the odds ratio was 1.41 (95% CI = 1.06, 1.88). Both crude odds ratio and asbestos exposure as well as lifetime smoking-adjusted odds ratio for the ≥65 years of age group were not significant.

Increasing years of DE exposure, categorized as ≥20 diesel years and 5 to 19 diesel years, with 0 to 4 years as the referent group, showed significantly increased risk in the ≤64 years of age group after adjusting for asbestos exposure and pack-year category of smoking. For individuals who had ≥20 years of DE exposure, the odds ratio was 1.64 (95% CI = 1.18, 2.29), whereas among individuals who had 5 to 19 years of DE exposure, the odds ratio was 1.02 (95% CI = 0.72, 1.45). In the ≥65 years of age group, only 3% of the workers were exposed to DE for more than 20 years. Relative odds for 5 to 19 years and ≥20 years of diesel exposure were less than 1 (p>0.01) after adjusting for smoking and asbestos exposure.

Alternative models to explain past asbestos exposure were tested. These were variables for regular and intermittent exposure groups and an estimate of years of exposure based on estimated years worked prior to 1959. No differences in results were seen. The interactions between DE exposure and the three pack-year categories (<50, >50, and missing pack-years) were explored. The cross-product terms were not significant. A model was also tested that excluded recent DE exposure occurring within the 5 years before death and gave an odds ratio of 1.43 (95% CI = 1.06, 1.94), adjusted for cigarette smoking and asbestos exposure, for workers with 15 years of cumulative exposure. For workers with 5 to 14 years of cumulative exposure, the OR were not significant.

The many strengths of the study are consideration of confounding factors such as asbestos exposure and smoking; classification of DE exposures by job titles and industrial hygiene sampling; exploration of interactions between smoking, asbestos exposure, and DE exposure; and good ascertainment (87%) of death certificates from the 15,059 deaths reported by the RRB.

The investigators also recognized and reported the following limitations: overestimation of cigarette consumption by surrogate respondents, which may have exaggerated the contribution of smoking to lung cancer risk, and use of the Interstate Commerce Commission (ICC) job classification as a surrogate for exposure, which may have led to misclassification of DE exposure jobs with low intensity and intermittent exposure, such as railroad police and bus drivers, as unexposed. These two limitations would result in underestimation of the lung cancer risk. This source of error could have been avoided if DE exposures were categorized by a specific dose range associated with a job title that could have been classified as heavy, medium, low, and zero exposure instead of a dichotomous variable. The use of death certificates to identify cases and controls may have resulted in misclassification. Controls may have had undiagnosed primary lung cancer, and lung cancer cases might have been secondary lesions misdiagnosed as primary lung cancer. However, the investigators quote a third National Cancer Survey report in which the death certificates for lung cancer were coded appropriately in 95% of the cases. Last, as in all previous studies, there is a lack of data on the contribution of unknown

occupational or environmental exposures and passive smoking. In conclusion, this study provides strong evidence that occupational DE emission exposure increases the risk of lung cancer.

7.2.2.5. *Benhamou et al. (1988): Occupational Risk Factors of Lung Cancer in a French Case-Control Study*

This is a case-control study of 1,625 histologically confirmed cases of lung cancer and 3,091 matched controls, conducted in France between 1976 and 1980. This study was part of an international study to investigate the role of smoking and lung cancer. Each case was matched with one or two controls, whose diseases were not related, to tobacco use, sex, age at diagnosis (± 5 years), hospital of admission, and interviewer. Information was obtained from both cases and controls on place of residence since birth, educational level, smoking, and drinking habits. A complete lifetime occupational history was obtained by asking participants to give their occupations from the most recent to the first. Women were excluded because most of them had listed no occupation. Men who smoked cigars and pipes were excluded because there were very few in this category. Thus, the study was restricted to nonsmokers and cigarette smokers. Cigarette smoking exposure was defined by age at the first cigarette (nonsmokers, ≤20 years, or >20 years), daily consumption of cigarettes (nonsmokers, <20 cigarettes a day, and ≥20 cigarettes a day), and duration of cigarette smoking (nonsmokers, <35 years, and ≥35 years). The data on occupations were coded by a panel of experts according to their own chemical or physical exposure determinations. Occupations were recorded blindly using the International Standard Classification of Occupations. Data on 1,260 cases and 2,084 controls were available for analysis. The remaining 365 cases and 1,007 controls were excluded because they did not satisfy the required smoking status criteria.

A matched logistic regression analysis was performed to estimate the effect of each occupational exposure after adjusting for cigarette status. Matched relative risk ratios were calculated for each occupation with the baseline category, which consisted of patients who had never been engaged in that particular occupation. The matched RR ratios, adjusted for cigarette smoking for the major groups of occupations, showed that the risks were significantly higher for production and related workers, transport equipment operators, and laborers (RR = 1.24, 95% CI = 1.04, 1.47). On further analysis of this group, for occupations with potential diesel emission exposure, significant excess risks were found for motor vehicle drivers (RR = 1.42, 95% CI = 1.07, 1.89) and transport equipment operators (RR = 1.35, 95% CI = 1.05, 1.75). No interaction with smoking status was found in any of the occupations. The only other significant excess was observed for miners and quarrymen (RR = 2.14, 95% CI = 1.07, 4.31). None of the significant associations showed a dose-response relationship with duration of exposure.

This study was designed primarily to investigate the relationship between smoking (not occupations or environmental exposures) and lung cancer. Although an attempt was made to obtain complete occupational histories, the authors did not clarify whether, in the logistic regression analysis, they used the subjects' first occupation, predominant occupation, last occupation, or ever worked in that occupation as the risk factor of interest. The most important limitation of this study is that the occupations were not coded into exposures for different chemical and physical agents, thus precluding the calculation of relative risks for diesel exposure. Using occupations as surrogate measures of diesel exposure, an excess significant risk was obtained for motor vehicle drivers and transport equipment operators, but not for motor mechanics. However, it is not known if subjects in these occupations worked with diesel engines or nondiesel engines.

7.2.2.6. *Hayes et al. (1989): Lung Cancer in Motor Exhaust-Related Occupations*

This study reports the findings from an analysis of pooled data from three lung cancer case-control studies that examine in detail the association between employment in motor exhaust-related (MER) occupations and lung cancer risk adjusted for confounding by smoking and other risk factors. The three studies were carried out by the National Cancer Institute in Florida (1976 to 1979), New Jersey (1980 to 1981), and Louisiana (1979 to 1983). These three studies were selected because the combined group would provide a sufficient sample to detect a risk of lung cancer in excess of 50% among workers in MER occupations. The analyses were restricted to males who had given occupational history. The Florida study was hospital based, with cases ascertained through death certificates. Controls were randomly selected from hospital records and death certificates, excluding psychiatric diseases, matched by age and county. The New Jersey study was population based, with cases ascertained through hospital records, cancer registry, and death certificates. Controls were selected from among the pool of New Jersey licensed drivers and death certificates. The Louisiana study was hospital based (it is not specified how the cases were ascertained), and controls were randomly selected from hospital patients, excluding those with lung diseases and tobacco-related cancers.

A total of 2,291 cases of male lung cancers and 2,570 controls were eligible, and the data on occupations were collected by next-of-kin interviews for all jobs held for 6 months or more, including the industry, occupation, and number of years employed. The proportion of next-of-kin interviews varied by site from 50% in Louisiana to 85% in Florida. The coding schemes were reviewed to identify MER occupations, which included truck drivers and heavy equipment operators (cranes, bulldozers, and graders); bus drivers, taxi drivers, chauffeurs, and other motor vehicle drivers; and automobile and truck mechanics. Truck drivers were classified as routemen and delivery men and other truck drivers. All jobs were also classified with respect to potential

exposure to known and suspected lung carcinogens. ORs were calculated by the maximum likelihood method, adjusting for age by birth year, usual amount smoked, and study area. Logistic regression models were used to examine the interrelationship of multiple variables.

A statistically significant excess risk was detected for employment of 10 years or more for all MER occupations (except truck drivers) adjusted for birth cohort, usual daily cigarette use, and study area. The odds ratio for lung cancer using data gathered by direct interviews was 1.4 (95% CI = 1.1, 2.0), allowing for multiple MER employment, and 2.0 (95% CI = 1.3, 3.0), excluding individuals with multiple MER employment. ORs for all MER employment, except truck drivers who were employed for less than 10 years, were 1.3 (95% CI = 1.0, 1.7) and 1.3 (95% CI = 0.9, 1.8) including and excluding multiple MER employment, respectively. ORs were then derived for specific MER occupations and, to avoid the confounding effects of multiple MER job classifications, analyses were also done excluding subjects with multiple MER job exposures. Truck drivers employed for more than 10 years had an odds ratio of 1.5 (95% CI = 1.1, 1.9). A similar figure was obtained excluding subjects with multiple MER employment. An excess risk was not detected for truck drivers employed less than 10 years. The only other job category that showed a statistically significant excess for lung cancer included taxi drivers and chauffeurs who worked multiple MER jobs for less than 10 years (OR = 2.5, 95% CI = 1.4, 4.8). For the same category, the risk for individuals working in that job for more than 10 years was 1.2 (95% CI = 0.5, 2.6). A statistically significant positive trend ($p<0.05$) with increasing employment of <2 years, 2 to 9 years, 10 to 19 years, and 20+ years was observed for truck drivers but not for other MER occupations. A statistically nonsignificant excess risk was also observed for heavy equipment operators, bus drivers, taxi drivers and chauffeurs, and mechanics employed for 10 years or more. All of the above-mentioned ORs were derived, adjusted for birth cohort, usual daily cigarette use, and State of residence. Exposure to other occupational suspect lung carcinogens did not account for the excess risks detected.

Results of this large study provide evidence that workers in MER jobs are at an excess risk of lung cancer that is not explained by their smoking habits or exposures to other lung carcinogens. Because no information on type of engine had been collected, it was not possible to determine if the excess risk was due to exposure to DE or gasoline exhaust or a mixture of the two. Among the study's other limitations are a possible bias due to misclassification of jobs reported by the large proportion of next-of-kin interviews. Such a bias would make the effect of DE harder to detect due to broad categorization of jobs and the problems in classifying individuals into uniform occupational groups based on the pooled data in the three studies that used different occupational classification schemes.

7.2.2.7. *Steenland et al. (1990): A Case-Control Study of Lung Cancer and Truck Driving in the Teamsters Union*

Steenland et al. conducted a case-control study of lung cancer deaths in the Teamsters Union to determine the risk of lung cancer among different occupations. Death certificates were obtained from the Teamsters Union files in the central States for 10,485 (98%) male decedents who had filed claims for pension benefits and who had died in 1982 and 1983. Individuals were required to have 20 years' tenure in the union to be eligible to claim benefits. Cases comprised all deaths (n = 1,288) from lung cancer, coded as ICD 162 or 163 for underlying or contributory cause on the death certificate. The 1,452 controls comprised every sixth death from the entire file, excluding deaths from lung cancer, bladder cancer, and motor vehicle accidents. Detailed information on work history and potential confounders such as smoking, diet, and asbestos exposure was obtained by questionnaire. Seventy-six percent of the interviews were provided by spouses and the remainder by some other next of kin. The response rate was 82% for cases and 80% for controls. Using these interview data and the 1980 census occupation and industry codes, subjects were classified either as nonexposed or as having held other jobs with potential DE exposure. Data on job categories were missing for 12% of the study subjects. A second work history file was also created based on the Teamsters Union pension application that lists occupation, employer, and dates of employment. A three-digit U.S. census code for occupation and industry was assigned to each job for each individual. This Teamsters Union work history file did not have information on whether men drove diesel or gasoline trucks, and the four principal occupations were long-haul drivers, short-haul or city drivers, truck mechanics, and dockworkers. Subjects were assigned the job category in which they had worked the longest.

The case-control analysis was done using unconditional logistic regression. Separate analyses were conducted for work histories from the Teamsters Union pension file and from next-of-kin interviews. Covariate data were obtained from next-of-kin interviews. Analyses were also performed for two time periods: employment after 1959 and employment after 1964. These two cut-off years reflect years of presumed dieselization: 1960 for most trucking companies and 1965 for independent driver and nontrucking firms. Data for analysis could be obtained for 994 cases and 1,085 controls using Teamsters Union work history and for 872 cases and 957 controls using next-of-kin work history. When exposure was considered as a dichotomous variable, for both Teamsters Union and next-of-kin work history, no single job category had an elevated risk. From the next-of-kin data, diesel truck drivers had an odds ratio of 1.42 (95% CI = 0.74, 2.47) and diesel truck mechanics had an odds ratio of 1.35 (95% CI = 0.74, 2.47). ORs by duration of employment as a categorical variable were then estimated. For the Teamsters Union work history data, when only employment after 1959 was considered, both long-haul ($p<0.04$) and short-haul drivers (not significant) showed an increase in risk with

increased years of exposure. The length-of-employment categories for which the trends were analyzed were 1 to 11 years, 12 to 17 years, and 18 years or more. Using 1964 as the cutoff date, long-haul drivers continued to show a significant positive trend (p=0.04), with an odds ratio of 1.64 (95% CI = 1.05, 2.57) for those who worked for 13+ years, the highest category. Short-haul drivers, however, did not show a positive trend when 1964 was used as the cutoff date. Similar trend analysis was done for most next-of-kin data. A marginal increase in risk with increasing duration of employment as a truck driver (p=0.12) was observed. For truck drivers who primarily drove diesel trucks for 35 years or longer, the odds ratio for lung cancer was 1.89 (95% CI = 1.04, 3.42). Similarly, the corresponding odds ratio was 1.34 (95% CI = 0.81, 2.22) for both gasoline truck drivers and drivers who drove both types of trucks, and 1.09 (95% CI = 0.44, 2.66) for truck mechanics.

No significant interactions between age and DE exposure or smoking and DE exposure were observed. All the ORs were adjusted for age, smoking, and asbestos in addition to various exposure categories.

This is a well-designed and analyzed study. The main strengths of the study are the availability of detailed records from the Teamsters Union, a relatively large sample size, availability of smoking data , and measurements of exposures. The authors acknowledge some limitations of this study, which include possible misclassifications of exposure and smoking habits, as information was provided by next of kin; lack of sufficient latency to observe lung cancer excess; and a small nonexposed group (n = 120). Also, they could not evaluate the concordance between Teamsters Union and next-of-kin job categories easily because job categories were defined differently in each data set. No data were available on levels of diesel exposure for the different job categories. Despite these limitations, the positive findings of this study, which are probably underestimated, provide a positive evidence toward causal association between DE exposure and excess lung cancer.

7.2.2.8. *Steenland et al. (1998): DE and Lung Cancer in the Trucking Industry: Exposure-Response Analyses and Risk Assessment*

Steenland et al. (1998) conducted an exposure-response analysis by supplementing the data from their earlier case-control study of lung cancer and truck drivers in the Teamsters Union (Steenland et al., 1990) with exposure estimates based on a 1990 industrial hygiene survey of elemental carbon exposure, a surrogate for DE in the trucking industry.

Study subjects were long-term Teamsters enrolled in the pension system who died during the period 1982-1983. Using death certificate information, the researchers identified 994 cases of lung cancer for the study period, and 1,085 non-lung-cancer deaths served as controls. Subjects were divided into job categories based on the job each held the longest. Most had held

only one type of job. The job categories were short-haul driver, long-haul driver, mechanic, dockworker, other jobs with potential diesel exposure, and jobs outside the trucking industry without occupational diesel exposure. Smoking histories were obtained from next of kin. ORs were calculated for work in an exposed job category at any time and after 1959 (an estimated date when the majority of heavy-duty trucks had converted to diesel) compared with work in nonexposed jobs. ORs were adjusted for age, smoking, and potential asbestos exposure. Trends in effect estimates for duration of work in an exposed job were also calculated.

An industrial hygiene survey by Zaebst et al. (1991) of elemental carbon exposures in the trucking industry provided exposure estimates for each job category in 1990. The elemental carbon measurements were generally consistent with the epidemiologic results, in that mechanics were found to have the highest exposures and relative risk, followed by long-haul and then short-haul drivers, although dockworkers had the highest exposures and the lowest relative risks.

Past exposures were estimated assuming that they were a function of (1) the number of heavy-duty trucks on the road, (2) the particulate emissions (grams/mile) of diesel engines over time, and (3) leaks from truck exhaust systems for long-haul drivers. Estimates of past exposure to elemental carbon, as a marker for DE exposure, for subjects in the case-control study were made by assuming that average 1990 levels for a job category could be assigned to all subjects in that category, and that levels prior to 1990 were directly proportional to vehicle miles traveled by heavy-duty trucks and the estimated emission levels of diesel engines. A 1975 exposure level of elemental carbon in terms of micrograms per cubic meter was estimated by the following equation: 1975 level = 1990 level*(vehicle miles 1975/vehicle miles 1990) (emissions 1975/emissions 1990). Once estimates of exposure for each year of work history were derived for each subject, analyses were conducted by cumulative level of estimated carbon exposure.

Estimates were made for long-haul drivers (n = 1,237), short-haul drivers (n = 297), dockworkers (n = 164), mechanics (n = 88), and those outside the trucking industry (n = 150). Logistic regression was used to estimate ORs adjusted for five categories of age, race, smoking (never, former-quitting before 1963, former-quitting in 1963 or later, current-with <1 pack per day, and current-with 1 or more packs per day), diet, and reported asbestos exposure. A variety of models for cumulative exposure were considered, including a log-linear model with cumulative exposure, a model adding a quadratic term for cumulative exposure, a log transform of cumulative exposure, dummy variables for quartile of cumulative exposure, and smoothing splines of cumulative exposure. The estimates of rate ratios from logistic regression for specific levels of exposure to elemental carbon were then used to derive excess risk estimates for lung cancer after lifetime exposure to elemental carbon.

The survey found that mechanics had the highest current levels of DE exposures and dockworkers who mainly used propane-powered forklifts had the lowest exposure. ORs of 1.69

and 0.93 were observed for the mechanics and dockworkers, respectively. The finding of the highest lung cancer risk for mechanics and lowest for dockworkers is indicative of causal association between the DE exposure and development of lung cancer. The log of cumulative exposure was found to be the best-fitting model and was a significant predictor ($p = 0.01$). However, the risk among mechanics did not increase with increasing duration of employment.

OR for quartile of cumulative exposure show a pattern of significantly increasing trends in risk with increasing exposure, ranging between 1.08 and 1.72, depending on the exposure level and lag structure used. The lifetime excess risk of lung cancer death (through age 75) for a male truck driver was estimated to be in the range of 1.4%-2.3% (95% confidence limits ranged from 0.3% to 4.6%) above the background risk, depending on the emissions scenarios assumed. The authors found that current exposures indicated that truck drivers are exposed to DE at levels about the same as ambient levels on the highways, which are about double the background levels in urban air. They conclude that the data suggest a positive and significant increase in lung cancer risk with increasing estimated cumulative exposure to DE among workers in the trucking industry. They assert that these estimates suggest that the lifetime excess risk for lung cancer is 10 times higher than the OSHA standards, but caution that the results should be viewed as exploratory.

The authors acknowledge that the increasing trend in risk with increasing estimates of cumulative exposure is partly due to the fact that a component of cumulative dose is simple duration of exposure, and that analyses by simple duration also exhibit a positive trend with duration. This analysis essentially weights the duration by contrived estimates of exposure intensity, and the authors acknowledge that this weighting depends on very broad assumptions.

This is not an analysis of new data that provides independent estimates of relative risk for DE and lung cancer incidence. Instead, it is an attempt to convert the data from Steenland's earlier study of lung cancer for the purpose of estimating a different risk metric, "lifetime excess risk of lung cancer," by augmenting these data with limited industrial hygiene data and rationalizations about plausible models for cumulative exposure.

The Health Effects Institute (HEI, 1999) and others have raised some concerns about the exposure estimations, selection of controls, and control for confounding variables, and hence, this study's usefulness for quantitative risk assessment. EPA and NIOSH will address these concerns in the year 2001. The HEI (1999) panel noted that some of the strengths of this study include the relevance of exposure levels to the general population and the use of an exposure marker for diesel engine emissions that was an improvement over the concentration of respirable-size particles (RSP). The number of study subjects (996 lung cancer cases) is large. Histories of exposures to asbestos and smoking were obtained, and confounding by these two variables was controlled in the analysis. Thus, it should be noted that these concerns are about

the use of these data for quantitative risk assessment, due to limitations of the exposure data. As far as qualitative risk assessment is concerned, this study is still considered to be positive and strong.

7.2.2.9. *Boffetta et al. (1990): Case-Control Study on Occupational Exposure to DE and Lung Cancer Risk*

This is an ongoing (since 1969) case-control study of tobacco-related diseases in 18 hospitals (six U.S. cities). Cases comprise 2,584 males with histologically confirmed primary lung cancers. Sixty-nine cases were matched to 1 control, whereas 2,515 were matched to 2 controls. Controls were individuals who were diagnosed with non-tobacco-related diseases. The matching was done for sex, age (±2 years), hospital, and year of interview. The interviews were conducted at the hospitals at the time of diagnosis. In 1985, the occupational section of the questionnaire was modified to include the usual occupation and up to five other jobs as well as duration (in years) worked in those jobs. After 1985, information was also obtained on exposure to 45 groups of chemicals, including DE at the workplace or during hobby activities. A priori aggregation of occupations was categorized into low probability of DE exposure (reference group), possible exposure (19 occupations), and probable exposure (13 occupations). Analysis was conducted based on "usual occupation" on all study subjects, and any occupation with sufficient cases was eligible for further analysis. In addition, cases enrolled after 1985 for which there were self-reported DE exposure and detailed work histories were also analyzed separately.

Both matched and unmatched analyses were done by calculating the adjusted (for smoking and education) relative odds using the Mantel-Haenzael method and calculating the test-based 95% confidence interval using the Miettinen method. Unconditional logistic regression was used to adjust for potential confounders (the PROC LOGIST of SAS). Linear trends for risk were also tested according to Mantel.

Adjusted relative odds for possible and probable exposure groups as well as the truck drivers were slightly below unity, none being statistically significant for the entire study population. Although slight excesses were observed for the self-reported DE exposure group and the subset of post-1985 enrollees for highest duration of exposure (for self-reported exposure, occupations with probable exposure, and truck drivers), none was statistically significant. Trend tests for the risk of lung cancer among self-reported DE exposure, probable exposure, and truck drivers with increasing exposure (duration of exposure used as surrogate for increasing dose) were nonsignificant too. Statistically significant lung cancer excesses were observed for cigarette smoking only.

The major strength of this study is availability of detailed smoking history. Even though detailed information was obtained for the usual and five other occupations (1985), because it

was difficult to estimate or verify the actual exposure to DE, duration of employment was used as a surrogate for dose instead. The numbers of cases and controls were large; however, the number of individuals exposed to DE was relatively few, thus reducing the power of the study. This study did not attempt latency analysis either. Due to these limitations, the findings of this study are unable to provide either positive or negative evidence for a causal association between DE and occurrence of lung cancer.

7.2.2.10. *Emmelin et al. (1993): DE Exposure and Smoking: A Case-Referent Study of Lung Cancer Among Swedish Dock Workers*

This case-control study of lung cancer was drawn from a cohort defined as all male workers who had been employed as dockworkers for at least 6 months between 1950 and 1974. In the population of 6,573 from 20 ports, there were 90 lung cancer deaths (cases), identified through Swedish death and cancer registers, during the period 1960 to 1982. Of these 90 deaths, the 54 who were workers at the 15 ports for which exposure surrogate information was available were chosen for the case-control study. Four controls, matched on port and age, were chosen for each case from the remaining cohort who had survived to the time of diagnosis of the case. Both live and deceased controls were included. The final analyses were done on 50 cases and 154 controls who had complete information on employment dates and smoking data. The smoking strata were created by classifying ex-smokers as nonsmokers if they had not smoked for at least 5 years prior to the date of diagnosis of the case; otherwise they were classified as smokers.

Relative odds and regression coefficients were calculated using conditional logistic regression models. Comparisons were made both with and without smoking included as a variable, and the possible interaction between smoking and DE was tested. Both the weighted linear regressions of the adjusted relative odds and the regression coefficients were used to test mortality trends with all three exposure variables.

Exposure to DE was assessed indirectly by initially measuring: (1) exposure intensity based on exhaust emission, (2) characteristics of the environment in terms of ventilation, and (3) measures of proportion of time in higher exposed jobs. For exhaust emissions, annual diesel fuel consumption at a port was used as the surrogate. For ventilation, the annual proportion of ships with closed or semiclosed holds was used as the surrogate. The proportion of time spent below decks was used as the surrogate for more exposed jobs. Although data were collected for all three measures, only the annual fuel consumption was used for analysis. Because every man was likely to rotate through the various jobs, the authors thought using annual consumption of diesel fuel was the appropriate measure of exposure. Consequently, in a second analysis, the annual fuel consumption was divided by the number of employees in the same port that year to come up with the fuel-per-person measure, which was further used to create a second measure,

"exposed time." The "annual fuel" and exposed-time data were entered in a calendar time-exposure matrix for each port, from which individual exposure measures were created. A third measure, "machine time" (years of employment from first exposure), was also used to compare the results with other studies. All exposure measures were accumulated from the first year of employment or first year of diesel machine use, whichever came later. The last year of exposure was fixed at 1979. All exposures up to 2 years before the date of lung cancer diagnosis were omitted from both cases and matched controls. A priori classification into three categories of low, medium, and high exposure was done for all three exposure variables: machine time, fuel, and exposed time.

Conditional logistic regression models, adjusting for smoking status and using low exposures and/or nonsmokers as a comparison group, yielded positive trends for all exposure measures, but no trend test results were reported, and only the relative odds for the exposed-time exposure measure in the high-exposure group (OR = 6.8, 90% CI = 1.3 to 34.9) was reported as statistically significant. For smokers, adjusting for DE exposure level, the relative odds were statistically significant and about equal for all three exposure variables: machine time, OR = 5.7 (90% CI = 2.4 to 13.3); fuel, OR = 5.5 (90% CI = 2.4 to 12.7); and exposed time, OR = 6.2 (90% CI = 2.6 to 14.6). Interaction between DE and smoking was tested by conditional logistic regression in the exposed-time variable. Although there were positive trends for both smokers and nonsmokers, the trend for smokers was much steeper: low, OR = 3.7 (90% CI = 0.9 to 14.6); medium, OR = 10.7 (90% CI = 1.5 to 78.4); and high, OR = 28.9 (90% CI = 3.5 to 240), indicating more than additive interaction between these two variables.

In the weighted linear regression model with the exposed-time variable, the results were similar to those using the logistic regression model. The authors also explored the smoking variable further in various analyses, some of which suggested a strong interaction between DE and smoking. However, with just six nonsmokers and no further categorization of smoking amount or duration, these results are of limited value.

The DE exposure matrices created using three different variables are intricate. Analyses by any of these variables yield essentially the same positive results and positive trends, providing consistent support for a real effect of DE exposure, at least in smokers. However, methodological limitations to this study prevent a more definitive conclusion. The numbers of cases and controls are small. There are very few nonsmokers; thus, testing the effects of DE exposure in them is futile. Lack of information on asbestos exposure, to which dockworkers are usually exposed, may also confound the results. Also, no latency analyses are presented. Overall, despite these limitations, this study supports the earlier findings of excess lung cancer mortality among individuals exposed to DE.

7.2.2.11. *Swanson et al. (1993): Diversity in the Association Between Occupation and Lung Cancer Among Black and White Men*

This population-based case-control study of lung cancer was conducted in metropolitan Detroit. The cases and controls for this study were identified from the Occupational Cancer Incidence Surveillance Study (OCISS). A total of 3,792 incident lung cancer cases and 1,966 colon and rectal cancer cases used as controls, diagnosed between 1984 and 1987 among white and black males aged 40 to 84 years, were selected for the study. Information was obtained by telephone interview either with the individual or a surrogate about lifetime work history and smoking history, as well as medical, demographic, and residential history. Occupation and industry data were coded using the 1980 U.S. Census Bureau classification codes. The investigators selected certain occupations and industries as having little or no exposure to carcinogens and defined them as an unexposed group. Analysis was done using logistic regression method and adjusting for age at diagnosis, pack-years of cigarette smoking, and race.

The results were presented by various occupations and industries; those with potential exposures to DE were drivers of heavy trucks and light trucks, farmers, and railroad workers, respectively. Among white males, increasing lung cancer risks were observed with increasing duration of employment for drivers of heavy trucks, drivers of light trucks, and farmers. Although none of the individual ORs were statistically significant, trend tests were significant for all three occupations ($p \leq 0.05$). On the other hand, among black males increasing lung cancer risks with increasing duration of employment were observed for farmers only, with an OR of 10.4 (95% CI = 1.4, 77.1) reaching significance for employment of 20+ years. As for the railroad industry, increasing lung cancer risks with increasing duration of employment were observed for both white and black males. The trend test was significant for white males only, with an OR of 2.4 (95% CI = 1.1, 5.1) reaching significance for employment of 10+ years.

The main strengths of the study are large sample size, availability of lifetime work history and smoking history, and the population-based study format, precluding selection bias. The major limitation, as in other studies, is lack of direct information on specific exposures. The interesting result of this study is lung cancer excesses observed in farmers, mainly among crop farmers, who have potential exposure to DE from their tractors in addition to pesticides, herbicides, and other PM_{10}. The authors point out that this is the first study to find excess lung cancer in this occupation.

7.2.2.12. *Hansen et al. (1998): Increased Risk of Lung Cancer Among Different Types of Professional Drivers in Denmark*

This is a population-based case-control study of lung cancer, conducted in professional drivers in Denmark. The cases first diagnosed as primary lung cancer between 1970 and 1989

among males born between 1897 and 1966 were identified from the Danish Cancer Registry. The registry provided the information on diagnosis from ICD-7, name, sex, and unique personal identification number (PIDN). Information about past employment was obtained by linkage with the nationwide pension fund. The fund keeps the records by name and PIDN about the date of start and end of each job and unique company number of the employer. The records are kept even after the employee has retired or died. Information about current employment was obtained from the Danish Central Population Registry (CPR) by linkage with the PIDN.

Of 37,597 cases identified from the Registry, 8,853 did not have any employment records. Controls (1:1) for 28,744 lung cancer cases with employment histories were selected randomly from CPR, matched with the case by year of birth and sex. Furthermore, these controls had to be alive, cancer free, and employed prior to the diagnosis of lung cancer in the corresponding case. Employment histories were obtained for the controls in the same fashion as cases from the pension fund. The employment record search resulted in a total of 1,640 lorry/bus drivers and 426 taxi drivers. They were further divided into subgroups by their duration of employment. Information about smoking in drivers was acquired from two national surveys conducted in 1970-72 and 1983. No direct information on smoking was available in either cases or controls. A separate case-control study of mesothelioma indirectly looked at asbestos exposure among professional drivers. OR, adjusting for socioeconomic status and 95% CI, were computed using conditional logistic regression (PECAN procedure in the statistical package EPICURE).

Significant ORs for lung cancer were found for lorry/bus drivers (OR = 1.31, 95% CI = 1.17, 1.46), taxi drivers (OR = 1.64, 95% CI = 1.22, 2.19), and unspecified drivers (OR = 1.39, 95% CI = 1.30, 1.51). Significant ORs were found for both lorry/bus drivers and taxi drivers by duration of employment in 1-5 years and >5 years categories, with no lag time and with a 10-year lag time. The ORs remained the same for lorry/bus drivers in these employment categories for no lag time and 10-year lag time. Among taxi drivers, on the other hand, the OR of 2.2 in >5 year employment in no-lag-time analysis increased to 3.0 in the 10-year lag time analysis. The authors asserted that the higher risk seen in the taxi drivers may be due to higher exposure attributable due to longer time spent in traffic congestion. The trend tests for increasing risk with increasing duration of employment (surrogate for exposure) were statistically significant ($p<0.001$) for both lorry/bus drivers and taxi drivers in no-lag-time and 10-year lag time analysis. All the ORs were adjusted for socioeconomic status.

The main strengths of the study are the large sample size, availability of information on socioeconomic status, and detailed employment records. The main limitation, however, is lack of information on what type of fuel these vehicles used. It is probably safe to assume that the lorry/buses were diesel powered, whereas the taxis could be either diesel or gasoline powered. A

personal communication with Dr. Johnni Hansen confirmed that dieselization in Denmark was completed in the late 1940s and lorries, buses, and taxis have been using diesel fuel since then. Although direct adjustments were not done for smoking and exposure to asbestos, indirect information on both these confounders indicates that they are unlikely to explain the observed excesses and the increasing risk with increasing duration of employment. Thus, the results of this study are strongly supportive of DE being associated with increased lung cancer.

7.2.2.13. *Brüske-Hohlfeld et al. (1999): Lung Cancer Risk in Male Workers Occupationally Exposed to Diesel Motor Emissions in Germany*

This paper presents a pooled analysis of two case-control studies of lung cancer. The first study, by Jöckel et al. (1995, 1998), was conducted between 1988 and 1993 and had 1,004 cases and 1,004 controls matched for sex, age, and region of residence, selected randomly from the compulsory municipal registries. The inclusion criteria for cases were: they should have been born in or after 1913, should have been of German nationality, and should have been diagnosed with lung cancer within 3 months prior to the interview. The second study, by Wichmann et al. (1998), was ongoing when it was included in this study. The study span covered the years 1990 to 1996. By 1994 a total of 3,180 cases and 3,249 controls, randomly selected from the compulsory population registries, were frequency matched on sex, age, and region. The cases were less than 76 years old, were residents of the region and living in Germany for more than 25 years, and had a diagnosis not more than 3 months old. Of 4,184 pooled cases and 4,253 pooled controls, the analysis was conducted on 3,498 male cases and 3,541 male controls. A personal interview was conducted with each study participant. Data were collected on basic demographic information, detailed smoking history, and lifelong occupational history about jobs held and industries worked in. The job titles and industries were classified into 33 and 21 categories, respectively, using the German Statistical Office codes.

Based on job codes with potential exposure to diesel motor emission (DME), four exposure groups were constituted. Group A comprised professional drivers of trucks, buses, taxis, etc. Group B comprised other traffic-related jobs such as switchmen, diesel locomotive drivers, and diesel forklift truck drivers. Group C comprised bulldozer operators, graders, and excavators. Group D comprised full-time farm tractor drivers. Validation of the jobs was done by written evaluation of the job task descriptions, which also avoided misclassification. The following information was acquired for the construction of job task descriptions: (1) What were your usual tasks at work and how often (in % of daily working hours) were they performed? (2) What did you produce, manufacture, or transport? (3) Which material was used? (4) What kind of machine did you operate? Some individuals had more than one job task

with DME exposure. The exposure assessment was done without knowing the status of the case/control.

For each individual, cumulative exposure was calculated for the complete work history by categorizing the duration of exposure as >0-3, >3-10, >10-20, >20-30, >30 years, and beginning and end of exposure. The first year of exposure was defined as ≤1945, 1946-1955, and ≥1956 while the last year of exposure was defined as ≤1965, 1966-1975, and ≥1976. For professional drivers, hours driven per day were accumulated and were classified as "driving hours."

A smoker was defined as any individual who had smoked regularly for at least 6 months. Smoking information was acquired in series with the starting time, type of tobacco, amount smoked, duration in years, and calender year of quitting. Asbestos exposure was estimated by certain job-specific supplementary questions.

The cases and controls were post-hoc stratified into 6 age and 17 region categories. ORs adjusted for smoking and asbestos exposure were calculated by conditional logistic regression, using "never exposed" workers as the reference group. The adjustment for cigarette smoking was done by using pack-years as a continuous variable; adjustment for other tobacco products was done by considering them as a binary variable. A total of 716 cases and 430 controls were found to be ever exposed to DME. The smoking- and asbestos-adjusted OR of 1.43 (95% CI = 1.23, 1.67) for all DME exposed was reduced from the crude OR of 1.91. For the entire group the various analyses yielded statistically significant ORs ranging from 1.25 to 2.31, adjusted for smoking and asbestos exposure (West Germany, >10-20 years and >20-30 years of exposure, first year of exposure in 1946-1955 and 1956+, end of exposure in 1966-1975 and 1976+, and for the job categories of Group A, B, and C). The risk increased with increasing years of exposure, and for both the first year of exposure (≤1945, 1946-1955, and ≥1956) and end year of exposure (≤1965, 1966-1975, and ≥1976).

Separate analyses by four job categories (all the ORs were adjusted for smoking and asbestos exposure) showed that for professional drivers (Group A) the overall OR was 1.25 (95% CI = 1.05, 1.47). Significant ORs were found for various factors in West Germany only. The factors were: >0-3 years and >10-20 years of exposure (OR = 1.69, 95% CI = 1.13, 2.53, and OR = 2.02, 95% CI = 1.32, 3.08, respectively), beginning of exposure in 1956+ and end of exposure in 1976+ (OR = 1.56, 95% CI = 1.21, 2.03, and OR = 1.5, 95% CI = 1.14, 1.98, respectively), and 1,000-49,999 driving hours (OR = 1.54, 95% CI = 1.15, 2.07). None of the ORs were significant in East Germany in this group.

For other traffic-related jobs (Group B) the overall OR was 1.53 (95% CI = 1.04, 2.24). The ORs for beginning of exposure in 1956+ and end of exposure in 1976+ were OR = 1.71, 95% CI = 1.05, 2.78, and OR = 2.68, 95% CI = 1.47, 4.90, respectively. The risk increased with

increasing duration of exposure and was statistically significant for >10-20 years (OR = 2.49) and more than 20 years (OR = 2.88). No separate analyses for West Germany and East Germany were presented in this category.

For heavy equipment operators (Group C) the overall OR of 2.31 (95% CI = 1.44, 3.7) was highest among all the job categories. Significant ORs were observed for beginning exposure in 1946-1955 (OR = 2.83, 95% CI = 1.10, 7.23) and end exposure in 1966-1975 (OR = 3.74, 95% CI = 1.20, 11.64). The risk increased with increasing duration of exposure and was statistically significant for more than 20 years of exposure (OR = 4.3). Although no separate analyses for West Germany and East Germany were presented, investigators mentioned that for this job group hardly any difference was seen between West Germany and East Germany.

For drivers of the farming tractors (Group D) the overall OR of 1.29 was not significant. Risk increased with increasing duration of exposure and was significant for exposure of more than 30 years (OR = 6.81, 95% CI = 1.17, 39.51). No separate analyses for West Germany and East Germany were presented in this category.

The professional drivers and the other traffic-related job categories probably have mixed exposures to gasoline exhaust in general traffic. On the other hand, it should be noted that exposure to DME among heavy equipment and farm tractor drivers is much higher and not as mixed as in professional drivers. The heavy equipment drivers usually drive repeatedly through their own equipment's exhaust. Therefore, the observed highest risk for lung cancer in this job category establishes a direct link with the DME. The only other study that found significantly higher risk for heavy equipment operators (RR = 2.6) was conducted by Boffeta et al. (1988). Although the only significant excess was observed for farming tractor operators among individuals with more than 30 years of exposure, a steady increase in risk was observed for this job category with increasing exposure. The investigators stated that the working conditions and the DME of tractors remained fairly constant over the years. This increase may be due mainly to exposure to DME and, in addition, PM_{10}.

This is a well-designed, well-conducted, and well-analyzed study. Its main strengths are large sample size, resulting in good statistical power; inclusion of incident cases that were diagnosed not more than 3 months prior to the interview; use of only personal interviews, reducing recall bias; diagnosis ascertained by cytology or histology; and availability of lifelong detailed occupational and smoking history. Exposure estimation for each individual was based on job codes and industry codes, which were validated by written job descriptions to avoid misclassification. The main limitation of the study is lack of data on actual exposure to DME. The cumulative quantitative exposures were calculated based on time spent in each job with potential exposure to DME and the type of equipment used. Thus, this study provides strong evidence for a causal association between exposure to DE and occurrence of lung cancer.

Table 7-2 summarizes the above lung cancer case-control studies.

Table 7-2. Epidemiologic studies of the health effects of exposure to DE: case-control studies of lung cancer

Authors	Population studied	DE exposure assessment	Results	Limitations
Hall and Wynder (1984)	502 histologically confirmed lung cancers Cases diagnosed 12 mo prior to interviews 502 matched hospital controls without tobacco-related diseases, matched for age, sex, race, and geographical area Population from 18 hospitals in controls	Based on previous Industrial Hygiene Standards for a particular occupation, usual lifetime occupation coded as "probably high exposure" and "no exposure" NIOSH standards used to classify exposures: High Moderate Low	SNS excess risk after adjustment for smoking for lung cancer: RR = 1.4 (1st criteria) and RR = 1.7 (NIOSH criteria)	Complete lifetime employment history not available Self-reported occupation history not validated No analysis by dose, latency, or duration of exposure No information on nonoccupational diesel exposure
Damber and Larsson (1987)	589 lung cancer cases who had died prior to 1979 reported to Swedish registry between 1972 and 1977 582 matched dead controls (sex, age, year of death, municipality) drawn from National Registry of Cause of Death 453 matched living controls (sex, year of birth, municipality) drawn from National Population Registry	Occupations held for at least 1 year or more A 5-digit code was used to classify the occupations according to Nordic Classification of Occupations	For underground miners: SS OR = 2.7 (≥1 year of employment) SS OR = 9.8 (≥20 years of employment) For professional drivers: SNS OR = 1.2 (≥20 years of employment) with dead controls All ORs adjusted for smoking	Uncertain DE exposure No validation of exposure done Underground miners data not adjusted for other confounders such as radon, etc.

Table 7-2. Epidemiologic studies of the health effects of exposure to DE: case-control studies of lung cancer (continued)

Authors	Population studied	DE exposure assessment	Results	Limitations
Lerchen et al. (1987)	506 lung cancer cases from New Mexico tumor registry (333 males and 173 females) Aged 25-84 years Diagnosed between January 1, 1980, and December 31, 1982 771 (499 males and 272 females) frequency matched with cases, selected from telephone directory	Lifetime occupational history and self-reported exposure history were obtained Coded according to Standard Industrial Classification Scheme	No excess of relative odds were observed for DE exposure	Exposure based on occupational history and self-report, which was not validated 50% occupational history provided by next of kin Absence of lung cancer association with asbestos suggests misclassification of exposure
Garshick et al. (1987)	1,319 lung cancer cases who died between March 1, 1981, and February 28, 1982 2,385 matched controls (two each, age and date of death) Both cases and controls drawn from railroad worker cohort who had worked for 10 or more years	Personal exposure assessed for 39 job categories This was corrected with job titles to dichotomize the exposure into: Exposed Not exposed Industrial hygiene sampling done	SS OR = 1.41 (≤64 year age group) SS OR = 1.64 (≤64 year age group) for ≥20 years DE exposure group when compared to 0- to 4-year exposure group All ORs adjusted for lifetime smoking and asbestos exposure	Probable misclassification of DE exposure jobs Years of exposure used as surrogate for dose 13% of death certificates not ascertained Overestimation of smoking history
Benhamou et al. (1988)	1,260 histologically confirmed lung cancer cases 2,084 non-tobacco-related disease matched controls (sex, age at diagnosis, hospital admission, and interviewer) Occurring between 1976 and 1980 in France	Based on exposures determined by panel of experts The occupations were recorded blindly using International Standard Classification of Occupations as chemical or physical exposures	Significant excess risks were found in motor vehicle drivers (RR = 1.42) and transport equipment operators (RR = 1.35) (smoking adjusted)	Exposure based on occupational histories not validated Exposures classified as chemical and physical exposures, not specific to DE

Table 7-2. Epidemiologic studies of the health effects of exposure to DE: case-control studies of lung cancer (continued)

Authors	Population studied	DE exposure assessment	Results	Limitations
Hayes et al. (1989)	Pooled data from three different studies consisting of 2,291 male lung cancer cases 2,570 controls	Occupational information from next of kin for all jobs held Jobs classified with respect to potential exposure to known and suspected pulmonary carcinogens	SS OR = 1.5 for truck drivers (>10 years of employment) SS positive trend with increasing employment as truck driver Adjusted for age, smoking, & study area	Exposure data based on job description given by next of kin, which was not validated Could have been mixed exposure to both diesel and gasoline exhausts Job description could have led to misclassification
Steenland et al. (1990)	1,058 male lung cancer deaths between 1982 and 1983 1,160, every sixth death from entire mortality file, sorted by Social Security number (excluding lung cancer, bladder cancer, and motor vehicle accidents) Cases and controls were from Central State Teamsters who had filed claims (requiring 20-year tenure)	Longest job held: diesel truck driver, gasoline truck driver, both types of trucks, truck mechanic, and dockworkers	As 1964 cut-off point: SS OR = 1.64 for long-haul drivers with 13+ years of employment Positive trend test for long-haul drivers (p=0.04) SS OR = 1.89 for diesel truck drivers of 35+ years of employment Adjusted for age, smoking, & asbestos	Exposure based on job titles not validated Possible misclassification of exposure and smoking, based on next-of-kin information Lack of sufficient latency
Steenland et al. (1998)	Exposure-response analyses of their 1990 case-control study	Industrial hygiene data of elemental carbon in trucking industry collected by Zaebst et al. (1991) used to estimate individual exposures Cumulative exposures calculated based on estimated lifetime exposures	For mechanics: OR = 1.69 (had the highest DE exposure) Lowest DE exposure and lowest OR = 0.93 observed for dockworkers Increasing risk of lung cancer with increasing exposure Adjusted for age & smoking	

Table 7-2. Epidemiologic studies of the health effects of exposure to DE: case-control studies of lung cancer (continued)

Authors	Population studied	DE exposure assessment	Results	Limitations
Boffetta et al. (1990)	From 18 hospitals (since 1969), 2,584 male lung cancer cases matched to either one control (69) or two controls (2,515) were drawn. Matched on age, hospital, and year of interview	A priori aggregation of occupations categorized into low probability, possible exposure (19 occupations), and probable exposure (13 occupations) to DE	OR slightly below unity SNS Adjusted for smoking	No verification of exposure Duration of employment used as surrogate for dose Number of individuals exposed to DE was small
Emmelin et al. (1993)	50 male lung cancer cases from 15 ports (worked for at least 6 months between 1950 and 1974), 154 controls matched on age and port	Indirect DE exposure assessment done based on (1) exposure intensity, (2) characteristics of ventilation, (3) measure of proportion of time in higher exposure jobs	SS OR for high-exposure group = 6.8 Positive trend for DE observed (trend much steeper for smokers than nonsmokers) Adjusted for smoking	Numbers of cases and controls are small Very few nonsmokers Lack of exposure information on asbestos No latency analysis
Swanson et al. (1993)	Population based case-control study in metropolitan Detroit 3,792 lung cancer cases and 1,966 colon cancer (cases) controls, diagnosed between 1984 and 1987 in white and black males (aged between 40-84)	Telephone interviews with the individual or surrogate about lifetime work history Occupation and industry data coded per 1980 U.S. Census Bureau classification codes Certain occupations and industries were selected as unexposed to carcinogens	SS excess ORs observed for - black farmers OR= 10.4 for 20+ years employment - white railroad industry workers OR= 2.4 for 10+ years employment Among white trend tests were SS for -drivers of heavy duty trucks - drivers of light duty trucks - farmers - railroad workers Among blacks trend test was SS for farmers only All the ORs were adjusted for age at diagnosis, pack-years of cigarette smoking and race	Lack of direct information on specific exposures No latency analysis

Table 7-2. Epidemiologic studies of the health effects of exposure to DE: case-control studies of lung cancer (continued)

Authors	Population studied	DE exposure assessment	Results	Limitations
Hansen et al. (1998)	Population-based case-control study of professional drivers in Denmark Male lung cancer cases diagnosed between 1970-1989, controls matched by year of birth and sex	Information about past employment obtained by linkage with nationwide pension fund Employment as lorry/bus drivers (n=1,640) and taxi drivers (n=426) was used as surrogate for exposure to DE	For lorry/bus drivers: SS OR = 1.31 For taxi drivers: SS OR = 1.64, which increased to 2.2 in > 5-year employment with no lag time & 3.0 in > 5 year employment with 10- year lag time SS trend test for increasing risk with increasing employment for both lorry/bus drivers & taxi drivers ($p<0.001$) All ORs adjusted for socioeconomic status	Lack of information on the type of fuel (personal communication with the principal investigator confirmed that diesel fuel is used for the lorry/buses and taxis since early 1960s) Even though direct adjustment was not done for smoking/asbestos, indirect methods indicate that the results are not likely to be confounded by these factors

Table 7-2. Epidemiologic studies of the health effects of exposure to DE: case-control studies of lung cancer (continued)

Authors	Population studied	DE exposure assessment	Results	Limitations
Brüske-Hohlfeld et al. (1999)	Pooled analysis of two case-control studies (3,498 cases & 3,541 controls) Controls frequency matched on sex, age, & region, randomly selected from the compulsory population registry Inclusion criteria: (1) born in or after 1913/less than 75 years old, (2) German nationality/resident of the region - lived in Germany for more than 25 years, & (3) lung cancer diagnosis should be 3 months prior to the study Information obtained by personal interview on:	Lifetime detailed occupational & smoking histories obtained from each individual in a personal interview Based on job codes (33 job titles & 21 industries) potential DE exposure classified in 4 categories: A- professional drivers of trucks, buses, & taxis; B- other traffic related i.e., switchman, locomotive, & forklift drivers; C- bulldozer operators, graders,& excavators; D- farm tractor drivers Cumulative DE exposures and pack-years (smoking) calculated for each individual	SS higher risk adjusted for smoking observed for all 4 categories: A- ORs ranged from 1.25 to 2.53 B- ORs ranged from 1.53 to 2.88 C- ORs ranged from 2.31 to 4.3 D- 6.81 (exposure < 30 years) Risk increased with increasing exposure	Lack of data on actual exposure to diesel exaust

Abbreviations: OR = odds ratio; RR = relative risk; SNS = statistically nonsignificant; SS = statistically significant.

7.2.3. Summaries of Studies and Meta-Analyses of Lung Cancer

7.2.3.1. *Cohen and Higgins (1995): Health Effects of DE: Epidemiology*

The Health Effects Institute (HEI) reviewed all published epidemiologic studies on the health effects of exposure to DE available through June 1993, identified by a MEDLINE search and by reviewing the reference sections of published research and earlier reviews. HEI identified 35 reports of epidemiologic studies (16 cohort and 19 case-control) of the relation of occupational exposure to diesel emissions and lung cancer published between 1957 and 1993. HEI reviewed the 35 reports for epidemiologic evidence of health effects of exposure to DE for lung cancer, other cancers, and nonmalignant respiratory disease. They found that the data were strongest for lung cancer. The evidence suggested that occupational exposure to DE from diverse sources increases the rate of lung cancer by 20% to 40% in exposed workers generally, and to a greater extent among workers with prolonged exposure. They also found that the results are not explicable by confounding caused by cigarette smoking or other known sources of bias.

Control for smoking was identified in 15 studies. Six studies (17%) reported relative risk estimates less than 1; 29 studies (83%) reported at least one relative risk greater than one indicating positive association. Twelve studies indicating a relative risk greater than 1 had 95% confidence intervals, which excluded unity.

The authors conclude that epidemiologic data consistently show weak associations between exposure to DE and lung cancer. They find that the evidence suggests that long-term exposure to DE in a variety of occupational circumstances is associated with a 1.2- to 1.5-fold increase in the relative risk of lung cancer compared with workers classified as unexposed. Most of the studies that controlled for smoking found that the association between increased risk of lung cancer and exposure to DE persisted after such controls were applied, although in some cases the excess risk was lower. None of the studies measured exposure to diesel emissions or characterized the actual emissions from the source of exposure for the time period most relevant to the development of lung cancer. Most investigators classified exposure based on work histories reported by subjects or their next of kin, or by retirement records. Although these data provide relative rankings of exposure, the absence of concurrent exposure information is the key factor that limits interpretation of the epidemiologic findings and subsequently their utility in making quantitative estimates of cancer risks.

This is a comprehensive and thorough narrative review of studies of the health effects of DE. It does not undertake formal estimation of summary measures of effect or evaluation of heterogeneity in the results. The conclusion drawn about the consistency of the results is based on the author's assessment of the failure of potential biases and alternative explanations for the increase in risk to account for the observed consistency. In many if not most studies, the quality of the data used to control confounding was relatively crude. Although the studies do include qualitative assessment of whether control for smoking is taken into account, careful scrutiny of

the quality of the control or adjustment for smoking among the studies is absent. This leaves open the possibility that prevalent residual confounding by inadequate control for smoking in many studies may account for the consistent associations seen.

7.2.3.2. *Bhatia et al. (1998): DE Exposure and Lung Cancer*

Bhatia et al. (1998) report a meta-analysis of 29 published[2] cohort and case-control studies of the relation between occupational exposure to DE and lung cancer. A search of the epidemiologic literature was conducted for all studies concerning lung cancer and DE exposure. Occupational studies involving mining were excluded because of concern about the possible influence of radon and silica exposures. Studies in which the minimum interval from time of first exposure to end of follow-up was less than 10 years, and studies in which work with diesel equipment or engines could not be confirmed or reliably inferred, were excluded. When studies presented risk estimates for more than one specific occupational category of DE-exposed workers, the subgroup risk estimates were used in the meta-analysis. Smoking-adjusted effect measures were used when present.

Of 29 studies 23 met the criteria for inclusion in the meta-analysis. The observed relative risk estimates were greater than 1 in 21 of these studies; this result is unlikely to be due to chance. The pooled relative risk weighted by study precision was 1.33 (95% CI = 1.24, 1.44), indicating increased relative risk for lung cancer from occupational exposure to DE. Subanalyses by study design (case-control and cohort studies) and by control for smoking produced results that did not differ from those of the overall pooled analysis. Cohort studies using internal comparisons showed higher relative risks than those using external comparisons (see Figure 7-1).

Bhatia and colleagues conclude that the analysis shows a small but consistent increase in the risk for lung cancer among workers with exposure to DE. The authors evaluate the dependence of the relative risk estimate on the presence of control for smoking among studies, and provide a table that allows assessment of whether the quality of the data contributing to control for smoking is related to the relative risk estimates (albeit in a limited number of studies). Bhatia et al. assert that residual confounding is not affecting the summary estimates or conclusions for the following reasons: (1) the pooled relative risks for studies adjusted for smoking were the same as those for studies not adjusting for smoking; (2) in those studies giving risk estimates adjusted for smoking and risk estimates not adjusted for smoking, there was only a small reduction in the pooled relative risk from DE exposure; and (3) in studies with internal

[2]Of 35 studies identified in the literature search, 6 pairs of studies represented analyses of the same study population, reducing the number of studies to 29.

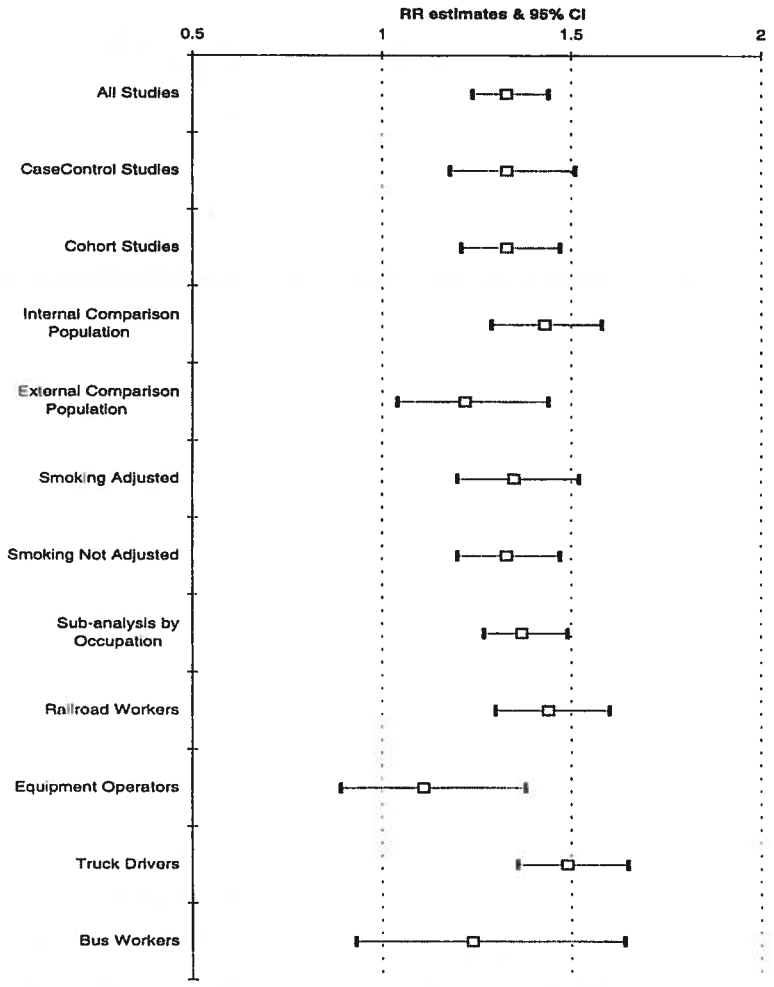


Figure 7-1. Pooled relative risk estimates and heterogeneity-adjusted 95% confidence intervals for all studies and subgroups of studies included in the meta-analysis.

Source: Bhatia et al., 1998.

comparison populations, in which confounding is less likely, the pooled relative risk estimate was 1.43.

The validity of this assessment depends on the adequacy of control for smoking in the individual studies. If inadequate adjustment for smoking is employed and residual confounding by cigarette smoking pertains in the result of the individual studies, then the comparisons and contrasts of the pooled estimates the authors cite as reasons for dismissing the effect of residual confounding by smoking will remain contaminated by residual confounding in the individual studies. In fact, Bhatia et al. erroneously identify the treatment of the smoking data in the main

analysis for the 1987 report by Garshick et al. as a continuous variable representing pack-years of smoking, whereas the analysis actually dichotomized the pack-years data into two crude dose categories (above and below the 50 pack-years level). This clearly reduced the quality of the adjustment for smoking, which already suffered from the fact that information on cumulative cigarette consumption was missing for more than 20% of the lung cancer cases. In this instance, the consistency between the adjusted and unadjusted estimates of the relative risk for DE exposure may be attributable to failure of adjustment rather than lack of confounding by cigarette smoking. A similar problem exists for the Bhatia et al. representation of the control for confounding in the study by Boffetta and Stellman (1988).

An evaluation of the potential for publication bias is presented that provides reassurance that the magnitude of published effects is not a function of the precision or study power; however, this assessment cannot rule out the possibility of publication bias.

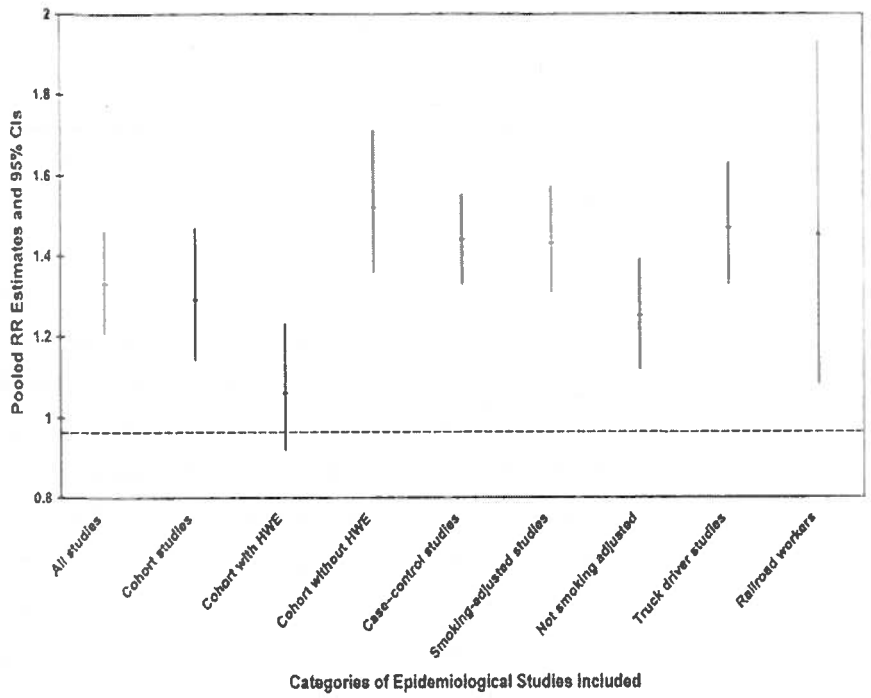
7.2.3.3. *Lipsett and Campleman (1999): Occupational Exposure to DE and Lung Cancer: A Meta-Analysis*

Lipsett and Campleman (1999) conducted electronic searches to identify epidemiologic studies published between 1975 and 1995 of the relationship of occupational exposure to DE and lung cancer. Studies were selected based on the following criteria: (1) Estimates of relative risks and their standard errors must be reported or derivable from the information presented. (2) Studies must have allowed for a latency period of 10 or more years for development of lung cancer after onset of exposure. (3) No obvious bias resulted from incomplete case ascertainment in follow-up studies. (4) Studies must be independent: that is, a single representative study selected from any set of multiple analyses of data from the same population. Studies focusing on occupations involving mining were excluded because of potential confounding by radon, arsenic, and silica, as well as possible interactions between cigarette smoking and exposure to these substances in lung cancer induction.

Thirty of the 47 studies initially identified as relevant met the specified inclusion criteria. Several risk estimates were extracted from six studies reporting results from multiple mutually exclusive diesel-related occupational subgroups. If a study reported effects associated with several levels or durations of exposure, the effect reported for the highest level or longest duration of exposure was used. If estimates for several occupational subsets were reported, the most diesel-specific occupation or exposure was selected. Adjusted risk estimates were used when available.

Thirty-nine independent estimates of relative risk and standard errors were extracted. Pooled estimates of relative risk were calculated using a random-effects model. Among study

populations most likely to have had substantial exposure to DE, the pooled smoking- adjusted relative risk was 1.47 (95% CI = 1.29, 1.67) (see Figure 7-2).



Note. CI = confidence interval; HWE = healthy worker effect.

Figure 7-2. Pooled estimates of relative risk of lung cancer in epidemiologic studies involving occupational exposure to DE (random-effects models).

Source: Lipsett and Campleman, 1999.

The between-study variance of the relative risks indicated the presence of significant heterogeneity in the individual estimates. The authors evaluated the potential sources of heterogeneity by subset analysis and linear meta-regressions. Major sources of heterogeneity included control for confounding by smoking, selection bias (a healthy worker effect), and exposure patterns characteristic of different occupational categories. A modestly higher, pooled relative risk was derived for the subset of case-control studies, which, unlike the cohort studies, showed little evidence of heterogeneity.

This meta-analysis also evaluated the potential for publication bias, which provides reassurance that the magnitude of published effects is not a function of the precision or study

power. Again, as stated in the Bhatia et al. (1998) review, this assessment cannot rule out the possibility of publication bias.

Although a relatively technical approach was used in deriving summary estimates of relative risk and the evaluation of possible sources of variation in the relative risks in this meta-analysis, this approach should not be confused with rigorous evaluation of the potential weaknesses among the studies included in the analysis. The heterogeneity attributable to statistical adjustment for smoking was evaluated based on a dichotomous assessment of whether control for smoking could be identified in the studies considered. This does not reflect the adequacy of the adjustment for smoking employed in the individual studies considered.

7.2.4. Summary and Discussion

Certain extracts of DE have been demonstrated as both mutagenic and carcinogenic in animals and in humans. Animal data suggest that DE is a pulmonary carcinogen among rodents exposed by inhalation to high doses over long periods of time. While rat lung cancer response to DE is not suitable for dose-response extrapolation to humans, the positive lung cancer response doses imply a hazard for humans. Because large working populations are currently exposed to DE and because nonoccupational ambient exposures currently are of concern as well, the possibility that exposure to this complex mixture may be carcinogenic to humans has become an important public health issue.

Because diesel emissions become diluted in the ambient air, it is difficult to study the health effects in the general population. Nonoccupational exposure to DE is worldwide in urban areas. Thus, "unexposed" reference populations used in occupational cohort studies are likely to contain a substantial number of individuals who are nonoccupationally exposed to DE. Furthermore, the "exposed" group in these studies is based on job titles, which in most instances are not verified or correlated with environmental hygiene measurement. The issue of health effect measurement is further complicated by the fact that occupational cohorts tend to be healthy and have below-average mortality, usually referred to as the "healthy worker effect." Hence, the usual standard mortality ratios observed in cohort mortality studies are likely to be underestimations of true risk.

A major difficulty with the occupational studies considered here was measurement of actual DE exposure. Because all the cohort mortality studies were retrospective, assessment of health effects from exposure to DE was naturally indirect. In these occupational settings, no systematic quantitative records of ambient air were available. Most studies compared men in job categories with presumably some exposure to DE with either standard populations (presumably no exposure to DE) or men in other job categories from industries with little or no potential for DE exposure. A few studies have included measurements of diesel fumes, but there is no

standard method for the measurement. No attempt is made to correlate these exposures with the cancers observed in any of these studies, nor is it clear exactly which extract should have been measured to assess the occupational exposure to DE. All studies have relied on the job categories or self-report of exposure to DE. Gustavsson et al. (1990), Emmelin et al. (1993), and Brüske-Hohlfeld et al. (1999) estimated exposure levels by getting detailed histories of job tasks/categories and computing cumulative exposures, which unfortunately were not verifiable due to of the lack of industrial hygiene data. In the studies by Garshick et al. (1987, 1988), the diesel-exhaust-exposed job categories were verified based on an industrial hygiene survey done by Woskie et al. (1988a,b). The investigators found that in most cases the job titles were good surrogates for DE exposure. Also, in the railroad industry, where only persons who had at least 10 years of work experience were included in the study, the workers tended not to change job categories over the years. Thus, a job known only at one point in time was a reasonable marker of past DE exposure. Unfortunately, the exposure was only qualitatively verified. Quantitative use of this information would have been much more meaningful. Zaebst et al. (1991) conducted an industrial hygiene survey of elemental carbon exposure in the trucking industry by job categories. Using these exposure measurements, Steenland et al. (1998) conducted an exposure-response analysis of their earlier lung cancer case-control study (Steenland et al., 1990). These exposure data are currently being verified and will be used for quantitative risk assessment in the near future.

Occupations involving potential exposure to DE are miners, truck drivers, transportation workers, railroad workers, and heavy equipment operators. No known studies in metal miners have assessed whether DE is associated with lung cancer. Currently, there are about 265 underground metal/nonmetal mines in the United States (Department of Labor, Mine Safety and Health Administration, 2001). Approximately 20,000 miners are employed, but not all of them are currently working in the mines. Diesel engines were introduced in metal mines in the United States in the early to mid-1960s. Although all these mines use diesel equipment, it is difficult to estimate how many of these miners were actually exposed to diesel fumes.

Diesel engines were introduced in coal mines at an even later date in the United States, and their use is still quite limited. There are 910 underground coal mines in the United States, of which only 145 currently use diesel powered equipment (Department of Labor, Mine Safety and Health Administration, 2001). Even if it were possible to estimate how many miners (metal and coal) were exposed to DE, it would be very difficult to separate out the confounding effects of other potential pulmonary carcinogens, such as radon decay products or heavy metals (e.g., arsenic, chromium). Furthermore, the relatively short latency period limits the usefulness of these cohorts of miners.

Both metal and coal mines in Europe and Australia, on the other hand, have been using diesel equipment for more than 50 years. The epidemiologic studies of coal miners conducted in these countries discuss only exposures to coal dust. In most of the coal miner studies, DE exposures are not even mentioned by the investigators as confounding exposures. Therefore, it is not known how many miners, if any, were exposed to DE, for how long, and at what concentrations. Although studies of coal miners reviewed by IARC (1997) generally found lower than expected lung cancer mortality (with some exceptions where some excess of lung cancer was observed), without knowing the concentrations, duration of exposure, and number of miners exposed to DE, it is inappropriate to conclude that the reported lung cancer mortality deficit in these studies provides a proof positive of absence of causal association between DE exposure and occurrence of lung cancer.

7.2.4.1. *Summary of the Cohort Mortality Studies*

The cohort studies mainly demonstrated an increase in lung cancer. Studies of bus company workers by Waller (1981), Rushton et al. (1983), and Edling et al. (1987) failed to demonstrate any statistically significant excess risk of lung cancer, but these studies have certain methodological problems, such as small sample sizes, short follow-up periods (just 6 years in the Rushton et al. study), lack of information on confounding variables, and lack of analysis by duration of exposure, duration of employment, or latency that preclude their use in determining the carcinogenicity of DE. Although the Waller (1981) study had a 25-year follow-up period, the cohort was restricted to employees (ages 45 to 64) currently in service. Employees who left the job earlier, as well as those who were still employed after age 64 and who may have died from cancer, were excluded.

Wong et al. (1985) conducted a mortality study of heavy equipment operators that demonstrated a nonsignificant positive trend for cancer of the lung with length of membership and latency. Analysis of deceased retirees showed a significant excess of lung cancer. Individuals without work histories who started work prior to 1967, when records were not kept, may have been in the same jobs for the longest period of time. Workers without job histories included those who had the same job before and after 1967 and thus may have worked about 12 to 14 years longer; these workers exhibited significant excess risks of lung cancer and stomach cancer. If this assumption about duration of jobs is correct, then these site-specific causes can be linked to DE exposure. One of the methodologic limitations of this study is that most of these men worked outdoors; thus, this cohort might have had relatively low exposure to DE. The authors did not present any environmental measurement data either. Because of the absence of detailed work histories for 30% of the cohort and the availability of only partial work histories for the remaining 70%, jobs were classified and ranked according to presumed diesel exposure.

Information is lacking regarding duration of employment in the job categories (used for surrogate of exposure) and other confounding factors (alcohol consumption, cigarette smoking, etc.). Thus, this study cannot be used to support or refute a causal association between exposure to DE and lung cancer.

A 2-year mortality analysis by Boffetta and Stellman (1988) of the American Cancer Society's prospective study, after controlling for age and smoking, demonstrated an excess risk of lung cancer in certain occupations with potential exposure to DE. These excesses were statistically significant among miners (RR = 2.67, 95% CI = 1.63, 4.37) and heavy equipment operators (RR = 2.6, 95% CI = 1.12, 6.06). Recently Brüske-Hohlfeld et al. (1999) also have observed significantly higher risk for lung cancer, in the range of 2.31 to 4.3, for heavy equipment operators. The elevated risks were nonsignificant in railroad workers (RR = 1.59) and truck drivers (RR = 1.24). A dose response was also observed for truck drivers. With the exception of miners, exposure to DE occurred in the three other occupations showing an increase in the risk of lung cancer. Despite methodologic limitations, such as the lack of representiveness of the study population (composed of volunteers only, who were probably healthier than the general population), leading to an underestimation of the risk, and the questionable reliability of exposure data based on self-administered questionnaires that were not validated, this study is suggestive of a causal association between exposure to DE and excess risk of lung cancer.

Two mortality studies were conducted by Gustavsson et al. (1990) and Hansen (1993) among bus garage workers (Stockholm, Sweden) and truck drivers, respectively. An SMR of 122 was found among bus garage workers, based on 17 cases. A nested case-control study was also conducted in this cohort. Detailed exposure matrices based on job tasks were assembled for both DE and asbestos exposures. Statistically significant increasing lung cancer relative risks of 1.34, 1.81, and 2.43 were observed for DE indices of 10 to 20, 20 to 30, and >30, respectively, using 0 to 10 as a comparison group. Adjustment for asbestos exposure did not change the results. The main strength of this study is the detailed exposure matrices; some of the limitations are low power (small cohort) and lack of smoking histories. But smoking is not likely to be different among study individuals irrespective of their exposure status to DE.

Hansen (1993), on the other hand, found statistically significant SMR of 160 from cancer of bronchus and lung. No dose response was observed, although the excesses were observed in most of the age groups (30 to 39, 45 to 49, 50 to 54, 55 to 59, 60 to 64, and 65 to 74). There are quite a few methodologic limitations to this study. Exposure to DE was assumed in truck drivers for diesel-powered trucks, but no validation of exposure was attempted. Follow-up period was short, no latency analysis was done, and smoking data were lacking. However, a population survey carried out in 1988 showed very little difference in smoking habits of residents of rural area and the total Danish male population, thus, smoking is unlikely to confound the finding of

excess lung cancer. The findings of both these studies are consistent with the findings of other truck driver studies and are supportive of causal association.

Two mortality studies of railroad workers were conducted by Howe et al. (1983) and Garshick et al. (1988). The Howe et al. study, which was conducted in Canada, found relative risks of 1.2 ($p<0.01$) and 1.35 ($p<0.001$) among "possibly" and "probably" exposed groups, respectively. The trend test showed a highly significant dose-response relationship with exposure to DE and the risk of lung cancer. The main limitation of the study was the inability to separate overlapping exposures of coal dust/combustion fumes and DE fumes. Information on jobs was available at retirement only. There also was insufficient detail on the classification of jobs by DE exposure. The exposures could have been nonconcurrent or concurrent, but because the data are lacking, it is possible that the observed excess could be due to the effect of both coal dust/combustion fumes and DE fumes and not just one or the other. It should be noted that, so far, coal dust has not been demonstrated to be a pulmonary carcinogen in studies of coal miners. However, lack of data on confounders such as asbestos and smoking (though use of the internal comparison group to compute relative risks minimizes confounding by smoking) makes interpretation of this study difficult. When three DE exposure categories were examined for smoking-related diseases such as emphysema, laryngeal cancer, esophageal cancer, and buccal cancer, positive trends were observed, raising a possibility that the dose response demonstrated for diesel exposure may have been due to smoking. The findings of this study are at best suggestive of DE being a lung carcinogen.

The strong evidence for linking DE exposure to lung cancer comes from the Garshick et al. (1988) railroad worker study conducted in the United States. Relative risks of 1.57 (95% CI = 1.19, 2.06) and 1.34 (95% CI = 1.02, 1.76) were found for ages 40 to 44 and 45 to 49, respectively, after the exclusion of workers exposed to asbestos. The investigators reported that the risk of lung cancer increased with increasing duration of employment. As this was a large cohort study with a lengthy follow-up and adequate analysis, including dose response (based on duration of employment as a surrogate) as well as adjustment for other confounding factors such as asbestos, the observed association between increased lung cancer and exposure to DE is more meaningful. Even though the reanalysis of these data by Crump et al. (1991) found that the relative risk could be positively or negatively related to duration of exposure depending on how age was controlled, additional analysis by Garshick et al. (letter from Garshick, Harvard Medical School, to Chao Chen, U.S. EPA, dated August 15, 1991) found that the relationship between years exposed when adjusted for the attained age and calendar years was flat to negative, depending on the choice of the model. They also found that deaths were underreported by approximately 20% to 70% between 1977 and 1980, and their analysis based on job titles, limited to 1959-1976, showed that the youngest workers still had the highest risk of dying of

lung cancer. On the other hand, an analysis of the same data by California EPA (CalEPA, 1998) yielded a positive dose response set using age at 1959 and adding an interaction term of age and calendar year in the model. However, Crump (1999) reported that the negative dose-response continued to be upheld in his latest analysis when age was controlled more carefully and years of exposure quantified more accurately. Crump (1999) asserted that the negative dose-response trends for lung cancer observed with either the cumulative exposure or duration of exposure may be due to underascertainment of deaths in the last 4 years of follow-up of the Garshick et al. (1988) study, as well as incomplete follow-up in earlier years. The HEI (1999) special panel conducted its own analyses using Garshick et al. (1988) data to evaluate their usefulness for quantitative risk assessment and found results similar to those of Crump et al. (1991) and Garshick (letter from Garshick, Harvard Medical School, to Chao Chen, U.S. EPA, dated August 15, 1991). The HEI panel reported consistently elevated risk of lung cancer for train workers compared with clerks for each duration of employment, and that shop workers had an intermediate risk of lung cancer. But they found decreasing risk of lung cancer with increasing duration of employment. The panel discussed various possibilities (different types of biases) for the negative dose-response and advised against using the Garshick et al. (1988) data for quantitative risk assessment. The panel also reported the strengths of the Garshick et al. (1988) study such as large population, control for asbestos, and smoking, and concluded that the study was generally consistent with findings of weak association between exposure to DE and occurrence of lung cancer. Hence, the divergent results of these recent analyses do not negate the positive evidence this study provides for the qualitative evaluation. The observance of dose-response would have strengthened the causal association, but an absence of a dose-response does not negate it.

Suggestive evidence is provided by a recent study of potash miners in Germany. The information on the exposure (including elemental carbon and organics), work chronology, and work category was used by the investigators to calculate cumulative exposures for each worker. Furthermore, information on smoking habits indicated homogeneity in the cohort.
A statistically nonsignificant twofold increase in lung cancer was observed in the production workers as compared to workshop workers. The lack of significance for this finding could be due to short follow-up, not enough latency, and relatively young age of the cohort.

7.2.4.2. *Summary of the Case-Control Studies of Lung Cancer*

Among the 11 lung cancer case-control studies reviewed in this chapter, only 2 studies did not find any increased risk of lung cancer. Lerchen et al. (1987) did not find any excess risk of lung cancer, after adjusting for age and smoking, for diesel fume exposure. The major limitation of this study was a lack of adequate exposure data derived from the job titles obtained

from occupational histories. Next of kin provided the occupational histories for 50% of the cases that were not validated. The power of the study was small (analysis done on males only, 333 cases). Similarly, Boffeta et al. (1990) did not find any excess of lung cancer after adjusting for smoking and education. This study had a few methodological limitations. The lung cancer cases and controls were drawn from the ongoing study of tobacco-related diseases. It is interesting to note that the leading risk factor for lung cancer is cigarette smoking. The exposure was not measured. Instead, occupations were used as surrogates for exposure. Furthermore, there were very few individuals in the study who were exposed to DE. On the other hand, statistically nonsignificant excess risks were observed for DE exposure by Hall and Wynder (1984) in workers who were exposed to DE versus those who were not (OR = 1.4 and 1.7 with two different criteria) and by Damber and Larsson (1987) in professional drivers (OR = 1.2). These rates were adjusted for age and smoking. Hall and Wynder (1984) had a high nonparticipation rate of 36%. Therefore, the positive results found in this study are underestimated at best. In addition, the self-reported exposures used in the study by Hall and Wynder (1984) were not validated. This study also had low power to detect excess risk of lung cancer for specific occupations.

The study by Benhamou et al. (1988), after adjusting for smoking, found significantly increased risks of lung cancer among French motor vehicle drivers (RR = 1.42) and transport equipment operators (RR = 1.35). The main limitation of the study was the inability to separate exposures to DE from those to gasoline exhaust because both motor vehicle drivers and transport equipment operators probably were exposed to the exhausts of both types of vehicles.

Hayes et al. (1989) combined data from three studies (conducted in three different states) to increase the power to detect an association between lung cancer and occupations with a high potential for exposure to DE. They found that truck drivers employed for more than 10 years had
a significantly increased risk of lung cancer (OR = 1.5, 95% CI = 1.1, 1.9). This study also found a significant trend of increasing risk of lung cancer with increasing duration of employment among truck drivers. The relative odds were computed by adjusting for birth cohort, smoking, and State of residence. The main limitation of this study is again the mixed exposures to diesel and gasoline exhausts, because information on type of engine was lacking. Also, potential bias may have been introduced because the way in which the cause of death was ascertained for the selection of cases varied in the three studies. Furthermore, the methods used in these studies to classify occupational categories were different, probably leading to incompatibility of occupational categories.

Emmelin et al. (1993), in their Swedish dockworkers from 15 ports, found increased relative odds of 6.8 (90% CI = 1.3 to 34.9). A strong interaction between smoking and DE was

observed in this study. Of 50 cases and 154 controls, only 6 individuals were nonsmokers. Although intricate exposure matrices were created using three different variables, no direct exposure measurement was done. Despite the limitations of small number of cases and controls; lack of data on asbestos exposure, which is fairly common in dockworkers; and very few nonsmokers; this study provides consistent support for a real effect of DE exposure and occurrence of lung cancer, at least in smokers.

The most convincing evidence comes from the case-control studies among railroad workers by Garshick et al. (1987); among truck drivers of the Teamsters Union by Steenland et al. (1990, 1998); among truck drivers, railroad workers, and farmers in a population-based study by Swanson et al. (1993); among different professional drivers in Denmark by Hansen et al. (1998); and among male workers occupationally exposed to diesel motor emissions in Germany by Brüske-Hohlfeld et al. (1999). Garshick et al. (1987) found that after adjustment for asbestos and smoking, the relative odds for continuous exposure were 1.39 (95% CI = 1.05, 1.83). Among the younger workers with longer DE exposure, the risk of lung cancer increased with duration of exposure after adjusting for asbestos and smoking. Even after the exclusion of recent DE exposure (5 years before death), the relative odds increased to 1.43 (95% CI = 1.06, 1.94). This appears to be a well-conducted and well-analyzed study with reasonably good power. Potential confounders were controlled adequately, and interactions between DE and other lung cancer risk factors were tested. Some of the limitations of this study are misclassification of exposure because ICC job classification was used as surrogate for exposure and use of death certificates for identification of cases and controls.

Steenland et al. (1990), on the other hand, created two separate work history files, one from Teamsters Union pension files and the other from next-of-kin interviews. Using duration of employment as a categorical variable and considering employment after 1959 (when presumed dieselization occurred) for long-haul drivers, the risk of lung cancer increased with increasing years of exposure. Using 1964 as the cutoff, a similar trend was observed for long-haul drivers. For short-haul drivers, the trend was positive with a 1959 cutoff, but not when 1964 was used as the cutoff. For truck drivers who primarily drove diesel trucks and worked for 35 years, the relative odds were 1.89. The main strengths of the study are availability of detailed records from the Teamsters Union, a relatively large sample size, availability of smoking data, and measurements of exposure. The limitations of this study include possible misclassifications of exposure and smoking, lack of levels of diesel exposure, a smaller nonexposed group, and an insufficient latency period. Recently Steenland et al. (1998) conducted an exposure-response analysis on these cases and controls, using the industrial hygiene survey results of Zaebst et al. (1991). The estimates were made for long-haul drivers, short-haul drivers, dockworkers, mechanics, and those outside the trucking industry. The survey found that mechanics had the

highest current levels of DE exposures and dockworkers who mainly used propane- powered forklifts had the lowest exposure. The finding of the highest lung cancer risk for mechanics and lowest for dock workers is indicative of a causal association between the DE exposure and development of lung cancer. However, the risk among mechanics did not increase with increasing duration of employment. The ORs for quartile cumulative exposures, computed by using logistic regression adjusted for age, race, smoking, diet, and asbestos exposure, showed a pattern of increasing trends in risk with increasing exposure, between 1.08 and 1.72 depending upon exposure level and lag structure used.

In a population-based lung cancer case-control study Swanson et al. (1993) found statistically significant excess risks adjusted for age at diagnosis, smoking, and race, among white male drivers of heavy trucks employed for ≥20 years and railroad workers employed for ≥10 years (OR = 2.5, 95% CI = 1.1, 4.4, and OR = 2.4, 95 % CI = 1.1, 5.1, respectively), and among black farmers employed for ≥20 years (OR = 10.4, 95% CI = 1.4, 77.1). Although individual ORs were not significant for various occupations with potential exposure to DE, statistically significant trends were observed for drivers of heavy trucks, light trucks, farmers, and railroad industry workers among whites, and among black farmers ($p \leq 0.05$). The main strengths of the study are availability of data on lifetime work history and smoking history; the main limitation is absence of actual specific exposure data. This is the first study that found increased lung cancer risk for farmers, who are exposed to DE of their farm tractors.

Hansen et al. (1998), in their study of professional drivers in Denmark, found statistically significant ORs (adjusted for socioeconomic status) of 1.31, 1.64, and 1.39 for lorry/bus drivers, taxi drivers, and unspecified drivers, respectively. The lag time analyses for duration of employment were unchanged for lorry/bus drivers but increased to OR = 3 from 2.2 in taxi drivers with a lag time of 10 years and duration of employment of > 5 years. The authors asserted that the higher risk seen in the taxi drivers may be due to higher exposure to these drivers because of longer time spent in traffic congestion. Furthermore, the trend tests for increasing risk of lung cancer with increasing duration of employment were statistically significant for both lorry/bus drivers and taxi drivers in both 10-year lag time and no lag time. The main strengths of the study are the large sample size, availability of detailed employment records, and information on socioeconomic status. The main limitations are absence of individual data on smoking habits and asbestos exposure, and information about the type of fuel used for the vehicles driven by these professional drivers. A personal communication with the main investigator revealed that the lorries/buses and taxis have been using diesel fuel since the late 1940s. Moreover, indirect information about smoking and asbestos exposure indicated that these two confounders are unlikely to explain the observed excesses or the trends, resulting in strong support of earlier positive studies.

Brüske-Hohlfeld et al. (1999) recently conducted a pooled analysis of two case-control studies among male workers occupationally exposed to DME in Germany. The investigators collected data on demographic information, detailed smoking, and occupational history. Job titles and industries were classified in 33 and 21 categories respectively. Job descriptions were written and verified to avoid misclassification of estimated exposure to diesel emissions. Individual cumulative DME exposures and smoking pack-years were calculated. Asbestos exposures were estimated by certain job-specific supplementary questions. Analysis of 3,498 lung cancer cases and 3,541 controls yielded statistically significant ORs ranging from 1.25 to 2.31 adjusted for smoking and asbestos exposure. The risk increased with increasing years of exposure for both the first year of exposure and the end year of exposure. These investigators presented analyses by various job categories, by years of exposure, first and end years of exposure and, when possible, separately for West and East Germany. Significantly higher risks were found among all four job categories. For professional drivers (of trucks, buses, and taxis) ORs ranged from 1.25 to 2.53. For other traffic-related jobs (switchmen, diesel locomotive drivers, diesel forklift truck drivers), ORs ranged from 1.53 to 2.88. For heavy equipment operators (bulldozers, graders, and excavators), ORs ranged from 2.31 to 4.3, and for drivers of farming equipment the only significant excess (OR = 6.81) was for exposure for <30 years.

This study shows increased risk for all the DME-exposed job categories. The professional drivers and the other traffic-related jobs also have some mixed exposures to gasoline exhaust in general traffic. On the other hand, it should be noted that exposure to DME among heavy equipment and farm tractor drivers is much higher and not as mixed as in professional drivers. The heavy equipment drivers usually drive repeatedly through their own equipment's exhaust. Therefore, the observed highest risk for lung cancer in this job category establishes a strong link with the DME. The only other study that found significantly higher risk for heavy equipment operators (RR = 2.6) was conducted by Boffeta et al. (1988). Although the only significant excess in the group was observed for farming tractor operators with more than 30 years of exposure, a steady increase in risk was observed for this job category with increasing exposure. The investigators stated that the working conditions and the DME of tractors remained fairly constant over the years. This increase may be due mainly to exposure to DME and PM_{10}.

The main strengths of the study are large sample size, resulting in good statistical power; inclusion of incident cases diagnosed not more than 3 months prior to the interview; use of only personal interviews, reducing recall bias; diagnoses ascertained by cytology or histology; and availability of lifelong detailed occupational and smoking history. Exposure estimation done for each individual was based on job codes and industry codes, which were validated by written job descriptions to avoid misclassification.

The main limitation of the study is lack of data on actual exposure to DME. The cumulative quantitative exposures were calculated based on time spent in each job with potential exposure to DME and the type of equipment used. Thus, this study provides strong evidence for causal association between exposure to DE and occurrence of lung cancer.

7.2.4.3. *Summary of the Reviews and Meta-Analyses of Lung Cancer*

Three summaries of studies concerned with the relationship of DE exposure and lung cancer risk are reviewed. The HEI report is a narrative study of 35 epidemiologic studies (16 cohort and 19 case-control) of occupational exposure to diesel emissions published between 1957 and 1993. Control for smoking was identified in 15 studies. Six of the studies (17%) reported relative risk estimates less than 1, whereas 29 (83%) reported at least 1 excess relative risk, indicating a positive association. Twelve studies indicating a relative risk greater than 1 had 95% confidence intervals that excluded unity. These studies found that the evidence suggests that occupational exposure to DE from diverse sources increases the rate of lung cancer by 20% to 40% in exposed workers generally, and to a greater extent among workers with prolonged exposure. They also found that the results are not explicable by confounding due to cigarette smoking or other known sources of bias.

Bhatia et al. (1998) identified 23 studies that met criteria for inclusion in the meta-analysis. The observed relative risk estimates were greater than 1 in 21 of these studies. The pooled relative risk weighted by study precision was 1.33 (95% CI= 1.24, 1.44), which indicated increased relative risk for lung cancer from occupational exposure to DE. Subanalyses by study design (case-control and cohort studies) and by control for smoking produced results that did not differ from those of the overall pooled analysis. Cohort studies using internal comparisons showed higher relative risks than those using external comparisons.

Lipsett and Campleman (1999) identify 39 independent estimates of relative risk among 30 eligible studies of DE and lung cancer published between 1975 and 1995. Pooled relative risks for all studies and for study subsets were estimated using a random effect model. Interstudy heterogeneity was also modeled and evaluated. A pooled smoking-adjusted relative risk was 1.47 (95% CI = 1.29, 1.67). Substantial heterogeneity was found in the pooled-risk estimates. Adjustment for confounding by smoking, having a lower likelihood of selection bias, and increased study power were all found to contribute to lower heterogeneity and increased pooled estimates of relative risk.

There is some variability in the conclusions of these summaries of the association of DE and lung cancer. The three analyses find that smoking is unlikely to account for the observed effects, and all conclude that the data support a causal association between lung cancer and DE exposure. On the other hand, Stöber and Abel (1996), Muscat and Wynder (1995), and Cox

(1997) call into question the assertions by Cohen and Higgins (1995), Bhatia et al. (1998), and Lipsett and Campleman (1999) that the associations seen for DE and lung cancer are unlikely to be due to bias. They argue that methodologic problems are prevalent among the studies, especially in evaluation of diesel engine exposure and control of confounding by cigarette smoking, and thus, the observed association between exposure to DE and excess risk of lung cancer is more likely to be due to bias. The conclusions of the two meta-analyses are based on magnitude of pooled relative risk estimates and evaluation of potential sources of heterogeneity in the estimates. Despite the statistical sophistication of the meta-analyses, the statistical models used cannot compensate for deficiencies in the original studies and will remain biased to the extent that bias exists in the original studies.

7.2.4.4. *Discussion of Relevant Methodologic Issues*

A persistent association of risk for lung cancer and DE exposure has been observed in more than 30 epidemiologic studies published in the literature over the past 40 years. Evaluation of whether this association can be attributed to a causal relation between DE exposure and lung cancer requires careful consideration of whether chance, bias, or confounding might be likely alternative explanations.

A total of 10 cohort and 12 case-control studies are reviewed in this chapter. An increased lung cancer risk was observed in 8 cohort and 10 case-control studies, even though the results were not always statistically significant. There is a consistent tendency for point estimates of relative risk to be greater than one in studies that adjusted (either directly or indirectly) for smoking, had a long enough follow-up, and sufficient statistical power among truck drivers, railroad workers, dock workers, and heavy equipment workers. If this elevated risk was due to chance one would expect almost equal distribution of these point estimates to be above and below one. Many of the studies provide confidence intervals for their estimates of excess risk or statistical tests, which indicate that it is unlikely that the individual study findings were due to random variation. The persistence of this association between DE and lung cancer risk in so many studies indicates that the possibility is remote that the observed association in aggregate is due to chance. It is unlikely that chance alone accounts for the observed relation between DE and lung cancer.

The excess risk is observed in both cohort and case-control designs, which contradicts the concern that a methodologic bias specifically characteristic of either design (e.g., recall bias) might account for the observed effect. Selection bias is certainly present in some of the occupational cohort studies that use external population data in estimating relative risks, but this form of selection bias (a healthy worker effect) would only obscure, rather than spuriously produce, an association between DE and lung cancer. Several occupational epidemiologic

studies that use more appropriate data for their estimates are available. Selection biases may be operating in some case-control studies, but it is not obvious how such a bias could be sufficiently uniform in effect, prevalent, and strong enough to lead to the consistent association seen in the aggregate data. Given the variety of designs used in studying the DE and lung cancer association and the number of studies in different populations, it is unlikely that routinely studying noncomparable groups is an explanation for the consistent association seen. Exposure information bias is certainly a problem for almost all of the studies concerned. Detailed and reliable individual-level data on DE exposure for the period of time relevant to the induction of lung cancer are not available and are difficult to obtain. Generally, the only information from which diesel exposure can be inferred is occupational data, which is a poor surrogate for the true underlying exposure distribution. The variability in actual lifetime exposure to DE in an occupational cohort may not be reflected in differences in job title, and there might be considerable variability in actual exposure despite similar job titles. Study endpoints are frequently mortality data taken from death certificate information, which is frequently inaccurate and often does not fully characterize the lung cancer incidence experience of the population in question. Using inaccurate surrogates for lung cancer incidence and for diesel exposure can lead to substantial bias, and these shortcomings are endemic in the field. In most cases these shortcomings will lead to misclassification of exposure and of outcome, which is nondifferential. Nondifferential misclassification of exposure and/or outcome can bias estimates of a DE–lung cancer association, if one exists, toward the null; but it is unlikely that such misclassification would produce a spurious estimate in any one study. It is even more unlikely that it would bias a sufficient number of studies in a uniform direction to account for the consistent aggregate association observed.

Moreover, throughout this chapter, various methodologic limitations of individual studies have been discussed, such as small sample size, short follow-up period, lack of data on confounding variables, use of death certificates to identify the lung cancer cases, and lack of latency analysis. The studies with small sample sizes (i.e., not enough power) and short follow-up periods (i.e., not enough latent period) have been difficult to interpret due to these limitations.

The most important confounding variable is smoking which is a strong risk factor for lung cancer. All the studies considered for this report are either cohort retrospective mortality or case-control studies where history of exposures in the past is elicited. Smoking history is usually difficult to obtain in such instances. The smoking histories obtained from surrogates (next of kin, either spouse or offspring) were found to be accurate by Lerchen and Samet (1986) and McLaughlin et al. (1987). Lerchen and Samet did not detect any consistent bias in the report of cigarette consumption. In contrast, overreporting of cigarette smoking by surrogates was observed by Rogot and Reid (1975), Kolonel et al. (1977), and Humble et al. (1984). Kolonel et

al. found that the age at which an individual started smoking was reported within 4 years of actual age 84% of the time. These studies indicate that surrogates were able to provide fairly credible information on the smoking habits of the study subjects. If the surrogates of the cases were more likely to overreport cigarette smoking compared with the controls, then it might be harder to find an effect of DE because most of the increase in lung cancer would be attributed to smoking rather than to exposure to DE.

Some studies do not adjust for tobacco smoke exposure. Even though smoking is a strong risk for lung cancer, it is only a confounder if there are differential smoking habits among individuals exposed to DE versus individuals who are not exposed. Most of the occupational cohorts include workers from the same socioeconomic background or used an internal comparison group; hence, it is unlikely that confounding by cigarette smoking is substantial in these studies. Some studies have adjusted for socioeconomic status and some studies have compared the cigarette smoking habits by conducting rural and urban general population surveys. Besides, in studies with long enough latency, adjustment for cigarette smoking did not alter substantially the observed higher risk.

Another methodologic concern in these studies is use of death certificates to determine cause of death. Death certificates were used by all of the cohort mortality studies and some of the case-control studies of lung cancer to determine cause of death. Use of death certificates could lead to misclassification bias because of overdiagnosis. Studies of autopsies done between 1960 and 1971 demonstrated that lung cancer was overdiagnosed when compared with hospital discharge, with no incidental cases found at autopsy (Rosenblatt et al., 1971). Schottenfeld et al. (1982) also found an overdiagnosis of lung cancer among autopsies conducted in 1977 and 1978. On the other hand, Percy et al. (1981) noted 95% concordance when comparing 10,000 lung cancer deaths observed in the Third National Cancer Survey from 1969 to 1971 (more than 90% were confirmed histologically) to death-certificate-coded cause of death. These more recent findings suggest that the diagnosis of lung cancer on death certificates is better than anticipated. In reality, lung cancer is one cause of death that has been found to be generally reliably reported on the death certificate. Thus, the misclassification bias probably is minimal in the studies described in this chapter.

Finally, several investigators have not conducted latency analysis in their studies. The latent period for lung cancer development is from 20 to 30 years or more. Considering the fact that dieselization was not complete till almost 1959 for locomotives and the 1970s for the trucking industry in the United States, most of the cohort studies conducted in the U.S. population do not have a long enough follow-up period to allow for latency of 20 to 30+ years. In addition, the study inclusion criteria for most of the studies are individuals who worked in the industry for at least 6 months /1 year from the beginning of the follow-up period to the end of

the follow-up period. Hence, the later the individual enters the cohort, the shorter the follow-up period; thus, the latent period is insufficient for the occurrence of lung cancer in these late entrants. Therefore, the observed slight to moderate increase in risk of lung cancer could be due to insufficient latency. On the other hand, in certain case-control studies the elapsed period between the identification of the lung cancer cases and exposure to DE is long enough to allow for the 30+ years latency needed for the development of lung cancer (Hansen et al., 1998; Brüske-Hohlfeld et al., 1999). These investigators identified lung cancer cases in the early to mid-1990s and found significant excess risks for lung cancer among the individuals exposed to DE. It should be noted that the use of diesel fuel for trucks, buses, and taxis had started in their countries (Denmark and Germany, respectively) in the late 1940s.

7.2.4.5. *Evaluation of Causal Association*

In most situations, epidemiologic data are used to delineate the causality of certain health effects. Several cancers have been causally associated with exposure to agents for which there is no direct biological evidence. Insufficient knowledge about the biological basis for diseases in humans makes it difficult to identify exposure to an agent as causal, particularly for malignant diseases when the exposure was in the distant past. Consequently, epidemiologists and biologists have used the original or modified version of a set of criteria provided by Hill (1965)[3] that define a causal relationship between exposure and the health outcome. A causal interpretation is enhanced for studies that meet these criteria. None of these criteria actually proves causality; actual proof is rarely attainable when dealing with environmental carcinogens. None of these criteria should be considered either necessary (except temporality of exposure) or sufficient in itself. The absence of any one or even several of these criteria does not prevent a causal interpretation. However, if more criteria apply, this provides more credible evidence for causality.

Thus, applying the Hill criteria (1965) of causal inference, as modified by Rothman (1986), to the studies reviewed here resulted in the following:

- *Strength of association.* This phrase refers to the magnitude of the ratio of incidence or mortality (RRs or ORs). Several studies found statistically significant RRs and ORs that ranged from 1.2 to 2.6 (Howe et al., 1983; Rushton

[3]Hill in his address to the Royal Society of Medicine in 1965 on "The environment and disease: association or causation" explored several aspects of association between exposure and occurrence of an event before deciding that the most likely interpretation of it is causation. He provided nine different aspects of association that he characterized as his viewpoints before interpreting the association being causal. The epidemiologic community universally adopted these (aspects/viewpoints) later as criteria for causality/causal association.

et al., 1983; Wong et al., 1985; Gustavsson et al., 1990; Emmlin et al., 1993; Hansen, 1993; Hansen et al., 1998) and, after adjustment for smoking and/or asbestos, RRs and ORs remained statistically significant and in the same range in certain studies (Dambar and Larson 1987; Garshick et al., 1987, 1988; Benhamou et al., 1988; Boffetta and Stellman, 1988; Hays et al., 1989; Steenland et al., 1990; Swanson et al., 1993; Brüsk-Hohlfeld et al., 1999). In addition, two meta-analyses demonstrated that not only did excess in lung cancer remain the same after stratification/adjustment for smoking and occupation, but in several instances the pooled RRs showed modest increases, with little evidence of heterogeneity. Overall, the studies in epidemiologic terms show relatively modest to weak association between DE and occurrence of lung cancer. Even though strong associations are more likely to be causal than modest-to-weak associations, the fact that association is relatively modest or weak does not rule out the causal link.

- *Consistency.* Increased lung cancer risk has been observed in several cohort and case-control studies, conducted in several industries and occupations in which workers were potentially exposed to DE. However, not all the excesses were statistically significant. Statistically significant lung cancer excesses adjusted for smoking were observed in truck drivers (Hayes et al., 1989; Hansen, 1993; Swanson et al., 1993; Brüske-Hohlfeld et al., 1999), professional drivers (Benhamou et al., 1988; Brüske-Hohlfeld et al., 1999), railroad workers (Garshick et al., 1987; Swanson et al., 1993), heavy equipment drivers (Boffetta and Stellman, 1988; Brüske-Hohlfeld et al., 1999), and farm tractor drivers (Swanson et al., 1993; Brüske-Hohlfeld et al., 1999). Furthermore, the two recent meta-analyses by Bhatia et al. (1998) and Lipsett and Campleman (1999) found that even though a substantial heterogeneity existed in their initial pooled estimates, stratification on several factors demonstrated a relationship between exposure to DE and excess lung cancer that remained positive throughout various analyses.

- *Specificity.* This criterion requires that a single cause lead to a single effect. With respect to exposure to DE, excess for lung cancer is the only effect that is found to be consistently elevated and statistically significant in several studies. Quite a few studies have examined DE for other effects such as bladder cancer, leukemia,

gastrointestinal cancers, prostate cancer etc. The evidence for these effects is inadequate.

- *Temporality.* The only necessary, but not sufficient, criterion described by Hill for causality inference is that exposure to a causal agent precedes the effect in time. This criterion is clearly satisfied in the studies reviewed here. Temporality can be explored further in addressing the latency issue. A certain period is necessary for development of an effect after exposure to a causal agent has occurred. For instance, in cancer-causing agents a latent period can vary from 5 years (childhood leukemia) to ≥30 years (mesothelioma). Most of the studies reviewed here did not conduct the latency analysis. Some studies had a short follow-up period that did not allow enough time for the latency period (Waller, 1981; Howe et al., 1983; Rushton et al., 1983; Wong et al., 1985, Hansen, 1993) while several studies clearly allowed for an adequate latency period (Garshick et al., 1987; Gustavsson et al., 1990; Steenland et al., 1990; Swanson et al., 1993; Brüske-Hohlfeld et al., 1999). Both type of studies showed mixed results.

- *Biological gradient.* This criterion refers to the dose-response curve. Due to the lack of quantitative data on DE exposure in most studies reviewed here, analyzing the dose-response curve directly was not possible. In very few studies, exposure to DE was addressed specifically. Most investigators have used job titles/categories and duration of employment as surrogates for exposure and thus have presented response in relation to duration of employment. Significant dose-response (using duration of employment as a surrogate) was observed in various studies for railroad workers (Howe et al., 1983; Garshick et al., 1987; Garshick et al., 1988; Swanson et al., 1993; Cal EPA, 1998), truck drivers (Boffetta and Stellman, 1988; Hayes et al., 1989; Steenland et al., 1990; Swanson et al., 1993; Hansen et al., 1998; Brüske-Hohlfeld et al., 1999), transportation/heavy equipment operators (Wong et al., 1985; Gustavsson et al., 1990; Brüske-Hohlfeld et al., 1999), farmers/farm tractor users (Swanson et al., 1993; Brüske-Hohlfeld et al., 1999), and dockworkers (Emmelin et al., 1993).

- *Biological plausibility.* This criterion refers to the biologic plausibility of the hypothesis, an important concern that may be difficult to judge. The hypothesis considered for this review is that occupational exposure to DE is causally associated with the occurrence of lung cancer and is supported by the following:

First, DE has been shown to cause lung and other cancers in animals (Heinrich et al., 1986b; Iwai et al., 1986b; Mauderly et al., 1987; Pott et al., 1990; Mauderly, 1994). Second, it contains highly mutagenic substances such as polycyclic aromatic hydrocarbons as well as nitroaromatic compounds (Claxton, 1983; Ball et al., 1990; Gallagher et al., 1993; Sera et al., 1994; Nielsen et al., 1996a) that are recognized human pulmonary carcinogens (IARC, 1989). Third, DE consists of carbon core particles with surface layers of organics and gases; the tumorigenic activity may reside in one, some, or all of these components. As explained in Chapter 4, there is clear evidence that the mixture of organic constituents, both in particles and vapor phases, have the capacity to interact with DNA and give rise to mutations, chromosomal aberrations, and cell transformations, all well-established steps in the process of carcinogenesis. Further, increased levels of peripheral blood cell DNA adducts associated with occupational exposure to DE have been observed in humans (Nielsen et al., 1996a,b). Thus, the above evidence makes a convincing case that occupational exposures to DE are causally associated with the occurrence of lung cancer is highly plausible biologically.

In conclusion, the epidemiologic studies of exposure to DE and occurrence of lung cancer furnish evidence that is consistent with a causal association. This association observed in several studies is unlikely to be due to chance or bias. Although many studies did not have information on smoking, significant confounding by smoking is unlikely in these studies because the comparison population was from the same socioeconomic class. The strength of association (i.e., RRs/ORs between 1.2 and 2.6) was weak to modest by epidemiologic standards, with dose-response relationships observed in several studies. Last, but not least, there is highly plausible biological evidence that exposure to DE could result in excess risk of lung cancer in humans.

7.3. CARCINOGENICITY OF DIESEL EXHAUST IN LABORATORY ANIMALS

This chapter summarizes studies that assess the carcinogenic potential of DE in laboratory animals. The first portion of this chapter summarizes results of inhalation studies. Experimental protocols for the inhalation studies typically consisted of exposure (usually chronic) to diluted exhaust in whole-body exposure chambers using rats, mice, and hamsters as model species. Some of these studies used both filtered (free of particulate matter) DE and unfiltered (whole) DE to differentiate gaseous-phase effects from effects induced by diesel PM (DPM) and its adsorbed components. Other studies were designed to evaluate the relative importance of the carbon core of the diesel particle versus that of particle-adsorbed compounds.

Finally, a number of exposures were carried out to determine the combined effect of inhaled DE and tumor initiators, tumor promoters, or cocarcinogens.

Particulate matter concentrations in the DE used in these studies ranged from 0.1 to 12 mg DPM /m^3. In this chapter, any mention of statistical significance implies that $p \leq 0.05$ was reported in the reviewed publications. A summary of the animal inhalation carcinogenicity studies and their results is presented in Table 7-3.

Results of lung implantation and intratracheal instillation studies of whole diesel particles, extracted diesel particles, and particle extracts are reported in Section 7.3.3 and in Tables 7-4 and 7-5. Studies destined to assess the carcinogenic effects of DPM as well as solvent extracts of DPM following subcutaneous (s.c.) injection, intraperitoneal (i.p.) injection, or intratracheal (itr.) instillation in rodents are summarized in Section 7.3.5. Individual chemicals present in the gaseous phase or adsorbed to the particle surface were not included in this review because assessments of those of likely concern (i.e., formaldehyde, acetaldehyde, benzene, polycyclic aromatic hydrocarbons [PAHs]) have been published elsewhere (U.S. EPA, 1993).

7.3.1. Inhalation Studies (Whole Diesel Exhaust)

7.3.1.1. *Rat Studies*

The potential carcinogenicity of inhaled DE was first evaluated by Karagianes et al. (1981). Male Wistar rats (40 per group) were exposed to room air or diesel engine exhaust diluted to a DPM concentration of 8.3 (± 2.0) mg/m^3, 6 hr/day, 5 days/week for up to 20 months. The animals were exposed in 3,000 L plexiglass chambers. Airflow was equal to 50 liters per minute. Chamber temperatures were maintained between 25 °C and 26.5 °C. Relative humidity ranged from 45% to 80%. Exposures were carried out during the daytime. The connected to an electric generator and operated at varying loads and speeds to simulate operating conditions in an occupational situation. To control the CO concentration at 50 ppm, the exhaust was diluted 35:1 with clean air. Six rats per group were sacrificed after 4, 8, 16, and 20 months exposure for gross necropsy and histopathological examination.

The only tumor detected was a bronchiolar adenoma in the group exposed over 16 months to DE. No lung tumors were reported in controls. The equivocal response may have been caused by the relatively short exposure durations (20 months) and small numbers of animals examined. In more recent studies, for example, Mauderly et al. (1987), most of the tumors were detected in rats exposed for more than 24 months.

Table 7-3. Summary of animal inhalation carcinogenicity studies

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m^3)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]				Comments
								Adenomas				
Karagianes et al. (1981)	Rat/Wistar	M, 40 M, 40	Clean air Whole exhaust	8.3	None None	6 hr/day, 5 days/ week, for up to 20 mo	NA	0/6 (0) 1/6 (16.6)				
								Bronchoalveolar carcinoma				
Kaplan et al. (1983) White et al. (1983)	Rat/F344	M, 30 M, 30 M, 30 M, 30	Clean air Whole exhaust Whole exhaust Whole exhaust	0 0.25 0.75 1.5	None None None None	20 hr/day, 7 days/ week, for up to 15 mo	8 mo 8 mo 8 mo 8 mo	0/30 (0) 1/30 (3.3) 3/30 (10.0) 1/30 (3.3)				
								Adenomas	Carcinomas	Squamous cell tumors	All tumors	
Heinrich et al. (1986a,b) Mohr et al. (1986)	Rat/ Wistar	F, 96 F, 92 F, 95	Clean air Filtered exhaust Whole exhaust	4	None None None	19 hr/day, 5 days/ week for up to 35 mo	NA	0/96 (0) 0/92 (0) 8/95 (8.4)	0/96 (0) 0/92 (0) 0/95 (0)	0/96 (0) 0/92 (0) 9/95 (9.4)	0/96 (0) 0/92 (0) 17/95 (17.8)[c]	
								Adenomas	Adenocarcinoma and adenosquamous carcinoma	Large cell and squamous cell carcinomas	All tumors	
Iwai et al. (1986a,b)	Rat/F344	F, 24 F, 24 F, 24	Clean air Filtered exhaust Whole exhaust	4.9	None None None	8 hr/day, 7 days/ week, for 24 mo	NA	1/22 (4.5) 0/16 (0) 3/19 (0)	0/22 (0) 0/16 (0) 3/19 (15.8)	0/22 (0) 0/16 (0) 2/19 (10.5)	1/22 (4.5)[f] 0/16 (0) 8/19 (42.1)[c,g]	

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Table 7-3. Summary of animal inhalation carcinogenicity studies (continued)

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m^3)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]				Comments
								Adenoma	Carcinoma			
Takemoto et al. (1986)	Rat/F344	F, 12	Clean air	0	None	4 hr/day,	NA	0/12 (0)	0/12 (0)			
		F, 21	Clean air	0	DIPN[h]	4 days/		10/21 (47.6)	4/21 (19)			
		F, 15	Whole	2-4	None	week,		0/15 (0)	0/15 (0)			
		F, 18	exhaust	2-4	DIPN[h]	18-24 mo		12/18 (66.7)	7/18 (38.9)			
			Whole exhaust									
								Adenomas	Adenocarcinoma + squamous cell carcinoma	Squamous cysts	All tumors	
Mauderly et al. (1987)	Rat/F344	M + F, 230[b]	Clean air	0	None	7 hr/day,	NA	(0)	(0.9)	(0)	(0.9)	
			Whole	0.35	None	5 days/		(0)	(1.3)	(0)	(1.3)	
		M + F, 223	exhaust	3.5	None	week up to		(2.3)	(0.5)	(0.9)	(3.6)[c]	
		M + F, 221	Whole	7.1	None	30 mo		(0.4)	(7.5)	(4.9)	(12.8)[c]	
		M + F, 227	exhaust									
			Whole exhaust									
								Adenomas	Adenosquamous carcinomas	Squamous cell carcinomas	All tumors	
Ishinishi et al. (1988a)	Rat/F344	M + F, 123	Clean air	0	None	16 hr/day,	NA	0/123 (0)	1/123 (0.8)	0/123 (0)	1/123 (0.8)	
		M + F, 123	Whole	0.5	None	6 days/		0/123 (0)	0/123 (0)	1/123 (0.8)	1/123 (0.8)	
		M + F, 125	exhaust	1.0	None	week,		0/125 (0)	0/125 (0)	0/125 (0)	0/125 (0)	
Heavy-duty engine		M + F, 123	Whole	1.8	None	for up to		0/123 (0)	4/123 (3.3)	0/123 (0)	4/123 (3.3)	
		M + F, 124	exhaust	3.7	None	30 mo		0/124 (0)	6/124 (4.8)	2/124 (1.6)	8/124 (6.5)[c]	
			Whole exhaust									
			Whole exhaust									

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Table 7-3. Summary of animal inhalation carcinogenicity studies (continued)

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m^3)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]			Comments
								Adenomas	Carcinomas	All tumors	
Ishinishi et al. (1988a)	Rat/F344	NS, 5	Whole	0.1	None	16 hr/day,	6 mo	0/5 (0)	0/5 (0)	0/5 (0)	
		NS, 8	exhaust	0.1	None	6 days/	12 mo	0/8 (0)	0/8 (0)	0/8 (0)	
		NS, 11	Whole	0.1	None	week,	18 mo	0/11 (0)	0/11 (0)	0/11 (0)	
		NS, 5	exhaust	1.1	None	for 12 mo	6 mo	0/5 (0)	0/5 (0)	0/5 (0)	
Light duty		NS, 9	Whole	1.1	None		12 mo	0/9 (0)	0/9 (0)	0/9 (0)	
		NS, 11	exhaust	1.1	None		18 mo	0/11 (0)	0/11 (0)	0/11 (0)	
			Whole exhaust								
			Whole exhaust								
			Whole exhaust								
Heavy duty		NS, 5	Whole	0.5	None	16 hr/day,	6 mo	0/5 (0)	0/5 (0)	0/5 (0)	
		NS, 9	exhaust	0.5	None	6 days/	12 mo	0/9 (0)	0/9 (0)	0/9 (0)	
		NS 11	Whole	0.5	None	week,	18 mo	0/11 (0)	0/11 (0)	0/11 (0)	
		NS, 5	exhaust	1.8	None	for 12 mo	6 mo	0/5 (0)	0/5 (0)	0/11 (0)	
		NS, 6	Whole	1.8	None		12 mo	0/6 (0)	0/6 (0)	0/6 (0)	
		NS, 13	exhaust	1.8	None		18 mo	0/13 (0)	1/13 (0)	1/13 (0)	
			Whole exhaust								
			Whole exhaust								
			Whole exhaust								

Table 7-3. Summary of animal inhalation carcinogenicity studies (continued)

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m^3)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]			Comments
								Primary lung tumors			
Brightwell et al. (1989)	Rat/344	M + F, 260	Clean air	0	None	16 hr/day, 5 days/ week, for 24 mo	NA	3/260 (1.2)			Tumor incidence for all rats dying or sacrificed
		M + F, 144	Filtered exhaust (medium exposure)	0	None			0/144 (0)			
		M + F, 143	Filtered exhaust (high exposure)	0	None			0/143 (0)			
		M + F, 143	Whole exhaust	0.7	None			1/143 (0.7)			♀ 24/25 (96%) after 24 mo
		M + F, 144	Whole exhaust	2.2	None			14/144 (9.7)[c]			♂ 12/27 (44%) after 24 mo
		M + F, 143	Whole exhaust	6.6	None			55/143 (38.5)[c]			
								Squamous cell carcinoma	All lung tumors		
Henrich et al. (1989a)	Rat/Wistar	F, NS	Clean air	0	DPN[d]	19 hr/day, 5 days/ week for 24 to 30 mo	NA	(4.4)	(84.8)		
		F, NS	Whole exhaust	4.2	DPN[d]			(46.8)[c]	(83.0)		
		F, NS	Filtered exhaust	0	DPN[d]			(4.4)	(67.4)		
		F, NS	Clean air	0	DPN[e]				(93.8)		
		F, NS	Whole exhaust	4.2	DPN[e]			(16.7)	(89.6)		
		F, NS	Filtered exhaust	0	DPN[e]			(31.3)[c]	(89.6)		
								(14.6)			
Lewis et al. (1989)	Rat/F344	M + F, 288[n]	Clean air	2	None	7 hr/day, 5 days/ week, 24 mo	NA	No tumors	0/192 (0)		
			Whole exhaust		None				0/192 (0)		

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Table 7-3. Summary of animal inhalation carcinogenicity studies (continued)

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m^3)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]				Comments
								Adeno-squamous carcinomas	Squamous cell carcinomas	All tumors		
Takaki et al. (1989) Light-duty engine	Rat/F344	M + F, 123 M + F, 123 M + F, 125 M + F, 123 M + F, 124	Clean air Whole exhaust Whole exhaust Whole exhaust Whole exhaust	0 0.1 0.4 1.1 2.3	None None None None None	16 hr/day, 6 days/ week, for up to 30 mo	NA	1/23 (0.8) 1/23 (0.8) 1/25 (0.8) 0/23 (0) 1/24 (8.1)	2/123 (1.6) 1/23 (0.8) 0/125 (0) 5/123 (4.1) 2/124 (1.6)	1/23 (0.8) 1/23 (0.8) 0/125 (0) 0/123 (0) 0/124 (0)	4/123 (3.3) 3/123 (2.4) 1/125 (0.8) 5/123 (4.1) 3/124 (2.4)	
								Adenomas	Adenocarcinomas	Squamous cell carcinomas	Benign squamous cell tumors	
Heinrich et al. (1995)	Rat/Wistar	F, 220 F, 200 F, 200 F, 100 F, 100 F, 100	Clean air Whole exhaust Whole exhaust Whole exhaust Carbon black TiO_2	0 0.8 2.5 7.0 11.6 10.0	None None None None None None	18 hr/day, 5 days/ week, for up to 24 mo	6 mo	0/217 (0) 0/198 (0) 2/200 (1) 4/100 (4) 13/100 (13) 4/100 (4)	1/217 (<1) 0/198 (0) 1/200 (<1) 4/100 (4) 13/100 (13) 13/100 (13)	0/217 (0) 0/198 (0) 0/200 (0) 2/100 (2) 4/100 (4) 3/100 (3)	0/217 (0) 0/198 (0) 7/200 (3.5) 14/100 (14) 20/100 (20) 20/100 (20)	Tumor incidences after 30 mo
								Adenomas	Adenocarcinomas	Squamous cell carcinoma	Adeno-squamous carcinoma	Other neoplasms
Nikula et al. (1995)	Rat/F344	M + F, 214[b] M + F, 210 M + F, 212 M + F, 213 M + F, 211	Clean air Whole exhaust Whole exhaust Carbon black Carbon black	0 2.5 6.5 2.5 6.5	None None None None None	16 hr/day, 5 days/ week for up to 24 mo	6 weeks	1/214 (<1) 7/210 (3) 23/212 (11) 3/213 (1) 13/211 (6)	1/214 (<1) 4/210 (2) 22/212 (10) 7/213 (3) 21/211 (10)	1/214 (<1) 3/210 (1) 3/212 (1) 0/213 (0) 3/211 (1)	0/214 (0) 0/210 (0) 1/212 (<1) 0/213 (0) 2/211 (<1)	0/214 (0) 0/210 (0) 0/212 (0) 1/213 (<1) 0/211 (0)

Table 7-3. Summary of animal inhalation carcinogenicity studies (continued)

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m^3)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]	Comments
Iwai et al. (1997)	F/344	121, F 108, F 153, F	Clean air Filtered air Whole exhaust	0 0 3.2-9.4	None None None	NA 48-56 hr/day 48-56 hr/day	NA 6 mo 6 mo	5/121(4%) type not stated 2/108(4%) type not stated 53/153(35%) 61.3% adenoma, 25.8% adenocarcinoma, 2.2% benign squamous cell tumor, 7.5% squamous cell carcinoma, 3.2% adenosquamous carcinoma	Cumulative exposure dose ranged from 154-274 mg/m^3
Orthoefer et al. (1981) (Pepelko and Peirano, 1983)	Mouse/ Strong A	M, 25	Clean air	0	None	20 hr/day, 7 days/ week, for 7 weeks		3/22 (13.6)	0.13 tumors/ mouse
			Whole exhaust	6.4	None		26 weeks	7/19 (36.8)	0.63 tumors/ mouse
			Whole exhaust	6.4	UV irradiated		26 weeks	6/22 (27.3)	0.27 tumors/ mouse

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Table 7-3. Summary of animal inhalation carcinogenicity studies (continued)

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m^3)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]	Comments
								Lung tumors	
	Mouse/ Jackson A	M + F, 40	Clean air	0	None	20 hr/day, 7 days/ week, for 8 weeks	8 weeks	16/36 (44.4)	0.5 tumors/ mouse
		M + F, 40	Whole exhaust	6.4	None		8 weeks	11/34 (32.3)	0.4 tumors/ mouse
	Mouse/ Jackson A	F, 60	Clean air	0	None			4/58 (6.9)	0.09 tumors/ mouse
		F, 60	Clean air	0	Urethan[l]	20 hr/day, 7 days/ week, for approx. 7 mo.		9/52 (17.3)	0.25 tumors/ mouse
		F, 60	Whole exhaust	6.4	None			14/56 (25.0)	0.32 tumors/ mouse
		F, 60		6.4	Urethan[k]			22/59 (37.3)	0.39 tumors/ mouse
		M, 429	Whole exhaust	0	None			73/403 (18.0)	0.23 tumors/ mouse
		M, 430	Clean air	6.4	None			66/368 (17.9)	0.20 tumors/ mouse
			Whole exhaust						
Kaplan et al. (1982)	Mouse A/J	M, 458 M, 18 M, 485	Clean air Clean air Whole exhaust	1.5	None Urethan[k] None	20 hr/day, 7 days/ week, for 3 mo	6 mo	Pulmonary adenomas 144/458 (31.4) 18/18 (100) 165/485 (34.2)	
								Pulmonary adenoma	
Kaplan et al. (1983) White et al. (1983)	Mouse/ A/J	M, 388 M, 388 M, 399 M, 396	Clean air Whole exhaust Whole exhaust Whole exhaust	0 0.25 0.75 1.5	None None None None	20 hr/day, 7 days/ week, for up to 8 mo	NA	130/388 (33.5) 131/388 (33.8) 109/399 (27.3) 99/396 (25.0)	

Table 7-3. Summary of animal inhalation carcinogenicity studies (continued)

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m^3)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]			Comments
								Adenomas	Carcinomas	All tumors	
Pepelko and Peirano (1983)	Mouse/ Sencar	M + F, 260	Clean air	121212	None	Continuous for 15 mo	NA	(5.1)	(0.5)	(5.6)	
			Clean air		BHT[l]			(12.2)	(1.7)	(2.8)	
			Clean air		Urethan[k]			(8.1)	(0.9)	(9.0)	
			Whole exhaust		None			(10.2)[c]	(1.0)	(11.2)[c]	
			Whole exhaust		BHT[l]			(5.4)	(2.7)	(8.1)	
			Whole exhaust		Urethan[l]			(8.7)	(2.6)	(11.2)	

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Table 7-3. Summary of animal inhalation carcinogenicity studies (continued)

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m³)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]				Comments
								All tumors				
Pepelko and Peirano (1983)	Mouse/ Strain A	M + F, 90	Clean air	1212012	None		NA	21/87 (24)				0.29 tumors/ mouse
			Clean air		Exposure (darkness)			59/237 (24.9)				0.27 tumors/ mouse
			Whole exhaust		Exposure (darkness)			10/80 (12.5)				0.14
			Whole exhaust					22/250 (0.10)				0.10
					Urethan[m]			66/75 (88)				2.80
					Urethan[m]			42/75 (0.95)				0.95
			Clean air									
			Whole exhaust									
								Adenomas	Adenocarcinoma	Squamous cell tumors	All tumors	
Heinrich et al. (1986a,b)	Mouse/ NMRI	M + F, 84	Clean air	4	None	19 hr/day, 5 days/ week for up to 30 mo	NA	9/84 (11)	2/84 (2)	—	11/84 (13)	
		M + F, 93	Filtered exhaust		None			11/93 (12)	18/93 (19)[c]	—	29/93 (31)[c]	
		M + F, 76	Whole exhaust		None			11/76 (15)	13/76 (17)[c]	—	24/76 (32)[c]	
Takemoto et al. (1986)	Mouse/ IRC	M + F, 45	Clean air	0	None	4 hr/day, 4 days/ week, for 19-28 mo	NA					
		M + F, 69	Whole exhaust	2-4	None							
								Adenoma	Adenocarcinoma			
	Mouse/ C57BL	M + F, 12	Clean air	0	None	4 hr/day, 4 days/ week for 19-28 mo	NA	3/45 (6.7)	1/45 (2.2)			
		M + F, 38	Whole exhaust	2-4	None			6/69 (8.7)	3/69 (4.3)			

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Table 7-3. Summary of animal inhalation carcinogenicity studies (continued)

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m^3)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]					Comments
Heinrich et al. (1995)	Mouse/ C57BL/6N	F, 120	Clean air	4.5	None	18 hr/day, 5 days/ week, for up to 21 mo	6 mo	1/12 (8.3)	0/12 (0)				5.1% tumor rate
		F, 120	Whole exhaust		None			8/38 (21.1)	3/38 (7.9)				8.5% tumor rate
		F, 120	Particle-free exhaust		None								3.5% tumor rate
	Mouse/ NMRI	F, 120	Clean air	0	None	18 hr/day, 5 days/ week for up to 13.5 mo	9.5 mo	Adenomas	Adenocarcinomas				
		F, 120	Whole exhaust	4.5	None			(25)	(15.4)				
				11.6	None			(21.8)	(15.4)				
			Carbon black	10	None			(11.3)	(10)				
			TiO_2					(11.3)	(2.5)				
	Mouse/ NMRI	F, 120	Clean air	4.5	None	18 hr/day, 5 days/ week, 23 mo	None	(25)	(8.8)				
		F, 120	Whole exhaust		None			(18.3)	(5.0)				
		F, 120	Particle-free exhaust		None			(31.7)	(15)				
								Multiple adenomas	Multiple carcinomas	Adenomas/ carcinoma	Alveolar/ bronchiolar adenoma	Alveolar/ bronchiolar carcinoma	
Mauderly et al. (1996)	Mouse/ CD-1	M + F, 157[b]	Clean air	0	None	7 hr/day, 5 days/week, for up to 24 mo	None	1/157 (0.6)	2/157 (1.3)	1/157 (0.6)	10/157 (6.4)	7/157 (4.5)	
		M + F, 171	Whole exhaust	0.35	None			2/171 (1.2)	1/171 (0.6)	1/171 (0.6)	16/171 (9.4)	5/171 (2.9)	
		M + F, 155	Whole exhaust	3.5	None			0/155 (0)	1/155 (0.6)	0/155 (0)	8/155 (5.2)	6/155 (3.9)	
		M + F, 186	Whole exhaust	7.1	None			0/186 (0)	0/186 (0)	0/186 (0)	10/186 (5.4)	4/186 (2.2)	
								Adenomas	Adenocarcinoma	Squamous cell tumors	All tumors		
Heinrich et al. (1986a,b)	Hamster/ Syrian	M + F, 96	Clean air Filtered exhaust		None	19 hr/day 5 days/week for up to 30 mo		0/96(0)	0/96(0)	0/96	0/96(0)		
		M + F, 96			None			0/96(0)	0/96(0)	0/96	0/96(0)		
		M + F, 96	Whole exhaust	4	None		NA	0/96(0)	0/96(0)	0/96	0/96(0)		

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Table 7-3. Summary of animal inhalation carcinogenicity studies (continued)

Study	Species/ strain	Sex/total number	Exposure atmosphere	Particle concentration (mg/m^3)	Other treatment	Exposure protocol	Post-exposure observation	Tumor type and incidence (%)[a]	Comments
								Primary lung tumors	
Brightwell et al. (1989)	Hamster/ Syrian Golden	M + F,	Clean air	0	None	16 hr/day, 5 days/ week, for 24 mo	NA	7/202 (3.5)	Respiratory tract tumors not related to exhaust exposure for any of the groups
		M + F, 202	Clean air	0	DEN[j]			4/104 (3.8)	
		M + F, 104	Filtered exhaust (medium dose)	0	DEN[j]			9/104 (8.7)	
		M + F, 104	Filtered exhaust (high dose)	0	DEN[j]			2/101 (2.0)	
		M + F, 101	Whole exhaust	0.7	DEN[j]			6/102 (5.9)	
		M + F, 102		2.2	DEN[j]			4/101 (3.9)	
		M + F, 101	Whole exhaust	6.6	DEN[j]			1/204 (0.5)	
		M + F, 204	Whole exhaust	0	None			0/203 (0)	
		M + F, 203	Filtered exhaust (high dose)	6.6	None				
			Whole exhaust						

[a]Table values indicate number with tumors/number examined (% animals with tumors).
[b]Number of animals examined for tumors.
[c]Significantly different from clean air controls.
[d]Dipentylnitrosamine; 6.25 mg/kg/week s.c. during first 25 weeks of exposure.
[e]Dipentylnitrasamine; 12.5 mg/kg/week s.c. during first 25 weeks of exposure.
[f]Splenic lymphomas also detected in controls (8.3%), filtered exhaust group (37.5%) and whole exhaust group (25%).
[g]5.3% incidence of large cell carcinomas.
[h]1 g/kg, i.p. 1/week for 3 weeks starting 1 mo into exposure.
[i]Includes adenomas, squamous cell carcinomas, adenocarcinomas, adenosquamous cell carcinoma, and mesotheliomas.
[j]4.5 mg/diethylnitrosamine (DEN)/kg, s.c., 3 days prior to start of inhalation exposure.
[k]Single i.p. dose 1 mg/kg at start of exposure.
[l]Butylated hydroxytoluene 300 mg/kg, i.p. for week 1, 83 mg/kg for week 2, and 150 mg/kg for weeks 3 to 52.
[m]12 mg/m^3 from 12 weeks of age to termination of exposure. Prior exposure (in utero) and of parents was 6 mg/m^3.
[n]120-121 males and 71-72 females examined histologically.
[o]Not all animals were exposed for full term, at least 10 males were killed at 3, 6, and 12 mo of exposure.
NS = Not specified.
NA = Not applicable.

Table 7-4. Tumor incidences in rats following intratracheal instillation of DE particles (DPM), extracted DPM, carbon black (CB), benzo[*a*]pyrene (B[*a*]P), or particles plus B[*a*]P

Experimental group	Number of animals	Total dose	Animals with tumors (percent)	Statistical significance[a]
Control	47	4.5 mL	0 (0)	-
DPM (original)	48	15 mg	8 (17)	< 0.01
DPM (extracted)	48	30 mg	10 (21)	< 0.001
DPM (extracted)	48	15 mg	2 (4)	NS
CB (printex)	48	15 mg	10 (21)	< 0.001
CB (lampblack)	48	14 mg	4 (8)	NS
B[*a*]P	47	30 mg	43 (90)	< 0.001
B[*a*]P	48	15 mg	12 (25)	< 0.001
DEP + B[*a*]P	48	15 mg + 170 µg B[*a*]P	4 (8)	NS
CB (printex) + B[*a*]P	48	15 mg + 443 µg B[*a*]P	13 (27)	< 0.001

Table 7-5. Tumorigenic effects of dermal application of acetone extracts of DPM

Number of animals	Strain/sex	Sample material	Time to first tumor (mo)	Survivors at time of first tumor	Total tumors	Duration of experiment (mo)
52	C57BL/40 F C57BL/12 M	Extract of DPM obtained during warmup	13	33	2	22
50	Strain A/M	Extract of DPM obtained during full load	15	8	4	23
25	Strain A/F	Extract of DPM obtained during full load	13	20	17	17

Source: Kotin et al., 1955.

General Motors Research Laboratories sponsored chronic inhalation studies at the Southwest Research Institute using male Fischer 344 rats, 30 per group, exposed to DPM concentrations of 0.25, 0.75, or 1.5 mg/m^3 (Kaplan et al., 1983; White et al., 1983). The animals were exposed in 12.6 m^3 exposure chambers. Airflow was adjusted to provide 13 changes per hour. Temperature was maintained at 22 ± 2 °C. The exposure protocol was 20 hr/day, 7 days/week for 9 to 15 months. Exposures were halted during normal working hours for servicing. Some animals were sacrificed following completion of exposure, while others were returned to clean air atmospheres for an additional 8 months. Control animals received clean air. Exhaust was generated by 5.7-L Oldsmobile engines (four different engines used throughout the experiment) operated at a steady speed and load simulating a 40-mph driving speed of a full-size passenger car.

Although five instances of bronchoalveolar carcinoma were observed in 90 rats exposed to DE for 15 months and held an additional 8 months in clean air, compared with none among controls, statistical significance was not achieved in any of the exposure groups. These included one tumor in the 0.25 mg/m^3 group, three in the 0.75 mg/m^3 group, and one in the 1.5 mg/m^3 group. Rats kept in clean-air chambers for 23 months did not exhibit any carcinomas. No tumors were observed in any of the 180 rats exposed to DE for 9 or 15 months without a recovery period, or in the respective controls for these groups. Equivocal results may again have been due to less-than-lifetime duration of the study as well as insufficient exposure concentrations. Although the increases in tumor incidences in the groups exposed for 15 months and held an additional 8 months in clean air were not statistically significant, relative to controls, they were slightly greater than the historic background incidence of 3.7% for this specific lesion in this strain of rat (Ward, 1983). The first definitive studies linking inhaled DE to induction of lung cancer in rats were reported by researchers in Germany, Switzerland, Japan, and the United States in the mid-to-late 1980s. In a study conducted at the Fraunhofer Institute exhaust-generating system and exposure atmosphere characteristics are presented in Appendix A. The type of engine used (3-cylinder, 43 bhp diesel) is normally used in mining situations and was of Toxicology and Aerosol Research, female Wistar rats were exposed for 19 hr/day, 5 days/week to both filtered and unfiltered (total) DE at an average particulate matter concentration of 4.24 mg/m^3. Animals were exposed for a maximum of 2.5 years. The exposure system as described by Heinrich et al. (1986a) used a 40 kilowatt 1.6-L diesel engine operated continuously under the U.S. 72 FTP driving cycle. The engines used European Reference Fuel with a sulfur content of 0.36%. Filtered exhaust was obtained by passing engine exhaust through a Luwa FP-65 HT 610 particle filter heated to 80 °C and a secondary series of filters (Luwa FP-85, Luwa NS-30, and Drager CH 63302) at room temperature. The filtered and unfiltered exhausts were diluted 1:17 with filtered air and passed through respective 12 m^3 exposure chambers. Mass

median aerodynamic diameter of DPM was 0.35 ± 0.10 μm (mean ± SD). The gas-phase components of the DE atmospheres are presented in Appendix A.

The effects of exposure to either filtered or unfiltered exhaust were described by Heinrich et al. (1986b) and Stöber (1986). Exposure to unfiltered exhaust resulted in 8 bronchoalveolar adenomas and 9 squamous cell tumors in 15 of 95 female Wistar rats examined, for a 15.8% tumor incidence. Although statistical analysis was not provided, the increase appears to be highly significant. In addition to the bronchioalveolar adenomas and squamous cell tumors, there was a high incidence of bronchioalveolar hyperplasia (99%) and metaplasia of the bronchioalveolar epithelium (65%). No tumors were reported among rats exposed to filtered exhaust (n = 92) or clean air (n = 96).

Mohr et al. (1986) provided a more detailed description of the lung lesions and tumors identified by Heinrich et al. (1986a,b) and Stöber (1986). Substantial alveolar deposition of carbonaceous particles was noted for rats exposed to unfiltered DE. Squamous metaplasia was observed in 65.3% of the rats breathing unfiltered DE, but not in the control rats. Of nine squamous cell tumors, one was characterized as a Grade I carcinoma (borderline atypia, few to moderate mitoses, and slight evidence of stromal invasion), and the remaining eight were classified as benign keratinizing cystic tumors.

Iwai et al. (1986b) examined the long-term effects of DE inhalation on female F344 rats. The exhaust was generated by a 2.4-L displacement truck engine. The exhaust was diluted 10:1 with clean air at 20 °C to 25 °C and 50% relative humidity. The engines were operated at 1,000 rpm with an 80% engine load. These operating conditions were found to produce exhaust with the highest particle concentration and lowest NO_2 and SO_2 content. For those chambers using filtered exhaust, proximally installed high-efficiency particulate air (HEPA) filters were used. Three groups of 24 rats each were exposed to unfiltered DE, filtered DE, or filtered room air for 8 hr/day, 7 days/week for 24 months. Particle concentration was 4.9 mg/m^3 for unfiltered exhaust. Concentrations of gas-phase exhaust components were 30.9 ppm NO_x, 1.8 ppm NO_2, 13.1 ppm SO_2, and 7.0 ppm CO.

No lung tumors were found in the 2-year control (filtered room air) rats, although one adenoma was noted in a 30-months control rat, providing a spontaneous tumor incidence of 4.5%. No lung tumors were observed in rats exposed to filtered DE. Nineteen of the 24 exposed to unfiltered exhaust survived for 2 years. Of these, 14 were randomly selected for sacrifice at this time. Four of the rats developed lung tumors; two of these were malignant. Five rats of this 2-year exposure group were subsequently placed in clean room air for 3 to 6 months and four eventually (time not specified) exhibited lung tumors (three malignancies). Thus, the lung tumor incidence for total tumors was 42.1% (8/19) and 26.3% (5/19) for malignant tumors in rats exposed to whole DE. The tumor types identified were adenoma (3/19), adenocarcinoma

(1/19), adenosquamous carcinoma (2/19), squamous carcinoma (1/19), and large-cell carcinoma (1/19). The lung tumor incidence in rats exposed to whole DE was significantly greater than that of controls ($p \leq 0.01$). Tumor data are summarized in Table 7-3. Malignant splenic lymphomas were detected in 37.5% of the rats in the filtered exhaust group and in 25.0% of the rats in the unfiltered exhaust group; these values were significantly ($p \leq 0.05$) greater than the 8.2% incidence noted in the control rats. The study demonstrates production of lung cancer in rats following 2-year exposure to unfiltered DE. In addition, splenic malignant lymphomas occurred during exposure to both filtered and unfiltered DE. This is the only report to date of tumor induction at an extrarespiratory site by inhaled DE in animals.

A chronic (up to 24 months) inhalation exposure study was conducted by Takemoto et al. (1986), in which female Fischer 344 rats were exposed to DE generated by a 269-cc YANMAR-40CE NSA engine operated at an idle state (1,600 rpm). Exposures were 4 hours/day, 4 days/week. The animals were exposed in a 376-L exposure chamber. Air flow was maintained at 120 L/min. Exhaust was diluted to produce a particle concentration of 2-4 mg/m^3. When not exposed the animals were maintained in an air-conditioned room at a temperature of 24 ± 2°C and a relative humidity of 55 ± 5% with 12 hr of light and darkness. Temperature and humidity in the exposure chambers was not noted. The particle concentration of the DE in the exposure chamber was 2 to 4 mg/m^3. B[a]P and 1-nitropyrene concentrations were 0.85 and 93 μg/g of particles, respectively. No lung tumors were reported in the diesel-exposed animals. It was also noted that the diesel engine employed in this study was originally used as an electrical generator and that its operating characteristics (not specified) were different from those of a diesel-powered automobile. However, the investigators deemed it suitable for assessing the effects of diesel emissions.

Mauderly et al. (1987) provided data affirming the carcinogenicity of automotive diesel engine exhaust in F344/Crl rats following chronic inhalation exposure. Male and female rats were exposed to diesel engine exhaust at nominal DPM concentrations of 0.35 (n = 366), 3.5 (n = 367), or 7.1 (n = 364) mg/m^3 for 7 hr/day, 5 days/week for up to 30 mo. Sham-exposed (n = 365) controls breathed filtered room air. A total of 230, 223, 221, and 227 of these rats (sham-exposed, low-, medium-, and high-exposure groups, respectively) were examined for lung tumors. These numbers include those animals that died or were euthanized during exposure and those that were terminated following 30 months of exposure. The exhaust was generated by 1980 model 5.7-L Oldsmobile V-8 engines operated through continuously repeating U.S. Federal Test Procedure (FTP) urban certification cycles. The engines were equipped with automatic transmissions connected to eddy-current dynamometers and flywheels simulating resistive and inertial loads of a midsize passenger car. The D-2 diesel control fuel (Phillips Chemical Co.) met U.S. EPA certification standards and contained approximately 30% aromatic

hydrocarbons and 0.3% sulfur. Following passage through a standard automotive muffler and tailpipe, the exhaust was diluted 10:1 with filtered air in a dilution tunnel and serially diluted to the final concentrations. The primary dilution process was such that particle coagulation was retarded. Mokler et al. (1984) provided a detailed description of the exposure system. No exposure-related changes in body weight or lifespan were noted for any of the exposed animals, nor were there any signs of overt toxicity. Collective lung tumor incidence was greater (z statistic, $p \leq 0.05$) in the high (7.1 mg/m^3) and medium (3.5 mg/m^3) exposure groups (12.8% and 3.6%, respectively) versus the control and low (0.35 mg/m^3) exposure groups (0.9% and 1.3%, respectively). In the high-dose group the incidences of tumor types reported were adenoma (0.4%), adenocarcinomas plus squamous cell carcinomas (7.5%), and squamous cysts (4.9%). In the medium-dose group adenomas were reported in 2.3% of animals, adenocarcinomas plus squamous cell carcinomas in 0.5%, and squamous cysts in 0.9%. In the low-exposure group adenocarcinomas plus squamous cell carcinomas were detected in 1.3% of the rats. Using the same statistical analysis of specific tumor types, adenocarcinoma plus squamous cell carcinoma and squamous cyst incidence was significantly greater in the high-exposure group, and the incidence of adenomas was significantly greater in the medium-exposure group. A significant ($p<0.001$) exposure-response relationship was obtained for tumor incidence relative to exposure concentration and lung burden of DPM. These data are summarized in Table 7-3. A logistic regression model estimating tumor prevalence as a function of time, dose (lung burden of DPM), and sex indicated a sharp increase in tumor prevalence for the high dose level at about 800 days after the commencement of exposure. A less pronounced, but definite, increase in prevalence with time was predicted for the medium-dose level. Significant effects were not detected at the low concentration. DPM (mg per lung) of rats exposed to 0.35, 3.5, or 7.1 mg of DPM/m^3 for 24 months were 0.6, 11.5, and 20.8, respectively, and affirmed the greater-than-predicted accumulation that was the result of decreased particle clearance following high-exposure conditions.

In summary, this study demonstrated the pulmonary carcinogenicity of high concentrations of whole, diluted DE in rats following chronic inhalation exposure. In addition, increasing lung particle burden resulting from this high-level exposure and decreased clearance was demonstrated. A logistic regression model presented by Mauderly et al. (1987) indicated that both lung DPM burden and exposure concentration may be useful for expressing exposure-effect relationships.

A long-term inhalation study (Ishinishi et al., 1988a; Takaki et al., 1989) examined the effects of emissions from a light-duty (LD) and a heavy-duty (HD) diesel engine on male and female Fischer 344/Jcl rats. The LD engines were 1.8-L, 4-cylinder, swirl-chamber-type power plants, and the HD engines were 11-L, 6-cylinder, direct-injection-type power plants. The

engines were connected to eddy-current dynamometers and operated at 1,200 rpm (LD engines) and 1,700 rpm (HD engines). Nippon Oil Co. JIS No. 1 or No. 2 diesel fuel was used. The 30-months whole-body exposure protocol (16 h/day, 6 days/week) used DPM concentrations of 0, 0.5, 1, 1.8, or 3.7 mg/m^3 from HD engines and 0, 0.1, 0.4, 1.1, or 2.3 mg/m^3 from LD engines. The animals inhaled the exhaust emissions from 1700 to 0900 h. Sixty-four male rats and 59 to 61 female rats from each exposure group were evaluated for carcinogenicity.

For the experiments using the LD series engines, the highest incidence of hyperplastic lesions plus tumors (72.6%) was seen in the highest exposure (2.3 mg/m^3) group. However, this high value was the result of the 70% incidence of hyperplastic lesions; the incidence of adenomas was only 0.8% and that of carcinomas 1.6%. Hyperplastic lesion incidence was considerably lower for the lower exposure groups (9.7%, 4.8%, 3.3%, and 3.3% for the 1.1, 0.4, and 0.1 mg/m^3 and control groups, respectively). The incidence of adenomas and carcinomas, combining males and females, was not significantly different among exposure groups (2.4%, 4.0%, 0.8%, 2.4%, and 3.3% for the 2.3, 1.1, 0.4, and 0.1 mg/m^3 groups and the controls, respectively).

For the experiments using the HD series engines, the total incidence of hyperplastic lesions, adenomas, and carcinomas was highest (26.6%) in the 3.7 mg/m^3 exposure group. The incidence of adenomas plus carcinomas for males and females combined equaled 6.5%, 3.3%, 0%, 0.8%, and 0.8% at 3.7, 1.8, 1, and 0.4 mg/m^3 and for controls, respectively. A statistically significant difference was reported between the 3.7 mg/m^3 and the control groups for the HD series engines. The carcinomas were identified as adenomas, adenosquamous carcinomas, and squamous cell carcinomas. Although the number of each was not reported, it was noted that the majority were squamous cell carcinomas. A progressive dose-response relationship was not demonstrated. Tumor incidence data for this experiment are presented in Table 7-3.

The Ishinishi et al. (1988a) study also included recovery tests in which rats exposed to whole DE (DPM concentration of 0.1 or 1.1 mg/m^3 for the LD engine and 0.5 or 1.8 mg/m^3 for the HD engine) for 12 months were examined for lung tumors following 6-, 12-, or 18-month recovery periods in clean air. The incidences of neoplastic lesions were low, and pulmonary DPM burden was lower than for animals continuously exposed to whole DE and not provided a recovery period. The only carcinoma observed was in a rat examined 12 months following exposure to exhaust (1.8 mg/m^3) from the HD engine.

Brightwell et al. (1986, 1989) studied the effects of DE on male and female F344 rats. The DE was generated by a 1.5-L Volkswagen engine that was computer-operated according to the U.S. 72 FTP driving cycle. The engine was replaced after 15 mo. The engine emissions were diluted by conditioned air delivered at 800 m^3/h to produce the high-exposure (6.6 mg/m^3) DE atmosphere. Further dilutions of 1:3 and 1:9 produced the medium- (2.2 mg/m^3) and low-

(0.7 mg/m^3) exposure atmospheres. The CO and NO_x concentrations (mean ± SD) were 32 ± 11 ppm and 8 ± 1 ppm in the high-exposure concentration chamber. The inhalation exposures were conducted overnight to provide five 16-h periods per week for 2 years; surviving animals were maintained for an additional 6 mo.

For males and females combined, a 1.2% (3/260), 0.7% (1/144), 9.7% (14/144), and 38.5% (55/143) incidence of primary lung tumors occurred in F344 rats following exposure to clean air or 0.7, 2.2, and 6.6 mg of DPM/m^3, respectively (Table 7-3). DE-induced tumor incidence in rats was dose-related and higher in females than in males (Table 7-3). These data included animals sacrificed at the interim periods (6, 12, 18, and 24 mo); therefore, the tumor incidence does not accurately reflect the effects of long-term exposure to the DE atmospheres. When tumor incidence is expressed relative to the specific intervals, a lung tumor incidence of 96% (24/25), 76% (19/25) of which were malignant, was reported for female rats in the high-dose group exposed for 24 months and held in clean air for the remainder of their lives. For male rats in the same group, the tumor incidence equaled 44% (12/27), of which 37% (10/27) were malignant. It was also noted that many of the animals exhibiting tumors had more than one tumor, often representing multiple histological types. The numbers and types of tumors identified in the rats exposed to DE included adenomas (40), squamous cell carcinomas (35), adenocarcinomas (19), mixed adenoma/adenocarcinomas (9), and mesothelioma (1). It should be noted that exposure during darkness (when increased activity would result in greater respiratory exchange and greater inhaled dose) could account, in part, for the high response reported for the rats.

Lewis et al. (1989) also examined the effects of inhalation exposure of DE and/or coal dust on tumorigenesis on F344 rats. Groups of 216 male and 72 female rats were exposed to clean air, whole DE (2 mg soot/m^3), coal dust (2 mg/m^3 respirable concentration; 5 to 6 mg/m^3 total concentration), or DE plus coal dust (1 mg/m^3 of each respirable concentration; 3.2 mg/m^3 total concentration) for 7 h/day, 5 days/week during daylight hours for up to 24 mo. Groups of 10 or more males were sacrificed at intermediate intervals (3, 6, and 12 mo). The DE was produced by a 7.0-L, 4-cycle, water-cooled Caterpillar Model 3304 engine using No. 2 diesel fuel (<0.5% sulfur by mass). The exhaust was passed through a Wagner water scrubber, which lowered the exhaust temperature and quenched engine backfire. The animals were exposed in 100-cubic-foot chambers. Temperature was controlled at 22 ± 2 °C and relative humidity at 50%±10%. The exhaust was diluted 27-fold with chemically and biologically filtered clean air to achieve the desired particle concentration.

Histological examination was performed on 120 to 121 male and 71 to 72 female rats terminated after 24 months of exposure. The exhaust exposure did not significantly affect the tumor incidence beyond what would be expected for aging F344 rats. There was no

postexposure period, which may explain, in part, the lack of significant tumor induction. The particulate matter concentration was also less than the effective dose in several other studies.

In a more recent study reported by Heinrich et al. (1995), female Wistar rats were exposed to whole DE (0.8, 2.5, or 7.0 mg/m^3) 18 h/day, 5 days/week for up to 24 mo, then held in clean air an additional 6 mo. The animals were exposed in either 6 or 12 m^3 exposure chambers. Temperature and relative humidity were maintained at 23-25 °C and 50%-70%, respectively. DE was generated by two 40-kw 1.6-L diesel engines (Volkswagen). One of them was operated according to the U.S. 72 cycle. The other was operated under constant load conditions. The first engine did not supply sufficient exhaust, which was filled by the second engine. Cumulative exposures for the rats in the various treatment groups were 61.7, 21.8, and 7.4 g/m^3 × h for the high, medium, and low whole-exhaust exposures. Significant increases in tumor incidences were observed in the high (22/100; $p<0.001$) and mid (11/200; $p<0.01$) exposure groups relative to clean-air controls (Table 7-3). Only one tumor (1/217), an adenocarcinoma, was observed in clean-air controls. Relative to clean-air controls, significantly increased incidences were observed in the high-exposure rats for benign squamous cell tumors (14/100; $p<0.001$), adenomas (4/100; $p<0.01$), and adenocarcinomas (5/100; $p<0.05$). Only the incidence of benign squamous cell tumors (7/200; $p<0.01$) was significantly increased in the mid-exposure group relative to the clean-air controls.

Particle lung burden and alveolar clearance also were determined in the Heinrich et al. (1995) study. Relative to clean air controls, alveolar clearance was significantly compromised by exposure to mid and high DE. For the high-diesel-exhaust group, 3-mo recovery time in clean air failed to reverse the compromised alveolar clearance.

In a study conducted at the Inhalation Toxicology Research Institute (Nikula et al., 1995) F344 rats (114-115 per sex per group) were exposed 16 hr/day, 5 days/week during daylight hours to DE diluted to achieve particle concentrations of 2.5 or 6.5 mg/m^3 for up to 24 mo. Controls (118 males, 114 females) were exposed to clean air. Surviving rats were maintained an additional 6 weeks in clean air, at which time mortality reached 90%. DE was generated with two 1988 Model LH6 General Motors 6.2-L V-8 engines burning D-2 fuel that met EPA certification standards. Chamber air flow was sufficient to provide about 15 exchanges per hour. Relative humidity was 40% to 70% and temperature ranged from 23 to 25 °C.

Following low and high DE exposure, the lung burdens were 36.7 and 80.7 mg, respectively, for females and 45.1 and 90.1 mg, respectively, for males. The percentages of susceptible rats (males and females combined) with malignant neoplasms were 0.9 (control), 3.3 (low DE), and 12.3 (high DE). The percentages of rats (males and females combined) with malignant or benign neoplasms were 1.4 (control), 6.2 (low DE), and 17.9 (high DE). All

primary neoplasms were associated with the parenchyma rather than the conducting airways of the lungs. The first lung neoplasm was observed at 15 mo. Among 212 males and females examined in the high-dose group, adenomas were detected in 23 animals, adenocarcinomas in 22 animals, squamous cell carcinomas in 3 animals, and an adenosquamous carcinoma in 1 animal. For further details see Table 7-3. Analysis of the histopathologic data suggested a progressive process from alveolar epithelial hyperplasia to adenomas and adenocarcinomas.

Iwai et al. (1997) carried out a series of exposures to both filtered and whole exhaust using a light-duty (2,369 mL) diesel engine. The protocol for engine operation was not stated. Groups of female SPF F344 Fischer rats were exposed for 2 years for 8 hr/day, 7 days/week, 8 hr/day, 6 days/week, or 18 hr/day, 3 days/week to either filtered exhaust or exhaust diluted to a particle concentration of 9.4, 3.2, and 5.1 mg/m^3, respectively. Cumulative exposure (mg/m^3 × hrs of exposure) equaled 274.4, 153.6, and 258.1 mg/m^3. The animals were then held for an additional 6 months in clean air. Lung tumors were reported in 5/121 (4%) of controls, 4/108 (4%) of those exposed to filtered exhaust, and 50/153 (35%) among those exposed to whole exhaust. Among rats exposed to whole DE the following number of tumors were detected; 57 adenomas, 24 adenocarcinomas, 2 benign squamous cell tumors, 7 squamous cell carcinomas, and 3 adenosquamous carcinomas. The authors stated that benign squamous cell tumors probably corresponded to squamous cysts in another classification.

7.3.1.2. *Mouse Studies*

A series of inhalation studies using strain A mice was conducted by Orthoefer et al. (1981). Strain A mice are usually given a series of intraperitoneal injections with the test agent; they are then sacrificed at about 9 months and examined for lung tumors. In the present series, inhalation exposure was substituted. DE was provided by one of two Nissan CN6-33 diesel engines having a displacement of 3244 cc and run on a Federal Short Cycle. Flow through the exposure chambers was sufficient to provide 15 air changes per hour. Temperature was maintained at 24 °C and relative humidity at 75%. In the first study, groups of 25 male Strong A strain (A/S) mice were exposed to irradiated DE (to simulate chemical reactions induced by sunlight) or nonirradiated DE (6 mg/m^3) for 20 h/day, 7 days/week. Additional groups of 40 Jackson A strain (S/J) mice (20 of each sex) were exposed similarly to either clean air or DE, then held in clean air until sacrificed at 9 months of age. No tumorigenic effects were detected at 9 months of age. Further studies were conducted in which male A/S mice were exposed 8 hr/day, 7 days/week until sacrifice (approximately 300 at 9 months of age and approximately 100 at 12 months of age). With the exception of those treated with urethan, the number of tumors per mouse did not exceed historical control levels in any of the studies. Exposure to DE,

however, significantly inhibited the tumorigenic effects of the 5-mg urethan treatment. Results are listed in Table 7-3.

Kaplan et al. (1982) also reported the effects of diesel exposure in strain A mice. Groups of male strain A/J mice were exposed for 20 h/day, 7 days/week for 90 days and held until 9 months of age. Briefly, the animals were exposed in inhalation chambers to DE generated by a 5.7-L Oldsmobile engine operated continuously at 40 mph at DPM concentrations of 0, 0.25, 0.75, or 1.5 mg/m^3. Controls were exposed to clean air. Temperature was maintained at 22 ± 2 °C and relative humidity at 50% ± 10% within the chambers. Among 458 controls and 485 exposed animals, tumors were detected in 31.4% of those breathing clean air versus 34.2% of those exposed to DE. The mean number of tumors per mouse also failed to show significant differences.

In a follow-up study, strain A mice were exposed to DE for 8 months (Kaplan et al., 1983; White et al., 1983). After exposure to the highest exhaust concentration (1.5 mg/m^3), the percentage of mice with pulmonary adenomas and the mean number of tumors per mouse were significantly less ($p<0.05$) than those for controls (25.0% vs. 33.5% and 0.30 ± 0.02 [S.E.] vs. 0.42 ± 0.03 [S.E.]) (Table 7-3).

Pepelko and Peirano (1983) summarized a series of studies on the health effects of diesel emissions in mice. Exhaust was provided by two Nissan CN 6-33, 6-cylinder, 3.24-L diesel engines coupled to a Chrysler A-272 automatic transmission and Eaton model 758-DG dynamometer. Sixty-day pilot studies were conducted at a 1:14 dilution, providing DPM concentrations of 6 mg/m^3. The engines were operated using the Modified California Cycle. These 20-hr/day, 7-days/week pilot studies using rats, cats, guinea pigs, and mice produced decreases in weight gain and food consumption. Therefore, at the beginning of the long-term studies, exposure time was reduced to 8 h/day, 7 days/week at an exhaust DPM concentration of 6 mg/m^3. During the final 12 months of exposure, however, the DPM concentration was increased to 12 mg/m^3. For the chronic studies, the engines were operated using the Federal Short Cycle. Chamber temperature was maintained at 24 °C and relative humidity at 50%. Airflow was sufficient for 15 changes per hour.

Pepelko and Peirano (1983) described a two-generation study using Sencar mice exposed to DE. Male and female parent-generation mice were exposed to DE at a DPM concentration of 6 mg/m^3 prior to (from weaning to sexual maturity) and throughout mating. The dams continued exposure through gestation, birth, and weaning. Groups of offspring (130 males and 130 females) were exposed to either DE or clean air. The exhaust exposure was increased to a DPM concentration of 12 mg/m^3 when the offspring were 12 weeks of age and was maintained until termination of the experiment when the mice were 15 months old.

The incidence of pulmonary adenomas (16.3%) was significantly increased in the mice exposed to DE compared with 6.3% in clean-air controls. The incidence in males and females combined was 10.2% in 205 animals examined compared with 5.1% in 205 clean-air controls. This difference was also significant. The incidence of carcinomas was not affected by exhaust exposure in either sex. These results provided the earliest evidence for cancer induction following inhalation exposure to DE. The increase in the sensitivity of the study, allowing detection of tumors at 15 mo, may have been the result of exposure from conception. It is likely that Sencar mice are sensitive to induction of lung tumors because they are also sensitive to induction of skin tumors. These data are summarized in Table 7-3.

Takemoto et al. (1986) reported the effects of inhaled DE (2 to 4 mg/m^3, 4 h/day, 4 days/week, for up to 28 mo) in ICR and C57BL mice exposed from birth. Details of the exposure conditions are presented in Section 7.3.2.1. All numbers reported are for males and females combined. Four adenomas and 1 adenocarcinoma were detected in 34 DE-exposed ICR mice autopsied at 13 to 18 mo, compared with 3 adenomas among 38 controls. Six adenomas and 3 adenocarcinomas were reported in 22 diesel-exposed ICR mice autopsied at 19 to 28 mo, compared with 3 adenomas and 1 adenocarcinoma in 22 controls. Four adenomas and 2 adenocarcinomas were detected in 79 C57BL mice autopsied at 13 to 18 mo, compared with none in 19 unexposed animals. Among males and females autopsied at 19 to 28 mo, 8 adenomas and 3 adenocarcinomas were detected in 71 exposed animals, compared with 1 adenoma among 32 controls. No significant increases in adenoma or adenocarcinoma were reported for either strain of exposed mice. However, the significance of the increase in the combined incidence of adenomas and carcinomas was not evaluated statistically. A statistical analysis by Pott and Heinrich (1990a) indicated that the difference in combined benign and malignant tumors between whole DE-exposed C57BL/6N mice and corresponding controls was significant at $p<.05$. See Table 7-3 for details of tumor incidence.

Heinrich et al. (1986b) and Stöber (1986), as part of a larger study, also evaluated the effects of DE in mice. Details of the exposure conditions reported by Heinrich et al. (1986a) are given in Section 7.3.1.1 and Appendix A. Following lifetime (19 h/day, 5 days/week, for a maximum of 120 weeks) exposure to DE diluted to achieve a particle concentration of 4.2 mg/m^3, 76 female NMRI mice exhibited a total lung tumor incidence of adenomas and adenocarcinomas combined of 32%. Tumor incidences reported for control mice (n = 84) equaled 11% for adenomas and adenocarcinomas combined. While the incidence of adenomas showed little change, adenocarcinomas increased significantly from 2.4% for controls to 17% for exhaust-exposed mice. In a follow-up study, however, Heinrich et al. (1995) reported a lack of tumorigenic response in either female NMRI or C57BL/6N mice exposed 17 h/day, 5

days/week for 13.5 to 23 months to whole DE diluted to produce a particle concentration of 4.5 mg/m^3. These data are summarized in Table 7-3.

The lack of a carcinogenic response in mice was reported by Mauderly et al. (1996). In this study, groups of 540 to 600 CD-1 male and female mice were exposed to whole DE (7.1, 3.5, or 0.35 mg DPM/m^3) for 7 hr/day, 5 days/week for up to 24 mo. Controls were exposed to filtered air. DE was provided by 5.7-L Oldsmobile V-8 engines operated continuously on the U.S. Federal Test Procedure urban certification cycle. The chambers were maintained at 25 °C-28 °C, relative humidity at 40%-60%, and a flow rate sufficient for 15 air exchanges per hour. Animals were exposed during the light cycle, which ran from 6:00 AM to 6:00 PM. DPM accumulation in the lungs of exposed mice was assessed at 6, 12, and 18 months of exposure and was shown to be progressive; DPM burdens were 0.2 ± 0.02, 3.7 ± 0.16, and 5.6 ± 0.39 mg for the low-, medium-, and high-exposure groups, respectively. The lung burdens in both the medium- and high-exposure groups exceeded that predicted by exposure concentration ratio for the low-exposure group. Contrary to what was observed in rats (Heinrich et al., 1986b; Stöber, 1986; Nikula et al., 1995; Mauderly et al., 1987), an exposure-related increase in primary lung neoplasms was not observed in the CD-1 mice, supporting the contention of a species difference in the pulmonary carcinogenic response to poorly soluble particles. The percentage incidence of mice (males and females combined) with one or more malignant or benign neoplasms was 13.4, 14.6, 9.7, and 7.5 for controls and low-, medium-, and high-exposure groups, respectively.

Although earlier studies provided some evidence for tumorigenic responses in diesel-exposed mice, no increases were reported in the two most recent studies by Mauderly et al. (1996) and Heinrich et al. (1995), which utilized large group sizes and were well designed and conducted. Overall, the results in mice must therefore be considered to be equivocal.

7.3.1.3. *Hamster Studies*

Heinrich et al. (1982) examined the effects of DE exposure on tumor frequency in female Syrian golden hamsters. Groups of 48 to 72 animals were exposed to clean air or whole DE at a mean DPM concentration of 3.9 mg/m^3. Inhalation exposures were conducted 7 to 8 hr/day, 5 days/week for 2 years. The exhaust was produced by a 2.4-L Daimler-Benz engine operated under a constant load and a constant speed of 2,400 rpm. Flow rate was sufficient for about 20 exchanges per hour in the 250-L chambers. No lung tumors were reported in either exposure group.

In a subsequent study, Syrian hamsters were exposed 19 hr/day, 5 days/week for a lifetime to DE diluted to a DPM concentration of 4.24 mg/m^3 (Heinrich et al., 1986b; Stöber, 1986). Details of the exposure conditions are reported in Appendix A. Ninety-six animals per

group were exposed to clean air or exhaust. No lung tumors were seen in either the clean-air group or in the DE-exposed group.

In a third study (Heinrich et al., 1989b), hamsters were exposed to exhaust from a Daimler-Benz 2.4-L engine operated at a constant load of about 15 kW and at a uniform speed of 2,000 rpm. The exhaust was diluted to an exhaust-clean air ratio of about 1:13, resulting in a mean particle concentration of 3.75 mg/m^3. Exposures were conducted in chambers maintained at 22 to 24 °C and 40% to 60% relative humidity for up to 18 mo. Surviving hamsters were maintained in clean air for up to an additional 6 mo. The animals were exposed 19 hr/day, 5 days/week beginning at noon each day, under a 12-hr light cycle starting at 7 AM. Forty animals per group were exposed to whole DE or clean air. No lung tumors were detected in either the clean-air or diesel-exposed hamsters.

Brightwell et al. (1986, 1989) studied the effects of DE on male and female Syrian golden hamsters. Groups of 52 males and 52 females, 6 to 8 weeks old, were exposed to DE at DPM concentrations of 0.7, 2.2, or 6.6 mg/m^3. They were exposed 16 hr/day, 5 days/week for a total of 2 years and then sacrificed. Exposure conditions are described in Section 7.3.1.1. No statistically significant (*t* test) relationship between tumor incidence and exhaust exposure was reported.

In summary, DE alone did not induce an increase in lung tumors in hamsters of either sex in several studies of chronic duration at high exposure concentrations.

7.3.1.4. *Monkey Studies*

Fifteen male cynomolgus monkeys were exposed to DE (2 mg/m^3) for 7 hr/day, 5 days/week for 24 months (Lewis et al., 1989). The same numbers of animals were also exposed to coal dust (2 mg/m^3 respirable concentration; 5 to 6 mg/m^3 total concentration), DE plus coal dust (1 mg/m^3 respirable concentration for each component; 3.2 mg/m^3 total concentration), or filtered air. Details of exposure conditions were listed previously in the description of the Lewis et al. (1989) study with rats (Section 7.3.1.1) and are listed in Appendix A.

None of the monkeys exposed to DE exhibited a significantly increased incidence of preneoplastic or neoplastic lesions. It should be noted, however, that the 24-mo time frame employed in this study may not have allowed the manifestation of tumors in primates, because this duration is only a small fraction of the monkeys' expected lifespan. In fact, there have been no near-lifetime exposure studies in nonrodent species.

7.3.2. Inhalation Studies (filtered DE)

Several studies have been conducted in which animals were exposed to DE filtered to remove PM. As these studies also included groups exposed to whole exhaust, details can be found in Sections 7.3.1.1 for rats, 7.3.1.2 for mice, and 7.3.1.3 for hamsters. Heinrich et al.

(1986b) and Stöber (1986) reported negative results for lung tumor induction in female Wistar rats exposed to filtered exhaust diluted to produce an unfiltered particle concentration of 4.24 mg/m^3. Negative results were also reported in female Fischer 344 rats exposed to filtered exhaust diluted to produce an unfiltered particle concentration of 4.9 mg/m^3 (Iwai et al., 1986a), in Fischer 344 rats of either sex exposed to filtered exhaust diluted to produce an unfiltered particle concentration of 6.6 mg/m^3 (Brightwell et al., 1989), in female Wistar rats exposed to filtered exhaust diluted to produce an unfiltered particle concentration of 7.0 mg/m^3 (Heinrich et al., 1995), and in female Fischer 344 rats exposed to filtered exhaust diluted to produce unfiltered particle concentrations of 5.1, 3.2, or 9.4 mg/m^3 (Iwai et al., 1997). In the Iwai et al. (1986a) study, splenic lymphomas were detected in 37.5% of the exposed rats compared with 8.2% in controls.

In the study reported by Heinrich at al. (1986a) and Stober (1986), primary lung tumors were seen in 29/93 NMRI mice (males and females combined) exposed to filtered exhaust, compared with 11/84 in clean-air controls, a statistically significant increase. In a repeat study by Heinrich et al. (1995), however, significant lung tumor increases were not detected in either female NMRI or C57BL/6N mice exposed to filtered exhaust diluted to produce an unfiltered particle concentration of 4.5 mg/m^3.

Filtered exhaust also failed to induce lung tumor induction in Syrian Golden hamsters (Heinrich et al., 1986a; Brightwell et al., 1989).

Although lung tumor increases were reported in one study and lymphomas in another, these results could not be confirmed in subsequent investigations. It is therefore concluded that little direct evidence exists for carcinogenicity of the vapor phase of DE in laboratory animals at concentrations tested.

7.3.3. Inhalation Studies (DE plus Cocarcinogens)

Details of the studies reported here have been described earlier and in Table 7-3. Tumor initiation with urethan (1 mg/kg body weight i.p. at the start of exposure) or promotion with butylated hydroxytolulene (300 mg/kg body weight i.p. week 1, 83 mg/kg week 2, and 150 mg/kg for weeks 3-52) did not influence tumorigenic responses in Sencar mice of both sexes exposed to concentrations of DE up to 12 mg/m^3 (Pepelko and Peirano, 1983).

Heinrich et al. (1986b) exposed Syrian hamsters of both sexes to DE diluted to a particle concentration of 4 mg/m^3. See Section 7.3.1.1 for details of the exposure conditions. At the start of exposure the hamsters received either one dose of 4.5 mg diethylnitrosamine (DEN) subcutaneously per kg body weight or 20 weekly intratracheal instillations of 250 μg B[*a*]P. Female NMRI mice received weekly intratracheal instillations of 50 or 100 μg B[*a*]P for 10 or 20 weeks, respectively, or 50 μg dibenz[ah]anthracene (DBA) for 10 weeks. Additional groups of 96 newborn mice received one s.c. injection of 5 or 10 μg DBA between 24 and 48 hr after birth. Female Wistar rats received weekly subcutaneous injections of dipentylnitrosamine

(DPN) at doses of 500 and 250 mg/kg body weight, respectively, during the first 25 weeks of exhaust inhalation exposure. Neither DEN, DBA, or DPN treatment enhanced any tumorigenic responses to DE. Response to B[*a*]P did not differ from that of BaP alone in hamsters, but results were inconsistent in mice. Although 20 B[*a*]P instillations induced a 71% tumor incidence in mice, concomitant diesel exposure resulted in only a 41% incidence. However, neither 10 B[*a*]P instillations nor DBA instillations induced significant effects.

Takemoto et al. (1986) exposed Fischer 344 rats for 2 years to DE at particle concentrations of 2 to 4 mg/m^3. One month after start of inhalation exposure one group of rats received di-isopropyl-nitrosamine (DIPN) administered i.p. at 1 mg/kg weekly for 3 weeks. Among injected animals autopsied at 18 to 24 mo, 10 adenomas and 4 adenocarcinomas were reported in 21 animals exposed to clean air, compared with 12 adenomas and 7 adenocarcinomas in 18 diesel-exposed rats. According to the authors, the incidence of adenocarcinomas was not significantly increased by exposure to DE.

Brightwell et al. (1989) investigated the concomitant effects of DE and DEN in Syrian hamsters exposed to DE diluted to produce particle concentrations of 0.7, 2.2, or 6.6 mg/m^3 for 2 years. The animals received a single dose of 4.5 mg DEN s.c. 3 days prior to start of inhalation exposure. DEN did not affect the lack of responsiveness to DE alone. Heinrich et al. (1989b) also exposed Syrian hamsters of both sexes to DE diluted to a particle concentration of 3.75 mg/m^3 for up to 18 mo. After 2 weeks of exposure, groups were treated with either 3 or 6 mg DEN/kg body weight, respectively. Again, DEN did not significantly influence the lack of tumorigenic responses to DE.

Heinrich et al. (1989a) investigated the effects of DPN in female Wistar rats exposed to DE diluted to achieve a particle concentration of 4.24 mg/m^3 for 2-2.5 years. DPN at doses of 250 and 500 mg/kg body weight was injected subcutaneously once a week for the first 25 weeks of exposure. The tumorigenic responses to DPN were not affected by exposure to DE. For details of exposure conditions of the hamster studies see Section 7.3.1.3.

Heinrich et al. (1986a) and Mohr et al. (1986) compared the effects of exposure to particles having only a minimal carbon core but a much greater concentration of PAHs than DPM does. The desired exposure conditions were achieved by mixing coal oven flue gas with pyrolyzed pitch. The concentration of B[a]P and other PAHs per milligram of DPM was about three orders of magnitude greater than that of DE. Female rats were exposed to the flue gas-pyrolyzed pitch for 16 hr/day, 5 days/week at particle concentrations of 3 to 7 mg/m^3 for 22 mo, then held in clean air for up to an additional 12 mo. Among 116 animals exposed, 22 tumors were reported in 21 animals, for an incidence of 18.1%. One was a bronchioloalveolar adenoma, one was a bronchioloalveolar carcinoma, and 20 were squamous cell tumors. Among the latter, 16 were classified as benign keratinizing cystic tumors and 4 were classified as carcinomas. No tumors were reported in 115 controls. The tumor incidence in this study was comparable to that reported previously for the DE-exposed animals.

In analyzing the studies of Heinrich et al. (1986a,b), Heinrich (1990b), Mohr et al. (1986), and Stöber (1986), it must be noted that the incidence of lung tumors occurring following exposure to whole DE, coal oven flue gas, or carbon black (15.8%, 18.1%, and 8% to 17%, respectively) was very similar. This occurred despite the fact that the PAH content of the PAH-enriched pyrolyzed pitch was more than three orders of magnitude greater than that of DE; carbon black, on the other hand, had only traces of PAHs. Based on these findings, particle-associated effects appear to be the primary cause of diesel-exhaust-induced lung cancer in rats exposed at high concentrations. This issue is discussed further in Chapter 7.

7.3.4. Lung Implantation or Intratracheal Instillation Studies

7.3.4.1. *Rat Studies*

Grimmer et al. (1987), using female Osborne Mendel rats (35 per treatment group), provided evidence that PAHs in DE that consist of four or more rings have carcinogenic potential. Condensate was obtained from the whole exhaust of a 3.0-L passenger-car diesel engine connected to a dynamometer operated under simulated city traffic driving conditions. This condensate was separated by liquid-liquid distribution into hydrophilic and hydrophobic fractions representing 25% and 75% of the total condensate, respectively. The hydrophilic, hydrophobic, or reconstituted hydrophobic fractions were surgically implanted into the lungs of the rats. Untreated controls, vehicle (beeswax/trioctanoin) controls, and positive (B[a]P) controls were also included in the protocol (Table 7-6). Fraction IIb (made up of PAHs with four to seven rings), which accounted for only 0.8% of the total weight of DPM condensate, produced the highest incidence of carcinomas following implantation into rat lungs. A carcinoma incidence of 17.1% was observed following implantation of 0.21 mg IIb/rat, whereas the nitro-PAH fraction (IId) at 0.18 mg/rat accounted for only a 2.8% carcinoma incidence. Hydrophilic fractions of the DPM extracts, vehicle (beeswax/trioctanoin) controls, and untreated controls failed to exhibit carcinoma formation. Administration of all hydrophobic fractions (IIa-d) produced a carcinoma incidence (20%) similar to the summed incidence of fraction IIb (17.1%) and IId (2.8%). The B[a]P positive controls (0.03, 0.1, 0.3 mg/rat) yielded a carcinoma incidence of 8.6%, 31.4%, and 77.1%, respectively. The study showed that the tumorigenic agents were primarily four- to seven-ring PAHs and, to a lesser extent, nitroaromatics. However, these studies demonstrated that simultaneous administration of various PAH compounds resulted in a varying of the tumorigenic effect, thereby implying that the tumorigenic potency of PAH mixtures may not depend on any one individual PAH. This study did not provide any information regarding the bioavailability of the particle-associated PAHs that might be responsible for carcinogenicity.

Kawabata et al. (1986) compared the effects of activated carbon and DE on lung tumor formation. One group of 59 F344 rats was intratracheally instilled with DPM (1 mg/week for 10

Table 7-6. Tumor incidence and survival time of rats treated by surgical lung implantation with fractions from DE condensate (35 rats/group)

Material portion by weight (%)	Dose (mg)	Median survival time in weeks (range)	Number of carcinomas[a]	Number of adenomas[b]	Carcinoma incidence (%)
Hydrophilic fraction (I) (25)	6.7	97 (24-139)	0	1	0
Hydrophobic fraction (II) (75)	20.00	99 (50-139)	50601	1000	14.2
Nonaromatics +					
PAC[c] 2 + 3 rings (IIa) (72)	19.22	103 (25-140)			0
PAH[d] 4 to 7 rings (IIb) (0.8)	0.21	102 (50-140)			17.1
Polar PAC (IIc) (1.1)	0.29	97 (44-138)			0
Nitro-PAH (IId) (0.7)	0.19	106 (32-135)			2.8
Reconstituted hydrophobics (Ia, b, c, d) (74.5)	19.91	93 (46-136)	70027113	101000	20.0
Control, unrelated		110 (23-138)			0
Control (beeswax/trioctanoin)		103 (51-136)			0
B[*a*]P	0.3	69 (41-135)			77.1
	0.1	98 (22-134)			31.4
	0.03	97 (32-135)			8.6

[a]Squamous cell carcinoma.

[b]Bronchiolar/alveolar adenoma.
[c]PAC = polycyclic aromatic compounds.
[d]PAH = polycyclic aromatic hydrocarbons.

Source: Adapted from Grimmer et al., 1987.

weeks). A second group of 31 rats was instilled with activated carbon using the same dosing regime. Twenty-seven rats received only the solvent (buffered saline with 0.05% Tween 80), and 53 rats were uninjected. Rats dying after 18 months were autopsied. All animals surviving 30 months or more postinstillation were sacrificed and evaluated for histopathology. Among 42 animals exposed to DPM surviving 18 months or more, tumors were reported in 31, including 20 malignancies. In the subgroup surviving for 30 mo, tumors were detected in 19 of 20 animals, including 10 malignancies. Among the rats exposed to activated carbon, the incidence of lung tumors equaled 11 of 23 autopsied, with 7 cases of malignancy. Data for those dying between 18 and 30 months and those sacrificed at 30 months were not reported separately. Statistical analysis indicated that activated carbon induced a significant increase in lung tumor incidence compared with no tumors in 50 uninjected controls and 1 tumor in 23 solvent-injected controls. The tumor incidence was significantly greater in the DPM-instilled group and was significantly greater than the increase in the carbon-instilled group.

A study reported by Rittinghausen et al. (1997) suggested that organic constituents of diesel particles play a role in the induction of lung tumors in rats. An incidence of 16.7% pulmonary cystic keratinizing squamous cell lesions was noted in rats intratracheally instilled with 15 mg whole DE particles, compared with 2.1% in rats instilled with 15 mg particles extracted to remove all organic constituents, and none among controls. Instillation of 30 mg of extracted particles induced a 14.6% incidence of squamous lesions, indicating the greater effectiveness of particles alone as lung particle overload increased.

Iwai et al. (1997) instilled 2, 4, 8, and 10 mg of whole diesel particles over a 2- to 10-week period into female F/344 rats, 50 or more per group. Tumors were reported in 6%, 20%, 43%, and 74% of the rats, with incidence of malignant tumors equal to 2%, 13%, 34%, and 48%, respectively. In a second experiment comparing whole with extracted diesel particles, tumor incidence equaled 1/48 (2%) in uninjected controls, 3/55 (5%) in solvent controls, 12/56 (21%) in extracted diesel particles, and 13/106 (12%) in animals injected with unextracted particles. Although the extracted particles appeared to be more potent, when converted to a lung burden basis (mg/100 mg dry lung) the incidence was only 14% among those exposed to extracted exhaust compared with 31% in those exposed to whole particles.

Dasenbrock et al. (1996) conducted a study to determine the relative importance of the organic constituents of diesel particles and particle surface area in the induction of lung cancer in rats. Fifty-two female Wistar rats were intratracheally instilled with 16-17 doses of DPM, extracted DPM, printex carbon black (PR), lampblack (LB), B[*a*]P, DPM + B[*a*]P, or PR + B[*a*]P. The animals were held for a lifetime or sacrificed when moribund. The lungs were necropsied and examined for tumors. Diesel particles were collected from a Volkswagen 1.6-L engine operating on a US FTP-72 driving cycle. The mass median aerodynamic diameter (MMAD) of the diesel particles was 0.25 μm and the specific surface area was 12 m^2/gm.

Following extraction with toluene, specific surface area increased to 138 m^2/gm. The MMAD for extracted PR was equal to 14 nm, while the specific surface area equaled 271 m^2/gm. The MMAD for extracted lampblack was equal to 95 nm, with a specific surface area equal to 20 m^2/gm. The B[*a*]P content of the treated particles was 11.3 mg per gm diesel particles and 29.5 mg B[*a*]P per gm PR. Significant increases in lung tumors were detected in rats instilled with 15 mg unextracted DPM and 30 mg extracted DPM, but not 15 mg extracted DPM. Printex CB was more potent than lampblack CB for induction of lung tumors, whereas B[*a*]P was effective only at high doses. Total dose and tumor responses are shown in Table 7-4.

A number of conclusions can be drawn from these results. First of all, particles devoid of organics are capable of inducing lung tumor formation, as indicated by positive results in the groups treated with high-dose extracted diesel particles and printex. Nevertheless, toluene extraction of organics from diesel particles results in a decrease in potency, indicating that the organic fraction does play a role in cancer induction. A relationship between cancer potency and particle surface area was also suggested by the finding that printex with a large specific surface area was more potent than either extracted DPM or lampblack, which have smaller specific areas. Finally, while very large doses of B[*a*]P are very effective in the induction of lung tumors, smaller doses adsorbed to particle surfaces had little detectable effect, suggesting that other organic components of DE may be of greater importance in the induction of lung tumors at low doses pf B[*a*]P (0.2-0.4 mg).

7.3.4.2. *Syrian Hamster Studies*

Kunitake et al. (1986) and Ishinishi et al. (1988b) conducted a study in which total doses of 1.5, 7.5, or 15 mg of a dichloromethane extract of DPM were instilled intratracheally over 15 weeks into male Syrian hamsters that were then held for their lifetimes. The tumor incidences of 2.3% (1/44), 0% (0/56), and 1.7% (1/59) for the high-, medium-, and low-dose groups, respectively, did not differ significantly from the 1.7% (1/56) reported for controls. Addition of 7.5 mg of B[a]P to a DPM extract dose of 1.5 mg resulted in a total tumor incidence of 91.2% and malignant tumor incidence of 88%. B[a]P (7.5 mg over 15 weeks) alone produced a tumor incidence rate of 88.2% (85% of these being malignant), which was not significantly different from the DPM extract + B[a]P group. Intratracheal administration of 0.03 μg B[a]P, the equivalent content in 15 mg of DPM extract, failed to cause a significant increase in tumors in rats. This study demonstrated a lack of detectable interaction between DPM extract and B[a]P, the failure of DPM extract to induce carcinogenesis, and the propensity for respiratory tract carcinogenesis following intratracheal instillation of high doses of B[a]P. For studies using the DPM extract, some concern must be registered regarding the known differences in chemical composition between DPM extract and DPM. As with all intratracheal instillation protocols, DPM extract lacks the complement of volatile chemicals found in whole DE.

The effects on hamsters of intratracheally instilled DPM suspension, DPM with Fe_2O_3, or DPM extract with Fe_2O_3 as the carrier were studied by Shefner et al. (1982). The DPM component in each of the treatments was administered at concentrations of 1.25, 2.5, or 5.0 mg/week for 15 weeks to groups of 50 male Syrian golden hamsters. The total volume instilled was 3.0 mL (0.2 mL/week for 15 weeks). The DPM and dichloromethane extracts were suspended in physiological saline with gelatin (0.5% w/v), gum arabic (0.5% w/v), and propylene glycol (10% by volume). The Fe_2O_3 concentration, when used, was 1.25 mg/0.2 mL of suspension. Controls received vehicle and, where appropriate, carrier particles (Fe_2O_3) without the DPM component. Two replicates of the experiments were performed. Adenomatous hyperplasia was reported to be most severe in those animals treated with DPM or DPM plus Fe_2O_3 particles and least severe in those animals receiving DPM plus Fe_2O_3. Of the two lung adenomas detected microscopically, one was in an animal treated with a high dose of DPM and the other was in an animal receiving a high dose of DPM extract. Although lung damage was increased by instillation of DPM, there was no evidence of tumorigenicity.

7.3.4.3. *Mouse Studies*

Ichinose et al. (1997a) intratracheally instilled 36 four-week-old male ICR mice per group weekly for 10 weeks with sterile saline or 0.05, 0.1, or 0.2 mg DPM. Particles were collected from a 2.74-L four-cylinder Isuzu engine run at a steady speed of 1,500 rpm under a load of 10 torque (kg/m). Twenty-four hours after the last instillation, six animals per group were sacrificed for measurement of lung 8-hydroxydeoxyguanosine (8-OHdG). The remaining animals were sacrificed after 12 months for histopathological analysis. Lung tumor incidence varied from 4/30 (13.3%) for controls to 9/30 (30%), 9/29 (31%), and 7/29 (24.1%) for mice instilled with 0.05, 0.1, and 0.2 mg/week, respectively. The increase in animals with lung tumors compared with controls was statistically significant for the 0.1 mg dose group, the only group analyzed statistically. Increases in 8-OHdG, an indicator of oxidative DNA damage, correlated well with the increase in tumor incidence in the 0.05 mg dose group, although less so with the other two. The correlation coefficients $r = 0.916$, 0.765, and 0.677 for the 0.05, 0.10, and 0.20 mg DPM groups, respectively.

In a similar study, 33 four-week-old male ICR mice per group were intratracheally instilled weekly for 10 weeks with sterile saline, 0.1 mg DPM, or 0.1 mg DPM from which the organic constituents were extracted with hexane (Ichinose et al., 1997b). Exhaust was collected from a 2.74-L four-cylinder Izuzu engine run at a steady speed of 2,000 rpm under a load of 6 torque (kg/m). Twenty-four hours after the last instillation, six animals per group were sacrificed for measurement of 8-OHdG. Surviving animals were sacrificed after 12 mo. The incidence of lung tumors increased from 3/27 (11.1%) among controls to 7/27 (25.9%) among those instilled with extracted diesel particles and 9/26 (34.6%) among those instilled with

unextracted particles. The increase in number of tumor-bearing animals was statistically significant compared with controls ($p<0.05$) for the group treated with unextracted particles. The increase in 8-OHdG was highly correlated with lung tumor incidence, r = 0.99.

7.3.5. Subcutaneous and Intraperitoneal Injection Studies

7.3.5.1. *Mouse Studies*

In addition to inhalation studies, Orthoefer et al. (1981) also tested the effects of i.p. injections of DPM on male (A/S) strain mice. Three groups of 30 mice were injected with 0.1 mL of a suspension (particles in distilled water) containing 47, 117, or 235 μg of DPM collected from Fluoropore filters in the inhalation exposure chambers. The exposure system and exposure atmosphere are described in Appendix A. Vehicle controls received injections of particle suspension made up of particulate matter from control exposure filters, positive controls received 20 mg of urethan, and negative controls received no injections. Injections were made three times weekly for 8 weeks, resulting in a total DPM dose of 1.1, 2.8, and 5.6 mg for the low-, medium-, and high-dose groups and 20 mg of urethan for the positive control group. These animals were sacrificed after 26 weeks and examined for lung tumors. For the low-, medium-, and high-dose DPM groups, the tumor incidence was 2/30, 10/30, and 8/30, respectively. The incidence among urethan-treated animals (positive controls) was 100% (29/29), with multiple tumors per animal. The tumor incidence for the DPM-treated animals did not differ significantly from that of vehicle controls (8/30) or negative controls (7/28). The number of tumors per mouse was also unaffected by treatment.

In further studies conducted by Orthoefer et al. (1981), an attempt was made to compare the potency of DPM with that of other environmental pollutants. Male and female Strain A mice were injected i.p. three times weekly for 8 weeks with DPM, DPM extracts, or various environmental mixtures of known carcinogenicity, including cigarette smoke condensate, coke oven emissions, and roofing tar emissions. Injection of urethan or dimethylsulfoxide (DMSO) served as positive or vehicle controls, respectively. In addition to DPM from the Nissan diesel previously described, an eight-cylinder Oldsmobile engine operated at the equivalent of 40 mph was also used to compare emission effects from different makes and models of diesel engine. The mice were sacrificed at 9 months of age and their lungs examined for histopathological changes. The only significant findings, other than for positive controls, were small increases in numbers of lung adenomas per mouse in male mice injected with Nissan DPM and in female mice injected with coke oven extract. Furthermore, the increase in the extract-treated mice was significant only in comparison with uninjected controls (not injected ones) and did not occur when the experiment was repeated. Despite the use of a strain of mouse known to be sensitive to tumor induction, the overall findings of this study were negative. The authors provided several possible explanations for these findings, the most likely of which were (1) the carcinogens that

were present were very weak, or (2) the concentrations of the active components reaching the lungs were insufficient to produce positive results.

Kunitake et al. (1986) conducted studies using DPM extract obtained from a 1983 HD MMC—6D22P 11-L V-6 engine. Five s.c. injections of DPM extract (500 mg/kg per injection) resulted in a significant ($p<0.01$) increase in subcutaneous tumors for female C57BL mice (5/22 [22.7%] vs. 0/38 among controls). Five s.c. doses of DPM extract of 10, 25, 30, 100, or 200 mg/kg failed to produce a significant increase in tumor incidence. One of 12 female ICR mice (8.3%) and 4 of 12 male ICR mice (33.3%) developed malignant lymphomas following neonatal s.c. administration of 10 mg of DPM extract per mouse. The increase in malignant lymphoma incidence for the male mice was statistically significant at $p<0.05$ compared with an incidence of 2/14 (14.3%) among controls. Treatment of either sex with 2.5 or 5 mg of DPM extract per mouse did not result in statistically significant increases in tumor incidence.

Additional studies using DPM extract from LD (1.8-L, 4-cylinder) as well as HD engines with female ICR and nude mice (BALB/c/cA/JCL-nu) were also reported (Kunitake et al., 1988). Groups of 30 ICR and nude mice each were given a single s.c. injection of 10 mg HD extract, 10 mg HD + 50 μg 12-O-tetradecanoylphorbol 13-acetate (TPA), 10 mg LD extract + 50 μg TPA, or 50 μg TPA. No malignant tumors or papillomas were observed. One papillomatous lesion was observed in an ICR mouse receiving LD extract + TPA, and acanthosis was observed in one nude mouse receiving only TPA.

In what appears to be an extension of the Kunitake et al. (1986) s.c. injection studies, Takemoto et al. (1988) presented additional data for subcutaneously administered DPM extract from HD and LD diesel engines. In this report, the extracts were administered to 5-week-old and neonatal (<24 hr old) C57BL mice of both sexes. DPM extract from HD or LD engines was administered weekly to the 5-week-old mice for 5 weeks at doses of 10, 25, 50, 100, 200, or 500 mg/kg, with group sizes ranging from 15 to 54 animals. After 20 weeks, comparison with a control group indicated a significant increase in the incidence of subcutaneous tumors for the 500 mg/kg HD group (5 of 22 mice [22.7%], $p<0.01$), the 100 mg/kg LD group (6 of 32 [18.8%],
$p<0.01$), and the 500 mg/kg LD group (7 of 32 [21.9%], $p<0.01$) in the adult mouse experiments. The tumors were characterized as malignant fibrous histiocytomas. No tumors were observed in other organs. The neonates were given single doses of 2.5, 5, or 10 mg DPM extract subcutaneously within 24 hr of birth. There was a significantly higher incidence of malignant lymphomas in males receiving 10 mg of HD extract and of lung tumors for males given 2.5 mg HD extract and for males given 5 mg and females given 10 mg LD extract. A dose-related trend that was not significant was observed for the incidences of liver tumors for both the HD extract- and LD extract-treated neonatal mice. The incidence of mammary tumors in female mice and multiple-organ tumors in male mice was also greater for some extract-treated

mice, but was not dose related. The report concluded that LD DPM extract showed greater carcinogenicity than did HD DPM extract.

7.3.6. Dermal Studies

7.3.6.1. *Mouse Studies*

In one of the earliest studies of diesel emissions, the effects of dermal application of extract from DPM were examined by Kotin et al. (1955). Acetone extracts were prepared from the DPM of a diesel engine (type and size not provided) operated at warmup mode and under load. These extracts were applied dermally three times weekly to male and female C57BL and strain A mice. Results of these experiments are summarized in Table 7-5. In the initial experiments using 52 (12 male, 40 female) C57BL mice treated with DPM extract from an engine operated in warmup mode, two papillomas were detected after 13 mo. Four tumors were detected 16 months after the start of treatment in 8 surviving of 50 exposed male strain A mice treated with DPM extract from an engine operated under full load. Among female strain A mice treated with DPM extract from an engine operated under full load, 17 tumors were detected in 20 of 25 mice surviving longer than 13 mo. This provided a significantly increased tumor incidence of 85%. Carcinomas as well as papillomas were seen, but the numbers were not reported.

Depass et al. (1982) examined the potential of DPM and dichloromethane extracts of DPM to act as complete carcinogens, carcinogen initiators, or carcinogen promoters. In skin-painting studies, the DPM was obtained from an Oldsmobile 5.7-L diesel engine operated under constant load at 65 km/h. The DPM was collected at a temperature of 100°C. Groups of 40 C3H/HeJ mice were used because of their low spontaneous tumor incidence. For the complete carcinogenesis experiments, DPM was applied as a 5% or 10% suspension in acetone. Dichloromethane extract was applied as 5%, 10%, 25%, or 50% suspensions. Negative controls received acetone, and positive controls received 0.2% B[a]P. For tumor-promotion experiments, a single application of 1.5% B[a]P was followed by repeated applications of 10% DPM suspension, 50% DPM extract, acetone only (vehicle control), 0.0001% phorbol 12-myristate 13-acetate (PMA) as a positive promoter control, or no treatment (negative control). For the tumor-initiation studies, a single initiating dose of 10% diesel particle suspension, 50% diesel particle extract, acetone, or PMA was followed by repeated applications of 0.0001% PMA. Following 8 months of treatment, the PMA dose in the initiation and promotion studies was increased to 0.01%. Animals were treated three times per week in the complete carcinogenesis and initiation experiments and five times per week in promotion experiments. All test compounds were applied to a shaved area on the back of the mouse.

In the complete carcinogenesis experiments, one mouse receiving the high-dose (50%) suspension of extract developed a squamous cell carcinoma after 714 days of treatment. Tumor

incidence in the B[a]P group was 100%, and no tumors were observed in any of the other groups. For the promotion studies, squamous cell carcinomas with pulmonary metastases were identified in one mouse of the 50% DPM extract group and in one in the 25% extract group. Another mouse in the 25% extract group developed a grossly diagnosed papilloma. Nineteen positive control mice had tumors (11 papillomas, 8 carcinomas). No tumors were observed for any of the other treatment groups. For the initiation studies, three tumors (two papillomas and one carcinoma) were identified in the group receiving DPM suspension and three tumors (two papillomas and one fibrosarcoma) were found in the DPM extract group. These findings were reported to be statistically insignificant using the Breslow and Mantel-Cox tests.

Although these findings were not consistent with those of Kotin et al. (1955), the occurrence of a single carcinoma in a strain known to have an extremely low spontaneous tumor incidence may be of importance. Furthermore, a comparison between studies employing different strains of mice with varying spontaneous tumor incidences may result in erroneous assumptions.

Nesnow et al. (1982) studied the formation of dermal papillomas and carcinomas following dermal application of dichloromethane extracts from coke oven emissions, roofing tar, DPM, and gasoline engine exhaust. DPM from five different engines, including a preproduction Nissan 220C, a 5.7-L Oldsmobile, a prototype Volkswagen Turbo Rabbit, a Mercedes 300D, and a HD Caterpillar 3304, was used for various phases of the study. Male and female Sencar mice (40 per group) were used for tumor initiation, tumor promotion, and complete carcinogenesis studies. For the tumor-initiation experiments, the DPM extracts were topically applied in single doses of 100, 500, 1,000, or 2,000 μg/mouse. The high dose (10,000 μg/mouse) was applied in five daily doses of 2,000 μg. One week later, 2 μg of the tumor promoter TPA was applied topically twice weekly. The tumor-promotion experiments used mice treated with 50.5 μg of B[a]P followed by weekly (twice weekly for high dose) topical applications (at the aforementioned doses) of the extracts. For the complete carcinogenesis experiments, the test extracts were applied weekly (twice weekly for the high doses) for 50 to 52 weeks. Only extracts from the Nissan, Oldsmobile, and Caterpillar engines were used in the complete carcinogenesis experiments.

In the tumor-initiation studies, both B[a]P alone and the Nissan engine DPM extract followed by TPA treatment produced a significant increase in tumor (dermal papillomas) incidence at 7 to 8 weeks postapplication. By 15 weeks, the tumor incidence was greater than 90% for both groups. No significant carcinoma formation was noted for mice in the tumor-initiation experiments following exposure to DPM extracts of the other diesel engines, although the Oldsmobile engine DPM extract at 2.0 mg/mouse did produce a 40% papilloma incidence in male mice at 6 mo. This effect, however, was not dose dependent.

B[a]P (50.5 μg/week), coke oven extract (at 1.0, 2.0, or 4.0 mg/week), and the highest dose of roofing tar extract (4.0 mg/week) all tested positive for complete carcinogenesis activity. DPM extracts from only the Nissan, Oldsmobile, and Caterpillar engines were tested for complete carcinogenic potential, and all three proved to be negative using the Sencar mouse assay.

The results of the dermal application experiments by Nesnow et al. (1982) are presented in Table 7-7. The tumor initiation-promotion assay was considered positive if a dose-dependent response was obtained and if at least two doses provided a papilloma-per-mouse value that was three times or greater than that of the background value. Based on these criteria, only emissions from the Nissan were considered positive. Tumor initiation and complete carcinogenesis assays required that at least one dose produce a tumor incidence of at least 20%. None of the DPM samples yielded positive results based on this criterion.

Kunitake et al. (1986, 1988) evaluated the effects of a dichloromethane extract of DPM obtained from a 1983 MMC M-6D22P 11-L V-6 engine. An acetone solution was applied in 10 doses every other day, followed by promotion with 2.5 μg of TPA three times weekly for 25 weeks. Exposure groups received a total dose of 0.5, 5, 15, or 45 mg of extract. Papillomas were reported in 2 of 50 animals examined in the 45 mg exposure group and in 1 of 48 in the 15 mg group compared with 0 of 50 among controls. Differences, however, were not statistically significant.

7.3.7. Summary and Conclusions of Laboratory Animal Carcinogenicity Studies

As early as 1955, Kotin et al. (1955) provided evidence for tumorigenicity and carcinogenicity of acetone extracts of DPM following dermal application and also provided data suggesting a difference in this potential depending on engine operating mode. Until the early 1980s, no chronic studies assessing inhalation of DE, the relevant mode for human exposure, had been reported. Since then long-term inhalation bioassays with DE have been carried out in the United States, Germany, Switzerland, and Japan, testing responses of rats, mice, and Syrian hamsters, and to a limited extent cats and monkeys.

Table 7-7. Dermal tumorigenic and carcinogenic effects of various emission extracts

	Tumor initiation		Complete carcinogenesis	Tumor promotion
Sample	**Papillomas[a]**	**Carcinomas[b]**	**Carcinomas[b]**	**Papillomas[a]**
Benzo[*a*]pyrene	+/+[c]	+/+	+/+	+/+
Topside coke oven	+/+	-/+	ND[d]	ND
Coke oven main	+/+	+/+	+/+	+/+
Roofing tar	+/+	+/+	+/+	+/+
Nissan	+/+	+/+	-/-	ND
Oldsmobile	+/+	-/-	-/-	ND
VW Rabbit	+/+	-/-	I[e]	ND
Mercedes	+/-	-/-	ND	ND
Caterpillar	-/-	-/-	-/-	ND
Residential furnace	-/-	-/-	ND	ND
Mustang	+/+	-/+	ND	ND

[a]Scored at 6 mo.

[b]Cumulative score at 1 year.

[c]Male/female.

[d]ND = Not determined.

[e]I = Incomplete.

Source: Nesnow et al., 1982.

It can be reasonably concluded that with adequate exposure, inhalation of DE is capable of inducing lung cancer in rats. Responses best fit cumulative exposure (concentration × daily exposure duration × days of exposure). Examination of rat data shown in Table 7-8 indicates a trend of increasing tumor incidence at exposures exceeding 1×10^4 mg·hr/m^3. Exposures greater than approximately this value result in lung particle overload, characterized by slowed particle clearance and lung pathology, as discussed in Chapters 3 and 5, respectively. Tumor induction at high doses may therefore be primarily the result of lung particle overload with associated inflammatory responses. Although tumorigenic responses could not be detected under non-particle-overload conditions, the animal experiments lack sensitivity to determine if a threshold exists. However, studies such as those reported by Driscoll et al. (1996) support the existence of a threshold if it is assumed that inflammation is a prerequisite for lung tumor induction. If low-dose effects do occur, it can be hypothesized that the organic constituents are playing a role. See Chapter 7 for a discussion of this issue.

Although rats develop adenomas, adenocarcinomas, and adenosquamous cell carcinomas, they also develop squamous keratinizing lesions. This latter spectrum appears for the most part to be peculiar to the rat. In a recent workshop aimed at classifying these tumors (Boorman et al., 1996), it was concluded that when these lesions occur in rats as part of a carcinogenicity study, they must be evaluated on a case-by-case basis and regarded as a part of the total biologic profile of the test article. If the only evidence of tumorigenicity is the presence of cystic keratinizing epitheliomas, it may not have relevance to human safety evaluation of a substance or particle. Their use in quantifying cancer potency is even more questionable.

The evidence for response of common strains of laboratory mice exposed under standard inhalation protocols is equivocal. Inhalation of DE induced significant increases in lung tumors in female NMRI mice (Heinrich et al., 1986b; Stöber, 1986) and in female Sencar mice (Pepelko and Peirano, 1983). An apparent increase was also seen in female C57BL mice (Takemoto et al., 1986). However, in a repeat of their earlier study, Heinrich et al. (1995) failed to detect lung tumor induction in either NMRI or C57BL/6N mice. No increases in lung tumor rates were reported in a series of inhalation studies using strain A mice (Orthoefer et al., 1981; Kaplan et al., 1982, 1983; White et al., 1983). Finally, Mauderly et al. (1996) reported no tumorigenic responses in CD-1 mice exposed under conditions resulting in positive responses in rats. The successful induction of lung tumors in mice by Ichinose et al. (1997a,b) via intratracheal instillation may have been the result of focal deposition of larger doses. Positive effects in Sencar mice may be due to use of a strain sensitive to tumor induction in epidermal tissue by organic agents, as well as exposure from conception, although proof for such a hypothesis is lacking.

Table 7-8. Cumulative (concentration × time) exposure data for rats exposed to whole DE

Study	Exposure rate/duration (hr/week, mo)	Total exposure time (hr)	Particle concentration (mg/m^3)	Cumulative exposure ($mg \cdot hr/m^3$) Per week	Cumulative exposure ($mg \cdot hr/m^3$) Total	Tumor incidence (%)[a]
Mauderly et al. (1987)	35, 30	4.20042004e+15	0	0	14701470029820	0.9
	35, 30		0.35	12.25		1.3
	35, 30		3.5	122.5		3.6
	35, 30		7.1	248.5		12.8
Nikula et al. (1995)	80, 23	736073607360	0	0	1840047840	1.0
	80, 23		2.5	200.0		7.0
	80, 23		6.5	520.0		18.0
Heinrich et al. (1986a)	95, 35	1330013300	4.24	402.8	56392	17.8
	95, 35					
Heinrich et al. (1995)	90, 24	8.64086409e+15	0	0	74002180061700	0
	90, 24		0.8	72.0		0
	90, 24		2.5	225.0		5.5
	90, 24		7.0	630.0		22.0
Ishinishi et al. (1988a)	96, 30	1.15201152e+49	0	0	1.1524	3.3
(Light-duty engine)	96, 30		0.1	9.6	60813e+37	2.4
	96, 30		0.4	38.4		0.8
	96, 30		1.1	105.6		4.1
(Heavy-duty engine)	96, 30		2.3	220.8		2.4
	96, 30		0	0		0.8
	96, 30		0.5	48.0		0.8
	96, 30		1.0	96.0		0
	96, 30		1.8	172.8		3.3
	96, 30		3.7	355.2		6.5

Table 7-8. Cumulative (concentration × time) exposure data for rats exposed to whole DE (continued)

Study	Exposure rate/duration (hr/week, mo)	Total exposure time (hr)	Particle concentration (mg/m^3)	Cumulative exposure ($mg \cdot hr/m^3$) Per week	Cumulative exposure ($mg \cdot hr/m^3$) Total	Tumor incidence (%)[a]
Brightwell et al. (1989)	80, 24	7.6807681e+15	0	0	53761689650688	1.2
	80, 24		0.7	56.0		0.7
	80, 24		2.2	176.0		9.7
	80, 24		6.6	528.0		38.5
Kaplan et al. (1983)	140, 15	8.4008401e+15	0	0	2100630012600	0
	140, 15		0.25	35.0		3.3
	140, 15		0.75	105.0		10.0
	140, 15		1.5	210.0		3.3
Iwai et al. (1986b)	56, 24	53765376	4.9	274.4	26342	36.8
	56, 24					
Takemoto et al. (1986)	16, 18-24	1,152-1,536	0	0	0	0
	16, 18-24	1,152-1,536	2-4	32-64	3,456-4,608	
Karagianes et al. (1981)	30, 20	24002400	8.3	249	19920	16.6
	30, 20					
Iwai et al. (1997)	56, 24	537649925616	9.4	526154275	5.47041597e+14	421242
	48, 24		3.2			
	54, 24		5.1			

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Attempts to induce significant increases in lung tumors in Syrian hamsters by inhalation of whole DE were unsuccessful (Heinrich et al., 1982, 1986b, 1989b; Brightwell et al., 1986). However, hamsters are considered to be relatively insensitive to lung tumor induction. For example, while cigarette smoke, a known human carcinogen, was shown to induce laryngeal cancer in hamsters, the lungs were relatively unaffected (Dontenwill et al., 1973).

Neither cats (Pepelko and Peirano, 1983 [see Chapter 7]) nor monkeys (Lewis et al., 1989) developed tumors following 2-year exposure to DE. The duration of these exposures, however, was likely to be inadequate for these two longer-lived species, and group sizes were quite small. Exposure levels were also below the maximum tolerated dose (MTD) in the monkey studies and, in fact, only borderline for detection of lung tumor increases in rats.

Long-term exposure to DE filtered to remove particulate matter failed to induce lung tumors in rats (Heinrich et al., 1986b; Iwai et al., 1986b; Brightwell et al., 1989), or in Syrian hamsters (Heinrich et al., 1986b; Brightwell, 1989). A significant increase in lung carcinomas was reported by Heinrich et al. (1986b) in NMRI mice exposed to filtered exhaust. However, in a more recent study the authors were unable to confirm earlier results in either NMRI or C57BL/6N mice (Heinrich et al., 1995). Although filtered exhaust appeared to potentiate the carcinogenic effects of DEN (Heinrich et al., 1982), because of the lack of positive data in rats and equivocal or negative data in mice it can be concluded that filtered exhaust is either not carcinogenic or has a low cancer potency.

Kawabata et al. (1986) demonstrated the induction of lung tumors in Fischer 344 rats following intratracheal instillation of DPM. Rittinghausen et al. (1997) reported an increase in cystic keratinizing epitheliomas following intratracheal instillation of rats with either original DPM or DPM extracted to remove the organic fraction, with the unextracted particles inducing a slightly greater effect. Grimmer et al. (1987) showed not only that an extract of DPM was carcinogenic when instilled in the lungs of rats, but also that most of the carcinogenicity resided in the portion containing PAHs with four to seven rings. Intratracheal instillation did not induce lung tumors in Syrian hamsters (Kunitake et al., 1986; Ishinishi et al., 1988b).

Dermal exposure and s.c. injection in mice provided additional evidence for tumorigenic effects of DPM. Particle extracts applied dermally to mice have been shown to induce significant skin tumor increases in two studies (Kotin et al., 1955; Nesnow et al., 1982). Kunitake et al. (1986) also reported a marginally significant increase in skin papillomas in ICR mice treated with an organic extract from an HD diesel engine. Negative results were reported by Depass et al. (1982) for skin-painting studies using mice and acetone extracts of DPM suspensions. However, in this study the exhaust particles were collected at temperatures of 100 °C, which would minimize the condensation of vapor-phase organics and, therefore, reduce the availability of potentially carcinogenic compounds that might normally be present on DE particles. A significant increase in the incidence of sarcomas in female C57Bl mice was reported by Kunitake et al. (1986) following s.c. administration of LD DPM extract at doses of

500 mg/kg. Takemoto et al. (1988) provided additional data for this study and reported an increased tumor incidence in the mice following injection of LD engine DPM extract at doses of 100 and 500 mg/kg. Results of i.p. injection of DPM or DPM extracts in strain A mice were generally negative (Orthoefer et al., 1981; Pepelko and Peirano, 1983), suggesting that the strain A mouse may not be a good model for testing diesel emissions.

Results of experiments using tumor initiators such as DEN, B[a]P, DPN, or DBA (Brightwell et al., 1986; Heinrich et al., 1986b; Takemoto et al., 1986) were generally inconclusive regarding the tumor-promoting potential of either filtered or whole DE. A report by Heinrich et al. (1982), however, indicated that filtered exhaust may promote the tumor-initiating effects of DEN in hamsters.

Several reports (Wong et al., 1985; Bond et al., 1990) affirm observations of the potential carcinogenicity of DE by providing evidence for DNA damage in rats. These findings are discussed in more detail in Chapter 3, Section 3.6. Evidence for the mutagenicity of organic agents present in diesel engine emissions is also provided in Chapter 4.

Evidence for the importance of the carbon core was initially provided by studies of Kawabata et al. (1986), which showed induction of lung tumors following intratracheal instillation of carbon black that contained no more than traces of organics, and studies of Heinrich (1990b) that indicated that exposure via inhalation to carbon black (Printex 90) particles induced lung tumors at concentrations similar to those effective in DPM studies. Additional studies by Heinrich et al. (1995) and Nikula et al. (1995) confirmed the capability of carbon particles to induce lung tumors. Induction of lung tumors by other particles of low solubility, such as titanium dioxide (Lee et al., 1986), confirmed the capability of particles to induce lung tumors. Pyrolyzed pitch, on the other hand, essentially lacking a carbon core but having much higher PAH concentrations than DPM, also was effective in tumor induction (Heinrich et al., 1986a, 1994).

The relative importance of the adsorbed organics, however, remains to be elucidated and is of some concern because of the known carcinogenic capacity of some of these chemicals. These include polycyclic aromatics as well as nitroaromatics, as described in Chapter 2. Organic extracts of particles also have been shown to induce tumors in a variety of injection, intratracheal instillation, and skin-painting studies, and Grimmer et al. (1987) have, in fact, shown that the great majority of the carcinogenic potential following instillation resided in the fraction containing four- to seven-ring PAHs.

In summary, based on positive inhalation studies in rats exposed to high concentrations, intratracheal instillation studies in rats and mice exposed to high doses, and supported by positive mutagenicity studies, the evidence for carcinogenicity of DE is considered to be adequate in animals. The contribution of the various fractions of DE to the carcinogenic response is less certain. Exposure to filtered exhaust generally failed to induce lung tumors. The presence of known carcinogens adsorbed to diesel particles and the demonstrated

tumorigenicity of particle extracts in a variety of injection, instillation, and skin-painting studies indicate a carcinogenic potential for the organic fraction. Studies showing that long-term exposure at high concentrations of poorly soluble particles (e.g., carbon black, TiO_2) can also induce tumors, on the other hand, have provided definitive evidence that the carbon core of the diesel particle is primarily instrumental in the carcinogenic response observed in rats under sufficient exposure conditions. The ability of DE to induce lung tumors at non-particle-overload conditions, and the relative contribution of the particles' core versus the particle-associated organics (if effects do occur at low doses) remains to be determined.

7.4. MODE OF ACTION OF DIESEL EXHAUST-INDUCED CARCINOGENESIS

As noted in Chapter 2, DE is a complex mixture that includes a vapor phase and a particle phase. The particle phase consists of an insoluble carbon core with a large number of organic compounds, as well as inorganic compounds such as sulfates, adsorbed to the particle surface. Some of the semivolatile and particle-associated compounds, in particular PAHs, nitro-PAHs, oxy-PAHs, and oxy-nitro-PAHs (Scheepers and Bos, 1992), are considered likely to be carcinogenic in humans. The vapor phase also contains a large number of organic compounds, including several known or probable carcinogens such as benzene and 1,3-butadiene. Because exposure to the vapor phase alone, even at high concentrations, failed to induce lung cancer in laboratory animals (Heinrich et al., 1986b), the mode-of-action discussion will focus on the particulate matter phase. Additive or synergistic effects of vapor-phase components, however, cannot be ruled out, as chronic inhalation bioassays involving exposure to diesel particles alone have not been carried out.

Several hypotheses regarding the primary mode of action of DE have been proposed. Initially it was generally believed that cancer was induced by particle-associated organics acting via a genotoxic mechanism. By the late 1980s, however, studies indicated that carbon particles virtually devoid of organics could also induce lung cancer at sufficient inhaled concentrations (Heinrich, 1990b). This finding provided support for a hypothesis originally proposed by Vostal (1986) that induction of lung tumors arising in rats exposed to high concentrations of DE is related to overloading of normal lung clearance mechanisms, accumulation of particles, and cell damage followed by regenerative cell proliferation. The action of particles is therefore mediated by epigenetic mechanisms that can be characterized more by promotional than initiation stages of the carcinogenic process. More recently several studies have focused upon the production of reactive oxygen species generated from particle-associated organics, which may induce oxidative DNA damage at exposure concentrations lower than those required to produce lung particle overload. Because it is likely that more than one of these factors is involved in the carcinogenic process, a key consideration is their likely relative contribution at different exposure levels. The following discussion will therefore consider the possible relationship of the organic components of exhaust, inflammatory responses associated with lung particle overload, reactive oxygen

species, and physical characteristics of diesel particles to cancer induction, followed by a hypothesized mode of action, taking into account the likely contribution of the factors discussed.

7.4.1. Potential Role of Organic Exhaust Components in Lung Cancer Induction

More than 100 carcinogenic or potentially carcinogenic components have been specifically identified in diesel emissions, including various PAHs and nitroarenes such as 1-nitropyrene (1-NP) and dinitropyrenes (DNPs). The majority of these compounds are adsorbed to the carbon core of the particulate phase of the exhaust and, if desorbed, may become available for biological processes such as metabolic activation to mutagens. Among such compounds identified from DE are B[*a*]P, dibenz[*a,h*]anthracene, pyrene, chrysene, and nitroarenes such as 1-NP, 1,3-DNP, 1,6-DNP, and 1,8-DNP, all of which are mutagenic, carcinogenic, or implicated as procarcinogens or cocarcinogens (Stenback et al., 1976; Weinstein and Troll, 1977; Thyssen et al., 1981; Pott and Stöber, 1983; Howard et al., 1983; Hirose et al., 1984; Nesnow et al., 1984; El-Bayoumy et al., 1988). More recently Enya et al. (1997) reported isolation of 3-nitrobenzanthrone, one of the most powerful direct-acting mutagens known to date, from the organic extracts of DE.

Grimmer et al. (1987) separated DE particle extract into a water- and a lipid-soluble fraction, and the latter was further separated into a PAH-free, a PAH-containing, and a polar fraction by column chromatography. These fractions were then tested in Osborne-Mendel rats by pulmonary implantation at doses corresponding to the composition of the original DE. The water-soluble fraction did not induce tumors; the incidences induced by the lipid-soluble fractions were 0% with the PAH-free fraction, 25% with the PAH and nitro-PAH- containing fractions, and 0% with the polar fraction. The PAH and nitro-PAH-containing fraction, comprising only 1% by weight of the total extract, was thus shown to be responsible for most, if not all, of the carcinogenic activity.

Exposure of rats by inhalation to 2.6 mg/m^3 of an aerosol of tar-pitch condensate with no carbon core but containing 50 μg/m^3 B[*a*]P along with other PAHs for 10 months induced lung tumors in 39% of the animals. The same amount of tar-pitch vapor condensed onto the surface of carbon black particles at 2 and 6 mg/m^3 resulted in tumor rates that were roughly two times higher (89% and 72%). Because exposure to 6 mg/m^3 carbon black almost devoid of extractable organic material induced a lung tumor rate of 18%, the combination of PAHs and particles increases their effectiveness (Heinrich et al., 1994). Although this study shows the tumor-inducing capability of PAHs resulting from combustion, it should be noted that the B[*a*]P content in the coal-tar pitch was about three orders of magnitude greater than in diesel soot. Moreover, because organics are present on diesel particles in a thinner layer and the particles are quite convoluted, they may be more tightly bound and less bioavailable. Nevertheless, these studies provide evidence supporting the involvement of organic constituents of diesel particles in the carcinogenic process.

Exposure of humans to related combustion emissions provides some evidence for the involvement of organic components. Mumford et al. (1989) reported greatly increased human lung cancer mortality in Chinese communes burning so-called smoky coal, but not wood, in unvented open-pit fires used for heating and cooking. Although particle concentrations were similar, PAH levels were five to six times greater in the air of communes burning smoky coal. Coke oven emissions, containing high concentrations of PAHs but lacking an insoluble carbon core, have also been shown to be carcinogenic in humans (Lloyd, 1971).

Adsorption of PAHs to a carrier particle such as hematite, CB, aluminum, or titanium dioxide enhances their carcinogenic potency (Farrell and Davis, 1974). As already noted, adsorption to carbon particles greatly enhanced the tumorigenicity of pyrolyzed pitch condensate containing B[*a*]P and other aromatic carcinogens (Heinrich et al., 1995). The increased effectiveness can be partly explained by more efficient transport to the deep lung. Slow release also enhances residence time in the lungs and prevents overwhelming of activating pathways. As discussed in Chapter 3, free organics are likely to be rapidly absorbed into the bloodstream, which may explain why the vapor-phase component of exhaust is relatively ineffective in the induction of pathologic or carcinogenic effects.

Even though the organic constituents may be tightly bound to the particle surface, significant elution is still likely because particle clearance half-times are nearly 1 year in humans (Bohning et al., 1982). Furthermore, Gerde et al. (1991) presented a model demonstrating that large aggregates of inert dust containing crystalline PAHs are unlikely to form at doses typical of human exposure. This allows the particles to deposit and react with the surrounding lung medium, without interference from other particles. Particle-associated PAHs can then be expected to be released more rapidly from the particles. Bond et al. (1984) provided evidence that alveolar macrophages from beagle dogs metabolized B[*a*]P coated on diesel particles to proximate carcinogenic forms. Unless present on the particle surface, B[*a*]P is more likely to pass directly into the bloodstream and escape activation by phagocytic cells.

The importance of DE-associated PAHs in the induction of lung cancer in humans may be enhanced because of the possibility that the human lung is more sensitive to these compounds than are rat lungs. Rosenkranz (1996) summarized information indicating that in humans and mice, large proportions of lung cancers contain both mutated *p*53 suppressor genes and K-*ras* genes. Induction of mutations in these genes by genotoxins, however, is much lower in rats than in humans or mice.

B[*a*]P, although only one of many PAHs present in DE, is the one most extensively studied. Bond et al. (1983, 1984) demonstrated metabolism of particle-associated B[*a*]P and free B[*a*]P by alveolar macrophages (AM) and by type II alveolar cells. The respiratory tract cytochrome P-450 systems have an even greater concentration in the nonciliated bronchiolar cells (Boyd, 1984). It is worth noting that bronchiolar adenomas that develop following diesel exposure have been found to resemble both Type II and nonciliated bronchiolar cells. It should

also be noted that any metabolism of procarcinogens by these latter two cell types probably involves the preextraction of carcinogens in the extracellular lining fluid and/or other endocytotic cells, as they are not especially important in phagocytosis of particles. Thus, bioavailability is an important issue in assessing the relative importance of PAHs.

Additionally, a report by Borm et al. (1997) indicates that incubating rat lung epithelial-derived cells with human polymorphonucleocytes (PMNs) (either unactivated or activated by preexposure to phorbol myristate acetate) increases DNA adduct formation caused by exposure to B[*a*]P; at 0.05 to 0.5 micromolar concentration, addition of more activated PMN in relation to the number of lung cells further increased adduct formation in a dose-dependent manner. The authors suggest that "an inflammatory response in the lung may increase the biologically effective dose of PAHs, and may be relevant to data interpretation and risk assessment of PAH-containing particles." These data raise the possibility that DE exposure at low concentrations may result in levels of neutrophil influx that would not necessarily be detectable via histopathological examination as acute inflammation, but that might be effective at amplifying any potential DE genotoxic effect.

Nitro-PAHs have also been implicated as potentially involved in diesel-exhaust-induced lung cancer. Although the nitro-PAH fraction of diesel was less effective than PAHs in the induction of lung cancer when implanted into the lungs of rats (Grimmer et al., 1987), in a study of various extracts of DE particles, 30%-40% of the total mutagenicity could be attributed to a group of six nitroarenes (Salmeen et al., 1984). Moreover, Gallagher et al. (1994) reported results suggesting that DNA adducts are formed from nitro-PAHs present in DNA and may play a role in the carcinogenic process. Nitroarenes, however, quantitatively represent a very small percentage of diesel particle extract (Grimmer et al., 1987), making their role in the tumorigenic response uncertain.

The induction of DNA adducts in humans occupationally exposed to DE indicates the likelihood that PAHs are participating in the tumorigenic response, and that these effects can occur at exposure levels less than those required to induce lung particle overload. Distinct adduct patterns were found among garage workers occupationally exposed to DE when compared with nonexposed controls (Nielsen and Autrup, 1994). Furthermore, the findings were concordant with the adduct patterns observed in groups exposed to low concentrations of PAHs from combustion processes. Hemminki et al. (1994) also reported significantly elevated levels of DNA adducts in lymphocytes from garage workers with known DE exposure compared with unexposed mechanics. Hou et al. (1995) found elevated adduct levels in bus maintenance workers exposed to DE. Although no difference in mutant frequency was observed between the groups, the adduct levels were significantly different (3.2 vs. 2.3×10^{-8}). Nielsen et al. (1996b) measured three biomarkers in DE-exposed bus garage workers: lymphocyte DNA adducts, hydroxyethylvaline adducts in hemoglobin, and 1-hydroxypyrene in urine. Significantly increased levels were reported for all three. Qu et al. (1996) detected increased adduct levels, as

well as increases in some individual adducts, in the blood of underground coal miners exposed to DE.

7.4.2. Role of Inflammatory Cytokines and Proteolytic Enzymes in the Induction of Lung Cancer in Rats by Diesel Exhaust

It is well recognized that the deposition of particles in the lung can result in the efflux of PMNs from the vascular compartment into the alveolar space compartment in addition to expanding the AM population size. Following acute exposures, the influx of the PMNs is transient, lasting only a few days (Adamson and Bowden, 1978; Bowden and Adamson, 1978; Lehnert et al., 1988). During chronic exposure the numbers of PMNs lavaged from the lungs of diesel-exposed rats generally increased with increasing exposure duration and inhaled DPM concentration (Strom, 1984). Strom (1984) also found that PMNs in diesel-exposed lungs remained persistently elevated for at least 4 months after cessation of exposure, a potential mechanism that may be related to an ongoing release of phagocytized particles. Evidence in support of this possibility was reported by Lehnert et al. (1989) in a study in which rats were intratracheally instilled with 0.85, 1.06, or 3.6 mg of polystyrene particles. The PMNs were not found to be abnormally abundant during the clearance of the two lower lung burdens, but they became progressively elevated in the lungs of the animals in which alveolar-phase clearance was inhibited. Moreover, the particle burdens in the PMNs became progressively greater over time. Such findings are consistent with an ongoing particle relapse process, in which particles released by dying phagocytes are ingested by new ones.

The inflammatory response, characterized by efflux of PMNs from the vascular compartment, is mediated by inflammatory chemokines. Driscoll et al. (1996) reported that inhalation of high concentrations of carbon black stimulated the release of macrophage inflammatory protein 2 (MIP-2) and monocyte chemotactic protein 1 (MCP-1). They also reported a concomitant increase in hprt mutants. In a following study it was shown that particle exposure stimulates production of tumor necrosis factor TNF-α, an agent capable of activating expression of several proteins that promote both adhesion of leucocytes and chemotaxis (Driscoll et al., 1997a). In addition, alveolar macrophages also have the ability to release several other effector molecules or cytokines that can regulate numerous functions of other lung cells, including their rates of proliferation (Bitterman et al., 1983; Jordana et al., 1988; Driscoll et al., 1996).

Another characteristic of AMs and PMNs under particle overload conditions is the release of a variety of potentially destructive hydrolytic enzymes, a process known to occur simultaneously with the phagocytosis of particles (Sandusky et al., 1977). The essentially continual release of such enzymes during chronic particle deposition and phagocytosis in the lung may be detrimental to the alveolar epithelium, especially to Type I cells. Evans et al. (1986) showed that injury to Type I cells is followed shortly thereafter by a proliferation of Type

II cells. Type II cell hyperplasia is a common feature observed in animals that have received high lung burdens of various types of particles, including unreactive polystyrene microspheres. Exaggerated proliferation as a repair or defensive response to DPM deposition may have the effect of amplifying the likelihood of neoplastic transformation in the presence of carcinogens beyond that which would normally occur with lower rates of proliferation, assuming an increase in the cycling of target cells and the probability of a neoplastic-associated genomic disturbance.

7.4.3. Role of Reactive Oxygen Species in Lung Cancer Induction by Diesel Exhaust

Phagocytes from a variety of rodent species produce elevated levels of oxidant reactants in response to challenges, with the physiochemical characteristics of a phagocytized particle being a major factor in determining the magnitude of the oxidant-producing response. Active oxygen species released by the macrophages and lymphatic cells can cause lipid peroxidation in the membrane of lung epithelial cells. These lipid peroxidation products can initiate a cascade of oxygen free radicals that progress through the cell to the nucleus, where they damage DNA. If this damage occurs during the epithelial cell's period of DNA synthesis, there is some probability that the DNA will be replicated unrepaired (Lechner and Mauderly, 1994). The generation of reactive oxygen species by both AMs and PMNs should therefore be considered as one potential factor of what probably is a multistep process that culminates in the development of lung tumors in response to chronic deposition of DPM.

Even though products of phagocytic oxidative metabolism, including superoxide anions, hydrogen peroxide, and hydroxyl radicals, can kill tumor cells (Klebanoff and Clark, 1978), and the reactive oxygen species can peroxidize lipids to produce cytotoxic metabolites such as malonyldialdehyde, some products of oxidative metabolism apparently can also interact with DNA to produce mutations. Cellular DNA is damaged by oxygen free radicals generated from a variety of sources (Ames, 1983; Trotter, 1980). Along this line, Weitzman and Stossel (1981) found that human peripheral leukocytes are mutagenic in the Ames assay. This mutagenic activity was related to PMNs and blood monocytes; blood lymphocytes alone were not mutagenic. These investigators speculated that the mutagenic activity of the phagocytes was a result of their ability to produce reactive oxygen metabolites, inasmuch as blood leukocytes from a patient with chronic granulomatous diseases, in which neutrophils have a defect in the NADPH oxidase generating system (Klebanoff and Clark, 1978), were less effective in producing mutations than were normal leukocytes. Of related significance, Phillips et al. (1984) demonstrated that the incubation of Chinese hamster ovary cells with xanthine plus xanthine oxidase (a system for enzymatically generating active oxygen species) resulted in genetic damage hallmarked by extensive chromosomal breakage and sister chromatid exchange and produced an increase in the frequency of thioguanidine-resistant cells (HGPRT test). Aside from interactions of oxygen species with DNA, increasing evidence also points to an important role of

phagocyte-derived oxidants and/or oxidant products in the metabolic activation of procarcinogens to their ultimate carcinogenic form (Kensler et al., 1987).

Driscoll et al. (1997b) have demonstrated that exposure to doses of particles producing significant neutrophilic inflammation are associated with increased mutation in rat alveolar type II cells. The ability of particle-elicited macrophages and neutrophils to exert a mutagenic effect on epithelial cells in vitro supports a role for these inflammatory cells for the in vivo mutagenic effects of particle exposure. The inhibition of bronchoalveolar lavage cell-induced mutations by catalase implies a role for cell-derived oxidants in this response.

Hatch and co-workers (1980) have demonstrated that interactions of guinea pig AMs with a wide variety of particles, such as silica, metal oxide-coated fly ash, polymethylmethacrylate beads, chrysotile asbestos, fugitive dusts, polybead carboxylate microspheres, glass and latex beads, uncoated fly ash, and fiberglass increase the production of reactive oxygen species. Similar findings have been reported by numerous investigators for human, rabbit, mouse, and guinea pig AMs (Drath and Karnovsky, 1975; Allen and Loose, 1976; Beall et al., 1977; Lowrie and Aber, 1977; Miles et al., 1977; Rister and Baehner, 1977; Hoidal et al., 1978). PMNs are also known to increase production of superoxide radicals, hydrogen peroxide, and hydroxyl radicals in response to membrane-reactive agents and particles (Goldstein et al., 1975; Weiss et al., 1978; Root and Metcalf, 1977). Although these responses may occur at any concentration, they are likely to be greatly enhanced at high exposure concentrations with slowed clearance and lung particle overload.

Reactive oxygen species can also be generated from particle-associated organics. Sagai et al. (1993) reported that DPM can nonenzymatically generate active oxygen species (e.g., superoxide [O_2^-] and hydroxyl radical [$^{\cdot}OH$] in vitro without any biologically activating systems) such as microsomes, macrophages, hydrogen peroxide, or cysteine. Because DPM washed with methanol could no longer produce these radicals, it was concluded that the active components were compounds extractable with organic solvents. However, the nonenzymatic contribution to the DPM-promoted active oxygen production was negligible compared with that generated via an enzymatic route (Ichinose et al., 1997a). They reported that O_2^- and $^{\cdot}OH$ can be enzymatically generated from DPM by the following process. Soot-associated quinone-like compounds are reduced to the semiquinone radical by cytochrome P-450 reductase. These semiquinone radicals then reduce O_2 to O_2^-, and the produced superoxide reduces ferric ions to ferrous ions, which catalyzes the homobiotic cleavage of H_2O_2 dismutated from O_2 by superoxide dismutase or spontaneous reactions to produce $^{\cdot}OH$. According to Kumagai et al. (1997), while quinones are likely to be the favored substrates for this reaction, the participation of nitroaromatics cannot be ruled out.

One of the critical lesions to DNA bases generated by oxygen free radicals is 8-hydroxydeoxyguanosine (8-OHdG). The accumulation of 8-OhdG as a marker of oxidative DNA damage could be an important factor in enhancing the mutation rate leading to lung cancer

(Ichinose et al., 1997a). For example, formation of 8-OHdG adducts leads to G:C to T:A transversions unless repaired prior to replication. Nagashima et al. (1995) demonstrated that the production of (8-OHdG) is induced in mouse lungs by intratracheal instillation of DPM. Ichinose et al. (1997b) reported further that although intratracheal instillation of DPM in mice induced a significant increase in lung tumor incidence, comparable increases were not reported when mice were instilled with extracted DPM (to remove organics). Lung injury was also less in the mice instilled with extracted DPM. Moreover, increases in 8-OHdG in the mice instilled with unextracted DPM correlated very well with increases in tumor rates. In a related study, Ichinose et al. (1997a) intratracheally instilled small doses of DPM, 0.05, 0.1, or 0.2 mg weekly for 3 weeks, in mice fed standard or high-fat diets either with or without β-carotene. High dietary fat enhanced DPM-induced lung tumor incidence, whereas β-carotene, which may act as a free radical scavenger, partially reduced the tumorigenic response. Formation of 8-OHdG was again significantly correlated with lung tumor incidence in these studies, except at the highest dose. Dasenbrock et al. (1996) reported that extracted DPM, intratracheally instilled into rats (15 mg total dose) induced only marginal increases in lung tumor induction, while unextracted DPM was considerably more effective. Although adducts were not measured in this study, it nevertheless provides support for the likelihood that activation of organic metabolites and/or generation of oxygen free radicals from organics are involved in the carcinogenic process.

Additional support for the involvement of particle-associated radicals in tissue damage was provided by the finding that pretreatment with superoxide dismutase (SOD), an antioxidant, markedly reduced lung injury and death due to instillation of DPM. Similarly, Hirafuji et al. (1995) found that the antioxidants catalase, deferoxamine, and MK-447 inhibited the toxic effects of DPM on guinea pig tracheal cells and tissues in vitro.

Although the data presented supported the hypothesis that generation of reactive oxygen species resulting from exposure to DPM is involved in the carcinogenic process, it should be noted that 8-OHdG is efficiently repaired and that definitive proof of a causal relationship in humans is still lacking. It is also uncertain whether superoxide or hydroxyl radicals chemically generated by DPM alone promote 8-OHdG production in vivo and induce lung toxicity, because SOD is extensively located in mammalian tissues. Nevertheless, demonstration that oxygen free radicals can be generated from particle-associated organics, that their presence will induce adduct formation and DNA damage unless repaired, that tumor induction in experimental animals correlates with OhdG adducts, and that treatment with antioxidant limits lung damage, provides strong support for the involvement of oxygen free radicals in the toxicologic and carcinogenic response to DE.

7.4.4. Relationship of Physical Characteristics of Particles to Cancer Induction

The biological potential of inhaled particles is strongly influenced by surface chemistry and character. For example, the presence of trace metal compounds such as aluminum and iron, as well as ionized or protonated sites, is important in this regard (Langer and Nolan, 1994). A

major factor is specific surface area (surface area/mg). PMNs characteristically are increased abnormally in the lung by DE exposure, but their presence in the lungs does not appear to be excessive following the pulmonary deposition of even high lung burdens of spherical TiO_2 particles in the 1-2 μm diameter range (Strom, 1984). In these studies lung tumors were detected only at an inhaled concentration of 250 $\mu g/m^3$. In a more recent study in which rats were exposed to TiO_2 in the 15-40 nm size range, inhibition of particle clearance and tumorigenesis were induced at concentrations of 10 mg/m^3 (Heinrich et al., 1995). Comparison of several chronic inhalation studies correlating particle mass and particle surface area retained in the lung with tumor incidence indicated that particle surface area is a much better dosimeter than particle mass (Oberdörster and Yu, 1990; Driscoll et al., 1996). Heinrich et al. (1995) also found that lung tumor rates increased with specific particle surface area following exposure to DE, carbon black, or titanium dioxide, irrespective of particle type. Langer and Nolan (1994) reported that the hemolytic potential of Min-U-Sil15, a silica flour, increased in direct relationship to specific surface area at nominal particle diameters ranging from 0.5 to 20 μm.

Ultrafine particles appear to be more likely to be taken up by lung epithelial cells. Riebe-Imre et al. (1994) reported that CB is taken up by lung epithelial cells in vitro, inducing chromosomal damage and disruption of the cytoskeleton, lesions that closely resemble those present in tumor cells. Johnson et al. (1993) reported that 20-nm polytetrafluoroethylene particles are taken up by pulmonary epithelial cells as well as polymorphonuclear leucocytes, inducing an approximate 4-, 8-, and 40-fold increase in the release of interleukin-1 alpha and beta, inducible nitric oxide synthetase, and macrophage inflammatory protein, respectively.

The carcinogenic potency of diesel particles, therefore, appears to be related, at least to some extent, to their small size and convoluted shape, which results in a large specific particle surface area. Toxicity and carcinogenicity increased with decreasing particle size into the submicron range. For example, Heinrich et al. (1995) have shown that ultrafine titanium dioxide (approximately 0.2 μm diameter) is much more toxic than particles with a 10-fold greater diameter of the same composition used in an earlier study by Lee et al. (1986). This increase in toxicity has been noted with even smaller particles. For example, carbon black particles 20 nm in diameter were shown to be significantly more toxic than 50 nm particles (Murphy et al., 1999). The relationship between particle size and toxicity is of concern because, as noted in Chapter 2, approximately 50%-90% of the number of particles in DE are in the size range from 5 to 50 nm. Other than disruption of the cytoskeleton of epithelial cells, there is little information regarding the means by which particle size influences carcinogenicity as well as noncancer toxicity.

7.4.5. Integrative Hypothesis for Diesel-Induced Lung Cancer

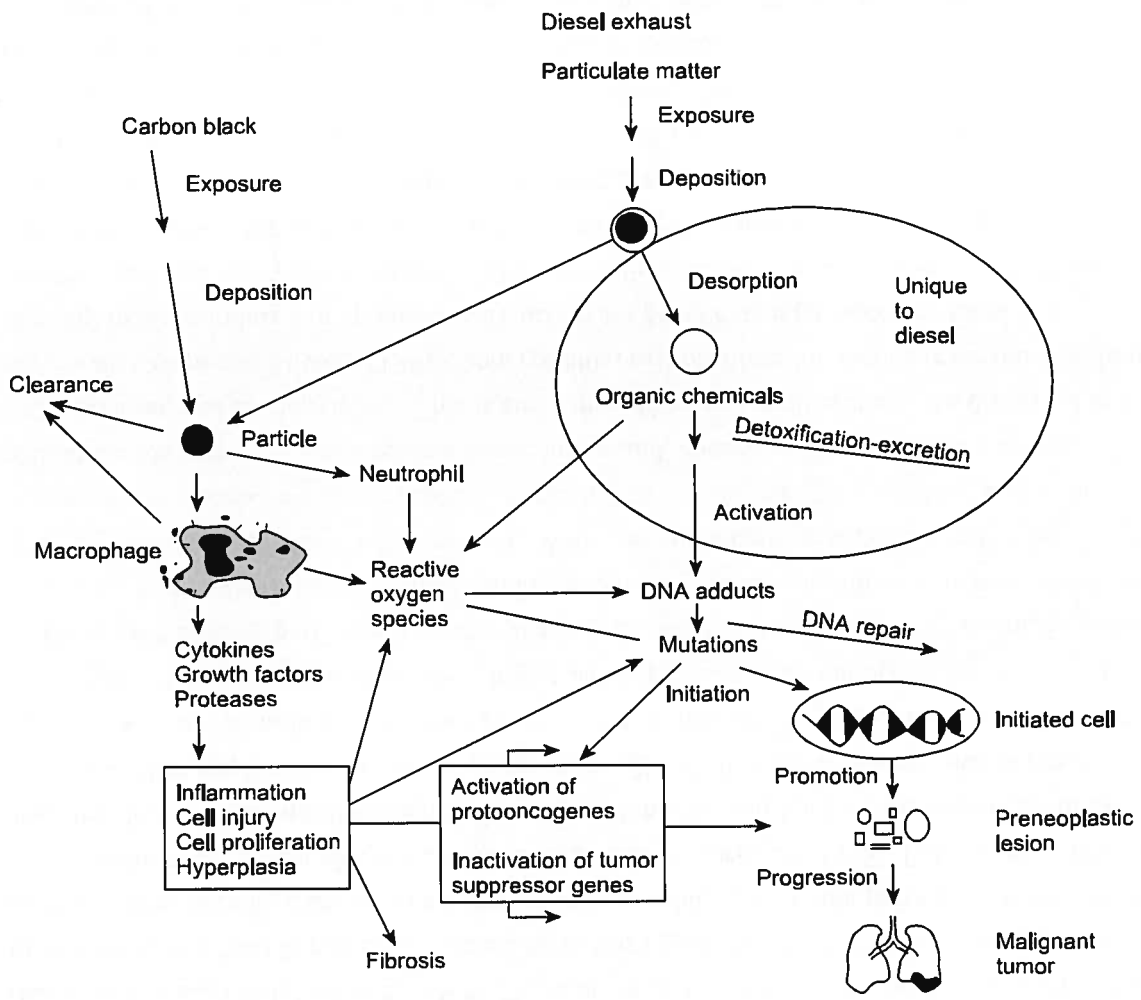
The induction of lung cancer in rats by large doses of carbon black via inhalation (Heinrich et al., 1995; Mauderly et al., 1991; Nikula et al., 1995) or intratracheal instillation (Kawabata et al., 1994; Pott et al., 1994; Dasenbrock et al., 1996) led to the development of the lung particle overload hypothesis. According to this hypothesis the induction of neoplasia by insoluble low- toxicity particles is associated with an inhibition of lung particle clearance and the involvement of persistent alveolar epithelial hyperplasia. Driscoll (1995), Driscoll et al. (1996), and Oberdörster and Yu (1990) outlined a proposed mechanism for the carcinogenicity of DE at high doses that emphasizes the role of phagocytic cells. Following exposure, phagocytosis of particles acts as a stimulant for oxidant production and inflammatory cytokine release by lung phagocytes. It was hypothesized that at high particle exposure concentrations the quantity of mediators released by particle-stimulated phagocytes exceeds the inflammatory defenses of the lung (e.g., antioxidants, oxidant-metabolizing enzymes, protease inhibitors, cytokine inhibitors), resulting in tissue injury and inflammation. With continued particle exposure and/or the persistence of excessive particle burdens, there then develops an environment of phagocytic activation, excessive mediator release-tissue injury and, consequently, more tissue injury, inflammation, and tissue release. This is accompanied by cell proliferation. As discussed in a review by Cohen and Ellwein (1991), conceptually, cell proliferation can increase the likelihood that any oxidant-induced or spontaneously occurring genetic damage becomes fixed in a dividing cell and is clonally expanded. The net result of chronic particle exposures sufficient to elicit inflammation and cell proliferation in the rat lung is an increased probability that the genetic changes necessary for neoplastic transformation will occur. A schematic of this hypothesis has been outlined by McClellan (1997) (see Figure 7-3). In support of this hypothesis, it was reported that concentrations of inhaled CB resulted in increased cytokine expression and inflammatory influx of neutrophils (Oberdörster et al., 1995), increased formation of 8-OhdG (Ichinose et al., 1997b), and increase in the yield of hprt mutants, an effect ameliorated by treatment with antioxidants (Driscoll, 1995; Driscoll et al., 1996). Metabolism of carcinogenic organics to active forms as well as the generation of reactive oxygen species from certain organic species are likely to contribute to the toxic and carcinogenic process.

At low exposure concentrations, the lung particle overload condition is not present and the overload-induced inflammatory effects are not present. Note, however, as discussed in Chapters 5 and 6, that other types of inflammation are present in the rat lung at exposures below those inducing lung particle overload. However, at low exposures, activation of organic carcinogens and generation of oxidants from the organic fraction can still be expected. Actual contribution depends upon elution/bioavailability and the effectiveness of antioxidants. Direct effects of ultrafine diesel particles taken up by epithelial cells are also likely to play a role.

Although high-dose induction of cancer is logically explained by this hypothesis, particle overload has not been clearly shown to induce lung cancer in other species. As noted in the quantitative chapter, the relevance of the rat pulmonary response is therefore problematic. The

rat pulmonary noncancer responses to DPM, however, have fairly clear interspecies and human parallels. In response to poorly soluble particles such as DPM, humans and rats both develop an alveolar macrophage response, accumulate particles in the interstitium, and show mild interstitial fibrosis (ILSI, 2000). Other species (mice, hamsters) also have shown similar noncancer pulmonary responses to DPM, but without accompanying cancer response. The rat response for noncancer pulmonary histopathology, however, seems to be more pronounced compared with humans or other species, i.e., rats appear to be more sensitive. Although many critical elements of interspecies comparison, such as the role of airway geometry and patterns of particle deposition, need further elucidation, this basic interspecies similarity and the possible greater sensitivity of pulmonary response seen after longer exposures at high doses make pulmonary histopathology in rats a valid basis for noncancer dose-response assessment.

Figure 7-3. Pathegenesis of lung disease in rats with chronic, high-level exposures to particles.



Source: Modified from McClellan, 1997.

7.4.6. Summary

Recent studies have shown rat lung tumor rates resulting from exposures to nearly organic-free carbon black (CB) particles at high concentrations to be similar to those observed for DE exposures, thus providing strong evidence for a particle overload mechanism for DE-induced pulmonary carcinogenesis in rats. Such a mechanism is also supported by the fact that carbon particles per se cause inflammatory responses and increased epithelial cell proliferation and that AM function may be compromised under conditions of particle overload.

The particle overload hypothesis appears sufficient to account for DE-induced lung cancer in rats. However, there is also biological plausibility for lung cancer induction in humans at concentrations insufficient to induce lung particle overload as seen in rats (Chapter 3, Section 3.4 and ILSI, 2000). The uptake of particles by epithelial cells at ambient or occupational exposure levels, DNA damage resulting from oxygen-free radicals generated from organic molecules, and the gradual in situ extraction and activation of procarcinogens associated with the diesel particles may play a role in this response and provide a basis for the plausibility. The slower particle clearance rates in humans (up to a year or more) may result in greater extraction of organics. This is supported by reports of increased DNA adducts in humans occupationally exposed to DE at concentrations unlikely to induce lung particle overload. Although these modes of action can be expected to function at lung overload conditions also, they are likely to be overwhelmed by inflammatory associated effects.

The evidence to date indicates that caution must be exercised in extrapolating observations made in animal models to humans when assessing the potential for DE-induced pulmonary carcinogenesis. The carcinogenic response and the formation of DNA adducts in rats exposed to DE and other particles at high exposure concentrations may be species-specific and not DPM specific. The likelihood that different modes of action predominate at high and low doses, such as lung particle overload, also renders high-dose extrapolation to lower ambient concentrations uncertain.

7.5. WEIGHT-OF-EVIDENCE EVALUATION FOR POTENTIAL HUMAN CARCINOGENICITY

A carcinogenicity weight-of-evidence evaluation is a synthesis of all pertinent information addressing the question of how likely an agent is to be a human carcinogen. EPA's 1986 Guidelines for Carcinogen Risk Assessment (U.S. EPA, 1986) provide a classification system for the characterization of the overall weight of evidence for potential human carcinogenicity based on human evidence, animal evidence, and other supportive data. This system includes Group A: *Human Carcinogen*; Group B: *Probable Human Carcinogen*; Group C: *Possible Human Carcinogen*; Group D: *Not Classifiable as to Human Carcinogenicity*; and Group E: *Evidence for Noncarcinogenicity to Humans*.

As part of the guidelines development and updating process, the Agency has developed revisions to the 1986 guidelines to take into account knowledge gained in recent years about the carcinogenic processes. With regard to the weight-of-evidence evaluation for potential human carcinogenicity, EPA's 1996 Proposed Guidelines for Carcinogen Risk Assessment (U.S. EPA, 1996b) and the subsequent revised external review draft (U.S. EPA, 1999) emphasize the need for characterizing cancer hazard, in addition to hazard identification. To express the weight of evidence for potential human carcinogenicity, EPA's proposed 1996 and 1999 guidelines utilize a hazard narrative in place of the 1986 A-E classification system. In order to provide some measure of consistency in using the 1996 and 1999 draft guidelines, standard hazard descriptors are used as part of the hazard narrative. The revised guidelines also stress the importance of considering the mode(s) of action information for making an inference about potential cancer hazard beyond the range of observation, typically encountered at levels of exposure in the general environment. "Mode of action" refers to a series of key biological events and processes that are critical to the development of cancer. This is contrasted with "mechanisms of action," which is defined as a more detailed description of the complete sequence of biological events at the molecular level that must occur to produce a carcinogenic response.

The sections to follow evaluate and weigh the individual lines of evidence and combine all evidence to make an informed judgment about the carcinogenicity hazard of DE. A conclusion in accordance with EPA's 1986 classification system (U.S. EPA, 1986) is provided, as well as a hazard narrative along with appropriate hazard descriptors according to EPA's Proposed Guidelines (U.S. EPA, 1996b, 1999). These sections draw on information reviewed in Chapters 2, 3, 4, and 7.

7.5.1. Human Evidence

Twenty-two epidemiologic studies about the carcinogenicity of workers exposed to DE in various occupations are reviewed in Section 7.2. Exposure to DE has typically been inferred based on job classification within an industry. Increased lung cancer risk, although not always statistically significant, has been observed in 8 out of 10 cohort and 10 of 12 case-control studies within several industries, including railroad workers, truck drivers, heavy equipment operators, and professional drivers. The increased lung cancer relative risks generally range from 1.2 to 1.5, though a few studies show relative risks as high as 2.6. Statistically significant increases in pooled relative risk estimates (1.33 to 1.47) from two independent meta-analyses further support a positive relationship between DE exposure and lung cancer in a variety of DE-exposed occupations.

The generally small increased lung cancer relative risk (less than 2) observed in the epidemiologic studies and meta-analyses potentially weakens the evidence of causality. When a relative risk is less than 2, if confounders (e.g., smoking, asbestos exposure) are having an effect on the observed risk increases, it could be enough to account for the increased risk. With the

strongest risk factor for lung cancer being smoking, there is a concern that smoking effects may be influencing the magnitude of the observed increased relative risks. However, in studies for which the effects of smoking were accounted for, increased relative risks for lung cancer prevailed. Though some studies did not have information on smoking, significant confounding by smoking is unlikely because the comparison populations were from the same socioeconomic class. Moreover, when the meta-analysis focused only on the smoking-controlled studies, the relative risks tended to increase.

As evaluated in Section 7.2.4.5, application of the criteria for causality (including the biological plausibility) leads to the conclusion that the increased risks observed in available epidemiologic studies are consistent with a causal association between exposure to DE and occurrence of lung cancer. Overall, the human evidence for potential carcinogenicity for DE is judged to be strong, but less than sufficient for DE to be considered as a human carcinogen because of exposure uncertainties (lack of historical exposure data for workers exposed to DE) and an inability to reach a fully and direct accounting for all possible confounders.

7.5.2. Animal Evidence

DE and its organic constituents, both in the gaseous and particle phase, have been extensively tested for carcinogenicity in many experimental studies using several animal species and with different modes of administration.

Several well-conducted lifetime rat inhalation studies have consistently demonstrated that chronic inhalation exposure to sufficiently high concentrations of DE produced dose-related increases in lung tumors (benign and malignant). However, the lung cancer responses in rats from high-concentration exposures appear to be mediated by impairment of lung clearance mechanisms through particle overload, resulting in persistent chronic inflammation and subsequent pathologic and neoplastic changes in the lung. Overload conditions are not expected to occur in humans as a result of environmental or most occupational exposures to DE. Thus, the rat lung tumor response is not considered relevant to an evaluation of the potential for a human environmental exposure-related hazard (Section 7.4).

The chronic inhalation studies of DE in mice showed equivocal results, whereas negative findings were consistently seen in hamsters. The gaseous phase of DE (filtered exhaust without particulate fraction) was found not to be carcinogenic in rats, mice, or hamsters.

In several intratracheal instillation studies, diesel particulate matter (DPM), carbon black, and the organic DPM extracts which were virtually devoid of PAHs, have been found to produce increased lung tumors in rats. When directly implanted into the rat lung, DPM condensate containing mainly four- to seven-ring PAHs induced increases in lung tumors. In several dermal studies in mice, DPM extracts have also been shown to cause skin tumors and sarcomas in mice following subcutaneous injection.

Available data and hypotheses suggest that both the carbon core and the adsorbed organics have potential roles in inducing lung tumors in the rat, although their relative contribution to the carcinogenic response remains to be determined.

The consistent findings of carcinogenic activity by DPM and the organic extracts of DPM in noninhalation studies (intratracheal instillation, lung implantation, skin painting) contribute to the overall evidence for a human hazard potential for DE. The lack of a tumor response from traditional animal inhalation studies in other rodent species is noted. Without understanding the mode(s) of action of DE's carcinogenicity in humans it is difficult to assess the meaning of nonpositive results from the mouse and hamster inhalation bioassays, and the unusable results from the rat, while having other evidence of carcinogenic potential and plausibility.

It should be noted that the animal studies used DE from engines available in the 1980s, and that present-day engine emissions have different characteristics (e.g., higher elemental carbon content and lesser amounts of adsorbed organics on the carbon particles), with uncertain impact on the outcome of the experimental studies. The same point can be made for the occupational epidemiologic studies.

7.5.3. Other Key Data

Other key data are judged to be supportive of potential carcinogenicity of DE. As discussed in Chapter 2, DE is a complex mixture of hundreds of constituents in either gaseous phase or particle phase. Although present in small amounts, several organic compounds in the gaseous phase (e.g. PAHs, formaldehyde, acetaldehyde, benzene, 1,3-butadiene) are known to exhibit mutagenic and/or carcinogenic activities. PAHs and PAH derivatives, including nitro-PAHs, present on the diesel particle are also known to be mutagenic and carcinogenic. As reviewed in Chapter 4, DPM and DPM organic extracts have been shown to induce gene mutations in a variety of bacteria and mammalian cell test systems. In addition, DE, DPM and DPM extracts have been found to cause chromosomal aberrations, aneuploidy, and sister chromatid exchange in both in vivo and in vitro tests.

There is also suggestive evidence for the bioavailability of the organics from DE (Chapter 3, Section3.5). Elevated levels of DNA adducts in lymphocytes have been reported in workers exposed to DE. In addition, animal studies showed that some of the radiolabeled organic compounds are eluted from DE particles following deposition in the lungs.

7.5.4. Mode of Action

As discussed in Section 7.4, the modes of action of DE-induced carcinogenicity in humans is not understood. It can be suggested that one or multiple modes of action may be involved. These may include: (a) mutagenic and genotoxic events (e.g., direct and indirect effects on DNA and effects on chromosomes) by organic compounds in the gaseous and particle

phases; (b) indirect DNA damage via the production of reactive oxygen species (ROS) induced by particle-associated organics; and (c) particle-induced chronic inflammatory response leading to oxidative DNA damage through the release of cytokines, ROS, etc., and an increase in cell proliferation.

The particulate phase or whole DE exposure, as measured by DPM, appears to have the greatest observable contribution to the carcinogenic effects, and both the particle core and the associated organic compounds have demonstrated carcinogenic properties, although a role for the gas-phase components cannot be ruled out. The carcinogenic activity of DE may also be related to the small size of the particles. Moreover, the relative contribution of the possible mode(s) of action may be different at different exposure levels. For example, available evidence from rat studies indicates the importance of the role of the DPM in mediating lung tumor response at high exposure levels. Thus, the role of the adsorbed organic compounds may take on increasing importance at lower exposure levels.

7.5.5. Characterization of Overall Weight of Evidence: EPA's 1986 Guidelines for Carcinogen Risk Assessment

The totality of evidence supports the conclusion that DE is a *probable human carcinogen (Group B1)*. This conclusion is based on:

- "Limited"evidence (i.e., strong but less than sufficient evidence for "known human carcinogen"), for a causal association between DE exposure and increased risk of lung cancer among workers in different occupations;
- Evidence of carcinogenicity of DPM in rats and mice by noninhalation routes of exposure (intratracheal instillation, lung implantation, skin painting, and subcutaneous injection); and
- Extensive supporting data including the demonstrated mutagenic and/or chromosomal effects of DE and its organic constituents, suggestive evidence for the bioavailability of the organics from DE, and knowledge of the known mutagenic and/or carcinogenic activity of a number of individual organic compounds present on the particles (e.g,. PAH and derivatives) and in the DE gases (e.g., benzene, 1,3-butadiene, and aldehydes).

7.5.6. Weight-of-Evidence Hazard Narrative: EPA's Proposed Guidelines for Carcinogen Risk Assessment (1996b, 1999)

The combined evidence supports the conclusion that DE is *likely to be carcinogenic to humans* by inhalation and that this hazard applies to environmental exposure conditions. The spectrum of evidence and the inferences drawn provide a substantial case for this hazard potential. The weight of evidence of human carcinogenicity is based on:

- Strong but less than sufficient epidemiologic evidence for a causal association between DE exposure and increased risk of lung cancer among workers in different occupations;
- Evidence of carcinogenicity of DPM in rats and mice by noninhalation routes of exposure (intratracheal instillation, lung implantation, skin painting, and subcutaneous injection); and
- Extensive supporting data including the demonstrated mutagenic and/or chromosomal effects of DE and its organic constituents, suggestive evidence for the local and systemic bioavailability of the organics from DE, and knowledge of the known mutagenic and/or carcinogenic activity of a number of individual organic compounds present on the particles (e.g., PAH and derivatives) and in the DE gases (e.g., benzene, 1,3 butadiene, and aldehydes).

The weight-of-evidence for the lung cancer hazard is considered strong, even though inferences and uncertainties are involved. Major uncertainties include:

- There is scientific debate about the significance of the occupational epidemiologic evidence for a causal association between occupational exposure and increased lung cancer risk. Some experts view the evidence as weak given that most of the relative risk increases are <2.0, whereas others consider the evidence as more than adequate and compelling. With relatively low relative risks (<2.0), the effects of possible confounding exposures or other factors could play a significant role in the risk increases. For example, there is specific concern about whether the effects of smoking, a known cause of lung cancer, has been adequately or fully accounted for in the key studies. In more general terms, the lack of historical exposure data to retrospectively validate estimated DE exposure levels is also a limitation.
- A lack of knowledge about the mode(s) of action of DE lung cancer in humans results in the use of a number of default risk assessment assumptions which, while justifiable by evidence or policy choice, introduce uncertainty. To date, available evidence for the role of DPM, both the adsorbed organics and the carbon core

particle, has been shown only for high exposure conditions in the rat lung. The tumor inducing mode-of-action in the rat lung appears to depend on particle overloading of the lung and subsequent pathology. This sequence is judged not to be relevant for assessing the hazard to humans exposed in the ambient environment. There is virtually no information about the relative role of DE constituents in mediating the carcinogenic effects at lower experimental exposure levels, though hypotheses exist.

While a major uncertainty relates to the incomplete understanding of DE's mode(s) of action for the induction of lung cancer in humans, available data and hypotheses suggest that DE-induced lung carcinogenicity may be mediated by mutagenic and nonmutagenic events from both the particles and the associated organic compounds, although a role for the organics in the gaseous phase cannot be ruled out. Given that there is some evidence for a mutagenic mode of action, a cancer hazard is presumed at environmental exposure levels. This is consistent with EPA's science policy position, which assumes a nonthreshold effect for carcinogens in the absence of definitive data demonstrating a nonlinear or threshold mechanism. It should also be noted that there are not orders of magnitude differences between lower level occupational and higher end environmental exposure levels, in fact, there appears to be exposure overlap. This observation means that an extrapolation of the occupational hazard to lower environmental exposure levels is minimal, and thus, the conclusion of an environmental hazard is supported. Given these circumstances, linear low-dose extrapolation also would be an appropriate default choice in dose-response assessment that is focused on environmental levels of exposure (Chapter 8, Section 8.2). Because of insufficient information, the human carcinogenic potential of DE by oral and dermal exposures cannot be determined.

7.6. EVALUATIONS BY OTHER ORGANIZATIONS

Several organizations have reviewed the relevant data and evaluated the potential human carcinogenicity of DE or its particulate component. The conclusions reached by these organizations are generally comparable to the evaluation made in this assessment using EPA's Carcinogen Risk Assessment Guidelines. A summary of available evaluations conducted by other organizations is provided in Table 7-9.

7.7. CONCLUSION

It is concluded that environmental exposure to DE may present a lung cancer hazard to humans. The particulate phase appears to have the greatest contribution to the carcinogenic effect, both the particle core and the associated organic compounds have demonstrated

Table 7-9. Evaluations of DE as to human carcinogenic potential

Organization	Human data	Animal data	Overall evaluation
NIOSH (1988)	Limited	Confirmatory	Potential occupational carcinogen
IARC (1989)	Limited	Sufficient	Probably carcinogenic to humans
IPCS (1996)	N/A[a]	N/A	Probably carcinogenic to humans
California EPA (1998)	"Consistent evidence for a causal association"	"Demonstrated carcinogenicity"	DPM as a "toxic air contaminant" (California Air Resources Board)
NTP (2000)	"Elevated lung cancer in occupationally exposed groups"	"Supporting animal and mechanistic data"	DPM-Reasonably anticipated to be a carcinogen

[a]Not applicable.

carcinogenic properties, although a role for the DE gas-phase components cannot be ruled out. Using either EPA's 1986 Guidelines for Carcinogen Risk Assessment (U.S. EPA, 1986) or the proposed revisions (U.S. EPA, 1996b, 1999), DE is judged to be a probable human carcinogen, or likely to be carcinogenic to humans by inhalation, respectively. The weight of evidence for potential human carcinogenicity for DE is considered strong, even though inferences are involved in the overall assessment. Major uncertainties of the hazard assessment include the following unresolved issues:

- There has been a considerable scientific debate about the significance of the available human evidence for a causal association between occupational exposure and increased lung cancer risk. Some experts view the evidence as weak given that most of the relative risk increases are <2.0 whereas others consider the evidence as more than adequate and compelling. Additionally, there is debate about whether the effects of smoking have been adequately accounted for in key studies, as well as the lack of historical DE exposure data to retrospectively validate estimated DE exposure levels for the available studies.
- A lack of knowledge about the mode(s) of action for DE lung cancer in humans results in the use of a number of default risk assessment assumptions which, while justifiable by evidence or policy choice, introduce uncertainty. To date, available evidence for the role of DPM, both the adsorbed organics and the carbon core particle, has been shown only for high-exposure conditions in the rat lung. The

tumor-inducing mode of action in the rat lung appears to depend on particle overloading of the lung but this is judged to be not relevant for assessing the human hazard of ambient exposures. There is virtually no information about the relative role of DE constituents in mediating carcinogenic effects at lower experimental or environmental exposure levels. Furthermore, there is only a limited understanding regarding the relationship between DPM particle size and carcinogenicity.

- DE is present in ambient PM (e.g., $PM_{2.5}$ or PM_{10}); however, a cancer hazard for ambient PM has not been identified, as of 1996 (EPA 1996b). An updated evaluation is expected in 2002.

Additional research is needed to address these issues to reduce the uncertainty associated with the potential cancer hazard of exposure to DE.

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8. DOSE-RESPONSE ASSESSMENT: CARCINOGENIC EFFECTS

8.1. INTRODUCTION

Dose-response assessment for carcinogenicity defines the relationship between the exposure/dose of an agent and the degree of carcinogenic response, and evaluates potential cancer risks to humans at exposure/dose levels of interest. Most often, the exposure/dose response of interest is well below the range of observation. As a result, dose-response assessment usually entails an extrapolation from the generally high exposures in studies on humans or laboratory animals to the exposure levels expected from human contact with the agent in the environment. It also includes considerations of the scientific validity of these extrapolations based on available knowledge about the underlying mechanisms or modes of carcinogenic action. The complete sequence of biological events that must occur to produce an adverse effect is defined as "mechanism of action." In cases where only partial information is available, the term "mode of action" is used to refer to the mechanisms for key events that are judged to be sufficient to inform about the shape of the dose-response curve beyond the range of observation.

This chapter evaluates the available exposure/dose-response data and discusses extrapolation issues in estimating the cancer risk of environmental exposure to diesel engine exhaust (DE). It concludes that available data are inadequate to confidently derive a cancer unit risk estimate for DE or its component, diesel particulate matter (DPM). Unit risk is one possible output from a dose-response assessment and is defined as the estimated upper-bound cancer risk at a specific exposure or dose from a continuous average lifetime exposure to a carcinogen (in this case, cancer risk per $\mu g/m^3$ of DPM). In lieu of unit-risk-based quantitative risk estimates, this chapter provides a perspective about potential risk at environmental levels. Subsequent sections of this chapter discuss issues related to dose-response evaluation of human cancer risk for DE exposure, including the target tumor site and underlying mode of action, suitable measures of dose, approaches to low-dose extrapolation, and appropriate data to be used in the dose-response analysis. This is followed by a simple analysis of the possible degree and extent of risk from environmental exposure to DE.

Appendix C provides a summary review of dose-response assessments conducted to date by other organizations and investigators. These risk estimations were performed on the basis of either epidemiologic and/or experimental data. As concluded in Section 8.5, EPA finds that available epidemiologic data are too uncertain to confidently derive a unit risk estimate for DE-induced lung cancer, and that rat data are not suitable for estimating human risk. Nevertheless, a review of dose-response evaluations is provided in the appendix for historical context.

8.2. MODE OF ACTION AND DOSE-RESPONSE APPROACH

According to EPA's 1996 Proposed Guidelines for Carcinogen Risk Assessment (U.S. EPA, 1996), dose-response assessment is performed in two steps: assessment of observed data to derive a point of departure, followed by extrapolation to lower exposures to the extent necessary. Human data are always preferred over animal data, if available, as their use obviates the need for extrapolation across species. Mode-of-action information is important to dose-response evaluation, as it informs about the relevance of animal data to assessment of human hazard and risk, the shape of the dose-response curve at low doses, and the most appropriate measure(s) of exposure/dose and response.

If there are sufficient quantitative data (humans and/or animals) and adequate understanding of the carcinogenic process, the preferred approach is to use a biologically based model for both the range of observation and extrapolation below that range. Otherwise, as a default procedure, a standard mathematical model is used to curve-fit the observed dose-response data to obtain a point of departure, which is the lower 95% confidence limit of the lowest exposure/dose that is associated with a selected magnitude of excesses of cancer risk in human or animal studies. Default approaches for low-dose extrapolation should be consistent with the current understanding of the mode(s) of action. These include approaches that assume linearity or nonlinearity, or both. Linear extrapolation is used when there is insufficient understanding of the modes of action, or the mode-of-action information indicates that the dose-response curve at low dose is, or is expected to be, linear. Linear extrapolation involves the calculation of the slope of the line drawn from the point of departure to zero exposure or dose (i.e., above background). When there is sufficient evidence for a nonlinear mode of action but not enough data to construct a biologically based model for the relationship, a margin of exposure is used as a default approach. A margin-of-exposure analysis compares the point of departure (i.e., the lowest exposure associated with some cancer risk) with the dose associated with the environmental exposure(s) of interest and determines whether or not the exposure margins are adequate. Both default approaches may be used for a tumor response if it is mediated by linear and nonlinear modes of action. The dose-response approaches considered in this chapter follow the principles of EPA's guidelines for carcinogen risk assessment (U.S. EPA, 1986, 1996, 1999).

As reviewed in Chapter 7, there is substantial evidence from combined human and experimental evidence that DE is likely to pose a cancer hazard to humans at anticipated levels of environmental exposure. The critical target organ is the lung. Evidence exists for a causal relationship between risk for lung cancer and occupational exposure to DE in certain occupational workers such as railroad workers, truck drivers, heavy equipment operators, transit workers, etc.

The mechanism(s) by which DE induces lung cancer in humans has not been established. As discussed in Chapter 7, Section 7.4, several modes of action have been postulated on the basis of available mechanistic studies, including direct DNA effects (gene mutations) by the adsorbed organic compounds and the gaseous fractions, indirect DNA effects (e.g., chromosomal aberrations, sister chromatid exchange [SCE], micronuclei) by DE and DPM, oxidative DNA damage by DPM via release of reactive oxygen species (ROS), and particle-induced chronic inflammatory response leading to epithelial cell cytotoxicity and regenerative cell proliferation via release of cytokines, growth factors, and ROS. It is likely that a combination of modes of action contributes to the overall carcinogenic activity of DE, and that the relative contribution of the various modes of action may vary with different exposure levels.

In the absence of a full understanding of the relative roles of DE constituents in inducing lung cancer in humans, and because there is some evidence for a mutagenic mode of action, linear low-dose extrapolation is an appropriate and prudent default choice for modeling dose-response, and if needed, risk extrapolation from high to lower exposures (U.S. EPA, 1986, 1996, 1999). It also should be noted that there are not order of magnitude differences between lower levels of occupational and higher end environmental exposure estimates. In fact, there appears to be exposure overlap. This means that an extrapolation of the occupational hazard to lower environmental exposure levels is minimal. Other individuals and organizations have used either linear risk extrapolation models and/or mechanistically based models to estimate cancer risk from environmental exposure to DE (e.g., IPCS, 1996; Cal EPA, 1998; also see Appendix C). These were examined but not found to provide a compelling basis for unit risk derivation because of database uncertainty and/or recent understandings about the suitability of the rat data for modeling a dose-response at environmental levels of exposure.

For example, there are an observable series of events showing how DE causes lung tumors in the rat under high exposure experimental conditions. Prolonged exposure to high concentrations of a variety of poorly soluble particles including DPM (and its carbon core, devoid of organics) causes lung tumors in rats through a mode of action that involves impairment of lung clearance mechanisms (referred to as "lung overload response"), leading to persistent chronic inflammation, cell proliferation, metaplasia, and ultimately the development of lung tumors (ILSI, 2000). Because this mode of action is not expected to be operative at environmental exposure conditions, the rat lung tumor dose-response data are not considered suitable for predicting human risk at low environmental exposure concentrations.

8.3. USE OF EPIDEMIOLOGIC STUDIES FOR QUANTITATIVE RISK ASSESSMENT

As discussed above, human data are considered more appropriate than animal data in estimating environmental cancer risk for DE. Still, there are many uncertainties in using the

available epidemiologic studies that have quantitative exposure data to extrapolate the risk to the general population for ambient-level DE exposure.

8.3.1. Sources of Uncertainty

The greatest uncertainty in estimating DE-induced cancer risk from epidemiologic studies is the lack of knowledge of actual historical exposures for individual workers, particularly for the early years. Reconstruction of historic exposures is based on job exposure categories, industrial hygiene measurements, and assumptions made about exposure patterns.

Another related uncertainty is the choice of markers of exposure to DE. As discussed above, the modes of action for DE-induced lung cancer in humans are not fully understood, and thus the best measure of DE exposure is unknown. Various markers of DPM (e.g., respirable-sized particles, elemental carbon [EC]) have been used as dosimeters for DE. Though EC is more sensitive and more specific than respirable-sized particles, both are considered appropriate dosimeters. Related to the choice of dosimeter, having a relatively constant relationship between the organics (on the particle) and the particle mass would be consistent with a possible mode-of-action role for both the particle and organic components. However, evidence of such a constant historic relationship remains unclear. As discussed in Chapter 2 (Section 2.5.2), it appears that newer model on-road engine exhaust has a lesser quantity of organics adsorbed onto the particle compared to older model engines. On the other hand, with regard to DE in the ambient air, there is significant variation in the amounts of DPM organic components emitted because of aged vehicles in the on-road fleet, driving patterns, and the additional presence of nonroad DE (e.g., marine vessels and locomotives, which generally use older technology than on-road engines).

Another major uncertainty associated with many of the DE epidemiologic studies was the inability to fully control for smoking effects, resulting in possible errors in estimating relative risk increases. Changes in adjustments for smoking could result in considerable changes in relative risk, because smoking has a much larger effect on relative lung cancer risk than is likely for DE. It is difficult to effectively control for a smoking effect in a statistical analysis because cigarette smoke contains an array of biologically active compounds and affects multiple steps of carcinogenesis, thus probably making smokers more susceptible to DE-induced lung cancer than are nonsmokers. A statistical analysis would not be able to adjust for such an effect without having a detailed record of the smoking history of individuals.

A potential uncertainty involves the use of occupational worker data to extrapolate cancer hazard risk to the general population and sensitive subgroups. By sex, age, and general health status, workers are not fully representative of the general population. For example, there is virtually no information to determine whether infants and children or people in poor health

respond differently to DE exposure than do workers. Finally, the use of linear low-dose extrapolation may contribute to uncertainty in estimating environmental risks.

8.3.2. Evaluation of Key Epidemiologic Studies for Potential Use in Quantitative Risk Estimates

Among the available epidemiologic studies, only the railroad worker studies and the Teamster truck driver studies have reconstructed quantitative historical exposure data for possible use in deriving a unit risk estimate for DE-induced lung cancer. This section evaluates the strengths and limitations of these data and their suitability for dose-response analysis.

8.3.2.1. *Railroad Worker Studies*

Garshick and colleagues conducted both cohort and case-control studies of lung cancer mortalities among U.S. railroad workers registered with the U.S. Railroad Retirement Board (RRB).

In the cohort study (Garshick et al., 1988), lung cancer mortality was ascertained through 1980 in 55,407 railroad workers, age 40 through 64 in 1959, with at least 10 years of work in selected railroad jobs (39 job titles). The cohort was selected on the basis of job titles in 1959. Industrial hygiene evaluations and descriptions of job activities were used to classify jobs as exposed or unexposed to diesel emissions. Workers with recognized asbestos exposure were excluded from the job categories selected for study. However, a few jobs with some potential for asbestos exposure were included in the cohort. Each subject's work history was determined from a yearly job report filed by his employer with the RRB from 1959 until death or retirement. The year 1959 was chosen as the effective start of DE exposure for this study because by this time 95% of the locomotives in the United States were diesel powered. The author reported statistically significant relative risk increases of 1.57 for the 40-44 year age group and 1.34 for the 45-49 year age group, after exclusion of workers exposed to asbestos and controls for smoking. Age groups were determined by their ages in 1959.

A main strength of the cohort study is the large sample size (55,407), which allowed sufficient power to detect small risks. This study also permitted the exclusion of workers with potential past exposure to asbestos. The stability of job career paths in the cohort ensured that of the workers 40 to 64 years of age in 1959 classified as DE-exposed, 94% of the cases were still in DE-exposed jobs 20 years later.

The main limitation of the cohort study is the lack of quantitative data on exposure to DE. The number of years exposed to DE was used as a surrogate for dose. The dose, based on duration of employment, has inaccuracies because individuals were working on both steam and diesel locomotives during the transition period. It should be noted that the investigators included

only exposures after 1959; the duration of exposure prior to 1959 was not known. Other limitations of this study include its inability to examine the effect of years of exposure prior to 1959 and the less-than-optimal latency period for lung cancer expression. No adjustment for smoking was made in this study. For a detailed description of this study please refer to Chapter 7, Section 7.2.1.7.

Garshick and colleagues also conducted a case-control study of railroad workers who died of lung cancer between 1981 and 1982 (Garshick et al., 1987). The author reported statistically significant increased odds ratios (with asbestos exposure accounted for) of 1.41 (95% confidence interval [CI] = 1.06, 1.88) for the ≤64 year age group and 1.64 (95% CI = 1.18, 2.29) for the ≤64 year age group with ≥20 years of exposure when compared with the 0-4 year exposure group. The population base for this case-control study was approximately 650,000 active and retired male U.S. railroad workers with 10 years or more of railroad service who were born in 1900 or later. The cases were selected from deaths with primary lung cancer, which was the underlying cause of death in most cases. Each case was matched to two deceased controls whose dates of birth were within 2.5 years of the date of birth of the case and whose dates of death were within 31 days of the date of death noted in the case. Controls were selected randomly from workers who did not have cancer noted anywhere on their death certificates and who did not die of suicide or of accidental or unknown causes. A total of 1,256 cases and 2,385 controls were selected for the study. Among younger workers, approximately 60% had exposure to DE, whereas among older workers, only 47% were exposed to DE. DE exposure surrogates for workers were similar to those in the cohort study. Asbestos exposure was categorized on the basis of jobs held in 1959, or on the last job held if the subject retired before 1959. Smoking history information was obtained from the next of kin.

The strengths of the case-control study are consideration of confounding factors such as asbestos exposure and smoking; classification of DE exposures by job titles and industrial hygiene sampling; and exploration of interactions between smoking, asbestos exposure, and DE exposure. Major limitations of this study include (a) possible overestimation of cigarette consumption by surrogate respondents; (b) use of the Interstate Commerce Commission (ICC) job classification as a surrogate for exposure, which may have led to misclassification of DE exposure jobs with low intensity and intermittent exposure, such as railroad police and bus drivers, as unexposed; (c) lack of data on the contribution of unknown occupational or environmental exposures and passive smoking; and (d) a suboptimal latency period of 22 years, which may not be long enough to observe a full expression of lung cancer. For a detailed description of this study, please see Chapter 7, Section 7.2.2.4.

As a part of these epidemiologic studies, Woskie et al. (1988a) conducted an industrial hygiene survey in the early 1990s for selected jobs in four small northern railroads. DE

exposure was considered as a yes/no variable based on job in 1959 and estimated years of work in a diesel- exposed job as an index of exposure. Thirty-nine job titles were originally identified and were then collapsed into 13 job categories and, for some statistical analyses, into 5 categories (clerks, signal maintainers, engineers/firers, brakers/conductors/hostlers, and shop workers) (Woskie et al., 1988b; Hammond et al., 1988). As discussed below, these exposure estimations were used by Crump et al. (1991) and by Cal EPA (1998) for their dose-response analyses.

8.3.2.1.1. ***Potential for the data to be used for dose-response modeling.*** Both case-control and cohort studies can be used for dose-response analysis if exposure for each worker is available. Control of a smoking effect is important when lung cancer is the disease of interest. However, as discussed previously (see Section 8.3.1), one may not be able to control smoking completely in a dose-response analysis because of the lack of detailed records of the smoking history of individuals.

Garshick et al. (1988) reported a positive relationship of relative risk and duration of exposure by modeling age in 1959 as a covariate in an exposure-response analysis. The positive relationship disappeared when attained age was used instead of age in 1959, and a negative dose-response was observed (Crump et al., 1991). This negative dose-response continued to be upheld in a subsequent reanalysis (Crump, 1999). Garshick (letter from Garshick, Harvard Medical School, to Chao Chen, U.S. EPA, dated August 15, 1991) performed further analysis and reported that the relationship between years of exposure and risk of lung cancer, when adjusted for attained age and calendar year, was flat to negative depending upon which model was used. In contrast, California EPA (Cal EPA, 1998) found a positive dose-response by using age in 1959 but allowing for an interaction term of age and calendar year in the model.

Crump et al. (1991) also found, and Garshick (letter from Garshick, Harvard Medical School, to Chao Chen, U.S. EPA, dated August 15, 1991) confirmed, that in the years 1977-1980 the death ascertainment was not complete. About 20% to 70% of deaths were unaccounted for, depending upon the calendar year. Further analysis, based on job titles in 1959 and limited to deaths occurring through 1976, showed that the youngest workers still had the highest risk of dying of lung cancer.

Extensive statistical analyses were conducted by a panel convened by HEI (1999) to investigate the utility of the railroad worker cohort for use in dose-response based quantitative risk assessment. Seven models were used to test the data, and the models were formed by varying a number of covariates in different combinations. The covariates included employment duration, cumulative exposure with and without correction for background exposure, and three job categories: clerks and signalmen, train workers (which include engineers/firers/brakers/

conductors), and shop workers. The coefficient for each covariate in a model is used to calculate relative risk for the associated covariate. In summary, the panel found that effects of exposure as defined by an exposure-response curve were either flat or negative in all of the models. In these analyses, relative risk for each job category was assumed to be constant with respect to age. Further exploration of the data showed that the relative risk for train workers was not constant. The panel's statistical analyses also revealed the complexity of the data and difficulties of providing an adequate summary measure of effect, probably because calendar year and cumulative exposure are highly correlated, which makes it especially difficult to sort out their separate effects. The difficulty of providing an adequate measure of DE effect was further demonstrated in Table C.3 of the HEI report, in which negative or positive effects for cumulative exposure (with background exposure adjustment) were obtained depending on whether or not job category was included in the model. A similar review of the divergent views about the railroad worker dose response also can be found in Chapter 7, Section 7.2.1.7.

The diverging results about the presence or absence of exposure response for the railroad worker data have become a source of continuing debate about the suitability of these data for estimating DE cancer risk. Although it is difficult to identify the exact reason for the diverging findings, the "age effect" appears to be a main source of uncertainty because age, calendar year, and cumulative exposure are not mutually independent. Therefore, an ideal dose-response analysis would account for the ages when exposure to DE began and terminated, along with the attained age and other covariates for each person, using age-dependent exposure concentration rather than cumulative exposure over lifetime as a dosimeter. This analysis would be possible for the railroad workers if information were available on the ages when exposure began and terminated.

Given the equivocal evidence for positive exposure response, EPA has not derived a unit risk on the basis of the available railroad worker data. This determination should not be construed, however, to imply that the railroad worker studies contain no useful information on lung cancer risk from exposure to DE.

8.3.2.2. *Teamsters Union Trucking Industry Studies*

Steenland et al. (1990) conducted a case-control study of lung cancer deaths in the Central States Teamsters Union to determine the risk of lung cancer among different trucking industry occupations. The study found statistically significant increased odds ratios for lung cancer of 1.89 and 1.64, depending on years of employment. Cases comprised all deaths from lung cancer (1,288). The 1,452 controls comprised every sixth death from the entire file, excluding deaths from lung cancer, bladder cancer, and motor vehicle accidents. Individuals were required to have 20 years tenure in the union to be eligible to claim benefits.

Detailed information on work history and potential confounders such as smoking, diet, and asbestos exposure was obtained by questionnaire. On the basis of interview data and the 1980 census occupation and industry codes, subjects were classified either as nonexposed or as having held other jobs with potential DE exposure. The Teamsters Union work history file did not have information on whether men drove diesel or gasoline trucks, and the four principal occupations were long-haul drivers, short-haul or city drivers, truck mechanics, and dockworkers. Subjects were assigned the job category in which they had worked the longest.

The main strengths of the study are the availability of detailed records from the Teamsters Union, a relatively large sample size, availability of smoking data, and measurement of possible asbestos exposures. Some limitations of this study include possible misclassifications of exposure and smoking habits, as information was provided by next-of-kin and lack of sufficient latency to observe lung cancer excess.

Steenland et al. (1998) conducted an exposure-response analysis by supplementing the data from their earlier case-control study of lung cancer and truck drivers in the Teamsters Union with exposure estimates based on a 1990 industrial hygiene survey of EC exposure (Zaebst et al., 1991), a surrogate for DE in the trucking industry. Available data indicate that exposure to workers in the trucking industry in 1990 averaged 2-27 $\mu g/m^3$ of EC. The 1990 exposure information was used by Steenland as a baseline exposure measurement to reconstruct past exposure (in the period of 1949 to 1983) by assuming that the exposure for workers in different job categories is a function of highway mileages traveled by heavy-duty vehicles and efficiency of the engine over the years.

The industrial hygiene survey by Zaebst et al. (1991) of EC exposures in the trucking industry provided exposure estimates for each job category in 1990. The EC measurements were generally consistent with the epidemiologic results, in that mechanics were found to have the highest exposures and relative risk, followed by long-haul and short-haul drivers. Dockworkers who had the lowest exposures also had the lowest relative risks.

Past exposures were estimated assuming that they were a function of (a) the number of heavy-duty trucks on the road, (b) the particulate emissions (grams/mile) of diesel engines over time, and (c) leaks from truck exhaust systems for long-haul drivers. Estimates of past exposure to EC (as a marker for DE exposure) were made based on the assumption that average 1990 levels for a particular job category could be assigned to all subjects in that category, and that levels prior to 1990 were directly proportional to vehicle miles traveled by heavy-duty trucks and the estimated emission levels of diesel engines. For example, a 1975 exposure level was estimated by the following equation: 1975 level = 1990 level × (vehicle miles 1975/vehicle miles 1990) × (emissions 1975/emissions 1990). Once estimates of exposure for each year of work history were derived for each subject, analyses were conducted by cumulative level of estimated

carbon exposure. As with most epidemiologic studies, the endeavors to reconstruct exposures for epidemiologic studies are subject to uncertainties.

8.3.2.2.1. ***Potential for the data to be used for dose-response modeling.*** Steenland et al. (1998) analyzed their case-control data and showed a significant positive trend in lung cancer risk with increasing cumulative exposure to DE. The study by Steenland et al. (1998) could provide a valuable database for calculating unit risk for DE emissions. The strength of this data set is that the smoking histories of workers were obtained to the extent possible. Smoking is especially important in assessing the lung cancer risk due to DE exposure because smoking has much higher relative risk (or odds ratio) of lung cancer than does DE. In the Steenland et al. (1998) study, the overall (ever-smokers vs. nonsmokers) odds ratio for developing lung cancer from smoking is about 7.2, which is about fivefold larger than the 1.4 relative risk increase from a large synthesis of many DE epidemiologic studies. It is possible that a modest change of information on smoking and diesel exposure might alter the conclusion and risk estimate.

Another strength of the Teamster data for use in environmental risk assessment for the general population is that exposures of Teamsters are closer to ambient exposures than are those of railroad workers. The Teamsters Union truck driver case-control workers had cumulative exposure ranging from 19 to 2,440 $\mu g/m^3$-years of EC, with the median and 95th percentile, respectively, of 358 and 754 $\mu g/m^3$-years of EC. The median and 95th percentile of an environmentally equivalent exposure would be 3 and 6 $\mu g/m^3$, respectively.[1] These environmental equivalent exposures for the Teamsters Union truck drivers are close to the estimated ambient exposures of <1.0 $\mu g/m^3$ to 4.0 $\mu g/m^3$ (see Table 2-31).

Steenland et al. (1998) stated that their risk assessment is exploratory because it depends on estimates about unknown past exposures. An EPA reanalysis of DE exposure for this study is underway. With a revised exposure assessment, a reevaluation of the dose-response would be appropriate. In a recent review, HEI (1999) concluded that the Teamsters studies may be useful for quantitative risk assessment, but significant further evaluation and development are needed. Given the ongoing reanalysis of exposure, EPA will not, at this time, use the Steenland et al. (1998) occupational risk assessment findings to derive equivalent environmental parameters and cancer unit risk estimates.

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[1]The conversion assumes (a) DPM = 40% EC as reported by Steenland et al. (1998), (b) environmental equivalent exposure is approximately = 0.21 × occupational exposure, and (c) 70 $\mu g/m^3$-years is equivalent to a lifetime of exposure at 1 $\mu g/m^3$.

8.3.3. Conclusion

Even though available evidence supports a conclusion that DE is likely to be a human lung carcinogen, the conclusion of the dose-response evaluation is that the available data are not sufficient to confidently estimate a cancer unit risk or unit risk range. The absence of such a cancer unit risk for DE limits the ability to quantify, with confidence, the potential impact of the hazard on exposed populations. Two significant short-term activities are underway to improve the epidemiologic database for dose-response assessment: (1) a follow-up study to correct the undercounting of mortality in the Garshick et al. (1988) railroad worker study, and (2) an EPA-sponsored effort to improve the exposure estimates for Teamsters Union truck drivers (Steenland et al., 1998). EPA will monitor this ongoing research as well as the ongoing NCI-NIOSH study of nonmetal miners and the recently NCI-funded epidemiologic study of truck drivers. As these studies or other new data become publicly available, EPA will reconsider the merit of conducting additional dose-response analysis and unit risk derivation.

8.4. PERSPECTIVES ON CANCER RISK

Although the available data are considered inadequate to confidently estimate a cancer unit risk, this does not mean that there is no information about the possible cancer risk of DE. To examine the significance of the potential cancer hazard from environmental exposure to DE, all relevant epidemiologic and exposure data as well as simple risk assessment tools can be used. Such an approach does not produce confident estimates of cancer unit risk. Rather, these exploratory approaches provide a perspective on the possible magnitude of cancer risk and thus insight about the potential significance of the hazard. This section describes approaches and methods that are used to gauge the magnitude of possible cancer risk from ambient exposure to DE.

The first approach involves examining the differences between the levels of occupational and ambient environmental exposures, while assuming that cancer risk to DE is linearly proportional with cumulative lifetime exposure. Risks to the general public would be low in comparison to occupational risk if the differences in exposure are large (e.g., about three orders of magnitude or more). On the other hand, if the exposure differences are smaller (i.e., within one to two orders of magnitude), environmental risks become more of a concern as they approach the range of workers' risk observed in epidemiologic studies of past occupational exposures. This assumes that the carcinogenic potency of historical and current-day DE is not significantly different, a reasonable assumption, though not without uncertainty.

Table 8-1 shows occupational exposure estimates for some of the occupational groups where increased relative risks of lung cancer (e.g., meta-analyses) have been analyzed. Given that no statistical properties associated with these exposure estimates are known, their use here is

Table 8-1. DPM exposure margins (ratio of occupational ÷ environmental exposures)

Occupational group	Estimated occupational exposure/concentration ---------- Environmental equivalent [a]	Exposure margin ratio - average environmental exposure for 0.8 μg/m³ of environmental exposure[b]	Exposure margin ratio - high-end environmental exposure for 4.0 μg/m³ of environmental exposure[b]	Reference[c]
Public transit workers	15-98 μg/m³ ---------- 3-21 μg/m³	4-26	0.8-5	Birch and Cary, 1996
U.S. railroad workers	39-191 μg/m³ ---------- 8- 40 μg/m³	10-50	2-10	Woskie et al., 1988b
Fork Lift Operators	7-403 μg/m³ ---------- 1- 85 μg/m³	2-106	0.37-21	Groves and Cain, 2000[d]
High end boundary estimate	1200 μg/m³ ---------- 252 μg/m³	315	63	see text discussion in Section 8.4

[a] Equivalent environmental exposure = occupational exposure × 0.21, see Chapter 2, Section 2.4.3.1, some values are rounded.
[b] 0.8 μg/m³ = average 1990 nationwide on-road exposure estimate from HAPEM model; the companion rural estimate is 0.5 μg/m³, and 4 μg/m³ is
a high-end estimate. The 1996 nationwide average is 0.7 μg/m³, the companion rural estimate is 0.2 μg/m³; however, a high-end estimate is not available for 1996. See Chapter 2, Sections 2.4.3.2.1 and 2.4.3.2.2.
[c] See Table 2-27 for more details about Birch and Cary, Woskie.
[d] 403 μg/m³ is a 99 percentile estimate of EC/μg/m³, the DPM equivalent of the EC measurement can be estimated as DPM = EC x 0.62 to 1.31.

not intended to be precise or to match with specific epidemiologic data, but rather to provide a broad range of possible exposures in the workplace. The purpose is to identify a high- and low-end occupational exposure consistent with the occupational groups of interest and then to compare these to estimates of environmental exposure. Given the special interest in discerning the lower risk magnitude, especially to see if the lower risk might be above or below one in 1 million, a high-end exposure estimate would be used, and as discussed later, the occupational exposure can be arbitrarily increased (e.g., toward an extreme value) to ensure that a low end of risk is identified, consistent with the reported occupational risk increases. Environmental exposure data from on-road vehicle emissions are based on the 1990 nationwide exposure estimates from the HAPEM model (see Chapter 2, Section 2.4.3.2.1). Both average (0.8 μg/m³) and high-end exposures (4 μg/m³) are used.

In order to compare differences between occupational and environmental exposures, it is necessary to convert occupational exposure to continuous exposure (i.e., environmental equivalent exposure = 0.21 × occupational exposure, see Section 2.4.3.1). Accordingly, Table 8-1 shows equivalent environmental levels and the ratios of occupational to environmental

exposures, referred to as exposure margins (EMs). An EM of 1 or less indicates that environmental exposure is comparable to occupational exposure. An EM >1 means that the occupational equivalent exposure is greater than the benchmarked environmental exposure.

Table 8-1 shows that the EMs based on the average nationwide environmental exposure (0.8 $\mu g/m^3$) approach three orders of magnitude. EM's that range from 1 to 10 also can be viewed as showing that adjusted occupational exposures are relatively close to the ambient environmental levels that were chosen as benchmarks. This closeness sets the stage for less uncertainty in hazard and risk extrapolation from the occupational to environmental setting. It also raises a concern that risks to the general public could approach worker risks that were observed in the occupational epidemiologic studies. Table 8-1 is based upon DE exposure estimates from on-road sources only. With the addition of exposure from nonroad sources, the average nationwide-based EM ratios would be lower. For example, using 1996 exposure data for urban populations (Table 2-30), the exposure from on-road sources is 0.5 $\mu g/m^3$, whereas nonroad sources contribute 0.9 $\mu g/m^3$, for a total of 1.4 $\mu g/m^3$. Using this exposure value in place of the EM calculation of Table 8-1 (1990 estimate of 0.8) produces a nearly 43% reduction in the EM ratio. A comparison of EM changes for the high-end on-road plus nonroad exposure is not possible at the present time because the 1996 data have not yet been modeled to obtain a high-end value similar to the 1990 value of 4.0 $\mu g/m^3$.

A second approach to explore the possible cancer risk to the general population from environmental exposure to DE is more quantitative. One begins by examining the risk observed in DE-exposed workers and then making reasoned assumptions as to how these risks can be translated to environmental exposure conditions. Such an approach involves three major assumptions: (1) the excess lung cancer risk as shown in numerous epidemiologic studies and in two meta-analyses is indeed due to DE exposure, (2) the increased lung cancer risk over background is linearly proportional to the lifetime exposure to DE, and (3) the past DE exposure for workers has the same cancer-inducing potential as the current DE in ambient air. Any of these assumptions could have an impact on the possible environmental risk by either increasing or decreasing the risk estimates, including the possibility of a lower or zero risk at environmental levels.

As reviewed in Chapter 7, Section 7.2, numerous epidemiologic studies have shown increased lung cancer risks (i.e., some are deaths, some are cases) among workers in certain occupations. The relative risks or odds ratios range from 1.2 to 2.6. Two independent meta-analyses show smoking-adjusted relative risk increases of 1.35 (Bhatia et al., 1997) and 1.47 (Lipsett and Campleman, 1999). For this analysis, a relative risk of 1.4 is selected as a reasonable estimate. This risk means that the workers faced an extra risk 40% higher than the

5% background lifetime lung cancer risk in the U.S. population.[2] Thus, using the relationship [excess risk = (relative risk-1) × background risk], these DE-exposed workers would have an excess risk of 2% (10^{-2}) (i.e., to develop lung cancer) due to occupational exposure to DE [(1.4 - 1) × (0.05) = 0.02]. The validity of this interpretation depends on an important assumption: that the observed incremental risk of 40% was due to DE exposure alone and not to other unknown extraneous factors. It should be noted, however, that the conclusion about the risk perspective would not be changed even if the incremental risk of 40% were greatly reduced (e.g., to 20%); the conclusion would be changed only if almost all of the incremental risk were due to nondiesel factors.

Next, one would consider the EM (i.e., the EM ratio) between the occupational exposures and general-population environmental exposures. DPM concentrations in the workplace, used as a surrogate for worker exposure, are shown for three occupational worker groups in Table 8-1. These range from 7-403 $\mu g/m^3$ (with an equivalent continuous exposure of 1-85 $\mu g/m^3$). These worker groups are consistent with many of those cited in the meta-analyses. For this exploratory risk estimation approach, we want to intentionally adopt a high-end boundary exposure estimate that is unlikely to be exceeded, so that a lower bounding of the risk would be identified. An occupational boundary exposure of 1,200 $\mu g/m^3$ with its environmental equivalent estimated value of 252 $\mu g/m^3$ has been purposefully adopted to represent a high-end boundary estimate. This happens to be about three times the forklift operator value shown in Table 8-1, and clearly a high-end estimate when Table 2-27 is examined, exclusive of the estimates for miners which are not included in the meta-analyses. It should be noted once again that none of these estimates are intended to be precise.

Table 8-1 shows that the DPM exposure margin ratio between occupational and environmental exposure, using the nationwide average exposure value of 0.8 $\mu g/m^3$, may range from 2 to 315 when the boundary estimate is used, and range from 0.37-63 when 4.0 $\mu g/m^3$ is used as a high-end environmental benchmark exposure. Some of these extreme values will be used, as discussed in the next paragraph.

Risks from environmental exposure depend on the shape of the dose-response curve in the range between occupational and environmental exposures. If lifetime risks in this range were

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[2]The background rate of 0.05 is an approximated lifetime risk calculated by the method of lifetable analysis using age-specific lung cancer mortality data and probability of death in the age group taken from the National Health Statistics (HRS) monographs of Vital Statistics of the U.S. (Vol. 2, Part A, 1992). Similar values based on two rather crude approaches also can be obtained: (1) $59.8 \times 10^{-5} / 8.8 \times 10^{-3} = 6.8 \times 10^{-2}$ where 59.8×10^{-5} and 8.8×10^{-3} are, respectively, the crude estimates of lung cancer deaths (including intrathoracic organs, estimated to be less than 105 of the total cases) and total deaths for 1996 reported in Statistical Abstract of the U.S. (Bureau of the Census, 1998, 118th Edition), and (2) 156,900/270,000,000 × 76 = 0.045, where 156,900 is the projected lung cancer deaths for the year 2000 as reported in Cancer Statistics J of the American Cancer Society, Jan/Feb 2000), 270,000,000 is the current U.S. population, and 76 is the expected lifespan.

to fall proportionately with reduced exposure, and if one assumes that past occupational exposures were at the high-boundary end, then the risk from average environmental exposure could be between 10^{-5} and 10^{-4} ($0.02 \div 315 = 6 \times 10^{-5}$). On the other hand, if occupational exposures for different groups were lower, risks from environmental exposure would be higher. For example, if occupational concentrations or exposures were closer to 100 $\mu g/m^3$, a value that is represented in several data sets shown in Table 8-1 (with an equivalent environmental exposure of 21 $\mu g/m^3$ and a corresponding EM of 26), then risks from environmental exposure would approach 10^{-3} ($0.02 \div 26 = 8 \times 10^{-4}$). If lifetime risks were to fall more than proportionately, then risks would be lower. The latter two sources of dose-response uncertainty (i.e., the actual occupational exposures and the shape of the dose-response curve at low exposures) cannot be further defined with currently available information. Use of higher environmental exposures (>0.8 up to 4.0 $\mu g/m^3$) lowers the EM value and increases the estimated risk.

The magnitude of the estimated lifetime cancer risk derived from using a very high-end occupational-to-environmental exposure difference, establishes a reasonable basis to believe that the general population could face possible risks high enough to be of concern. This does not directly address the segments of the population that may be at highest risk: those who are additionally exposed to nonroad sources of DE and children who may be more sensitive to early-life DE exposure, if not in fact, a longer period of potential lifetime exposure.

The analyses presented above are not intended to be precise but are useful in gauging the possible risk range using simple risk exploration methods. Best scientific judgment guided the selection of assumptions and other elements of this analysis which are deemed reasonable and appropriate for identifying possible risks based on the information currently available. These analyses provide a sense of where an upper limit (or "upper bound") of the cancer risk may be. The simple methodologies used are generic and are valid for any increased relative risk data, however, they are not unique to the DE data. These analyses are subject to numerous uncertainties, particularly the lack of actual exposure information in the epidemiologic studies and uncertainties related to the three major underlying assumptions mentioned earlier. Any of these uncertainties could have an impact on the possible risk levels discussed above. Lower risks are possible and one cannot rule out zero risk. The risks could be zero because (a) some individuals within the population may have a high tolerance to exposure from DE and therefore not be susceptible to the cancer risk from environmental exposure, and (b) although evidence of this has not been seen, there could be a threshold of exposure below which there is no cancer risk.

The estimated possible risk ranges (10^{-5} to 10^{-3} as well as lower and zero risk) provide a perspective of the potential significance of the lung cancer hazard. This perspective should not

be viewed as a definitive quantitative characterization of risk. The development of risk estimates does not constitute endorsement of their validity as surrogates for cancer unit risk or their suitability for estimating numbers of cancer cases. Further research is needed to more accurately assess and characterize environmental cancer risks of DE.

8.5. SUMMARY AND DISCUSSION

There are numerous published quantitative dose-response assessments to estimate human cancer risk from exposure to DE that use epidemiologic and/or experimental animal data (see Appendix C). These dose-response assessments were considered but failed to present a fully sufficient basis for a confident derivation of a cancer unit risk. This is because of epidemiologic exposure-related database uncertainties and the recent understanding about the lack of relevance of the rat lung cancer response to environmentally exposed humans. The dose-response analysis in this chapter has focused on the feasibility of using the occupational epidemiologic data to develop dose-response relationships and extrapolating them to the presumably lower levels of environmental exposure. Typically, this would result in the derivation of an exposure/dose-specific cancer unit risk. In the absence of an understanding about the mode(s) of action for DE-induced lung cancer in humans, coupled with the consideration that DE contains many mutagenic and carcinogenic constituents, linear low-dose extrapolation is judged to be an appropriate default choice for dose-response analysis, should there be satisfactory data to perform such an analysis.

This chapter specifically evaluated the suitability of using the railroad worker studies (Garshick et al., 1987, 1988) and the Teamster Union truck driver studies (Steenland et al., 1990, 1998) for dose-response analysis. However, because of uncertainties about the exposure response for the railroad workers and exposure uncertainties for the truck drivers, a dose-response-based cancer unit risk estimate for DE is not developed from these data sets at this time.

In the absence of a unit risk to assess environmental cancer risk, some insight about the possible significance of the hazard can be drawn from the available epidemiologic data and exploratory risk evaluation techniques. A discussion of possible risk is presented in the form of a perspective on the possible magnitude of risk from environmental exposure. The perspective discussion notes the small exposure margins and possible overlap between some occupational and environmental exposure levels. This lessens the uncertainty of extrapolating the occupational hazard and observed risk into the environmental setting. Furthermore, based on a more quantitative approach involving the observed lung cancer from occupational exposures and the magnitude of occupational and environmental exposure differences, an exploratory risk analysis shows that environmental cancer risks possibly range from 10^{-5} to nearly 10^{-3}, while a

consideration of the numerous uncertainties and assumptions also indicates that lower risk is possible and zero risk cannot be ruled out. These risk findings are only general indicators of the potential significance of the lung cancer hazard and should not be viewed as a definitive quantitative characterization of risk or be used to estimate an exposure-specific population impact, i.e., estimating numbers of cancer deaths. Best scientific judgment guided the selection of assumptions and other elements of the analysis which are deemed reasonable and appropriate for identifying possible risks based on the information currently available. Further research is needed to more accurately assess and characterize environmental cancer risks of DE.

This exploratory risk analysis uses data collected from engines built prior to the mid-1990s. While engine exhaust emissions have been decreasing and exhaust composition has been changing in recent years, particularly for on-road engines, EPA believes that the insight gained from the risk perspective is pertinent to current on-road and nonroad engine use. New and cleaner engines will become available in response to environmental concerns and strict new regulations. As cleaner engines replace a substantial number of existing engines, the risk perspective will need to be reevaluated.

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9. CHARACTERIZATION OF POTENTIAL HUMAN HEALTH EFFECTS OF DIESEL EXHAUST: HAZARD AND DOSE-RESPONSE ASSESSMENTS

9.1. INTRODUCTION

Human health risk assessment entails the evaluation of all pertinent information on the hazardous nature of environmental agents, on the extent of human exposure to them, and on the characterization of the potential risk to an exposed population. The information is typically organized into four components: hazard assessment, dose-response assessment, exposure assessment, and risk characterization. This health assessment document focuses only on the hazard and dose-response assessment components. The overall objectives of this diesel engine exhaust (DE) assessment are:

- to identify and characterize the human health effects, i.e., hazards that may result from environmental exposure to DE;
- to determine whether there is a quantitative exposure/dose-response relationship for DE exposure and the health effect in the range of observation, and if sufficient data are available (1) for noncancer effects to derive estimates of exposure that are believed to be without appreciable risk, and (2) for carcinogenicity to derive an exposure/dose-specific cancer unit risk; and
- to summarize and integrate the findings of the assessment into a characterization and discuss the uncertainties.

This chapter summarizes and integrates the key findings about the nature and characteristics of environmental exposure to DE (Chapter 2), health hazard information (Chapters 3, 4, 5, and 7), and dose-response analyses (Chapters 6 and 8) that are relevant to the potential human health effects associated with current-day environmental exposure to DE. It also discusses the uncertainties associated with the key findings, including critical data and knowledge gaps, key assumptions, and EPA's science policy choices that are used to bridge the data and knowledge gaps.

This assessment is the Agency's first health assessment for DE emissions and was developed to provide information about the potential for DE-related environmental health hazards that could be used in evaluating regulatory initiatives under provisions of the Clean Air Act.

9.2. PHYSICAL AND CHEMICAL COMPOSITION OF DIESEL EXHAUST

As reviewed in Chapter 2, DE is a complex mixture of hundreds of constituents in gas or particle phases. Gaseous components of DE include carbon dioxide, oxygen, nitrogen, water vapor, carbon monoxide, nitrogen compounds, sulfur compounds, and low molecular-weight hydrocarbons and their derivatives. The particulate matter of DE, diesel particulate matter (DPM), is composed of elemental carbon (EC), adsorbed organic compounds, and small amounts of sulfate, nitrate, metals, trace elements, water, and unidentified compounds. Incomplete combustion of fuel hydrocarbons as well as engine oil and other fuel components such as sulfur leads to the formation of DPM. DPM is either directly emitted from diesel-powered engines (primary particulate matter) or is formed from the gaseous compounds emitted by a diesel engine (secondary particulate matter).

DE emissions vary in chemical composition and particle sizes among different engine types, fuel formulations, and within engine types according to operating conditions. As the emissions age in the environment they also change. There also have been changes in DE emissions over time as a result of changes in engine technology and fuel reformulation. The following sections identify and characterize the key components of DE that are of concern in possible health outcomes, and discuss the changes in the composition of DE over time. The latter information is critical for making a scientific judgment about the appropriateness of using epidemiologic and toxicologic findings from past DE exposures to assess hazard and risk from current-day environmental exposures. It should be noted that available animal studies are based on exhaust exposures from various model year on-road diesel engines since 1980, whereas many of the epidemiologic studies refer to exposures from on-road and nonroad diesel engines in use from the 1950s through the mid-1990s.

After emission from the tailpipe, DE undergoes dilution, chemical and physical transformations, and dispersion and transport into the atmosphere. After a day or so in the ambient environment, the exhaust mixture is said to be aging, a recognition of the atmospheric transformation processes, mostly focused on the organics present, though some particle size changes also may occur. The public health impact of DE mixture transformations is not clear, as some atmospheric processes alter chemical forms to a less toxic form whereas others seem to produce a chemical form with increased toxicity (Chapter 2, Section 2.3).

9.2.1. Diesel Exhaust Components of Possible Health Concern

The components of DE that are of health concern for this assessment are the particles (elemental carbon core), the organic compounds adsorbed to the particles, and the organic compounds present in the gas phase. The gaseous oxides of carbon, nitrogen, and sulfur are also

of public health interest and the relevant health considerations for these are reviewed separately in EPA's Ambient Air Quality Criteria Documents.

9.2.1.1. *Diesel Particles*

Approximately 80%-95% of DPM mass is in the fine particle size range ($\leq$2.5 micrometers, ambient particulate matter [PM]), with a mean particle aerodynamic diameter of about 0.2 micrometers. Ultrafine particles (<0.1 micrometers), a smaller size component of the fine particles, average about 0.02 micrometers in aerodynamic diameter and account for about 1%-20% of the DPM mass and 50%-90% of the total number of particles in DPM (Chapter 2, Section 2.2.8.3).

Particle size is important for a number of reasons. Particles with aerodynamic diameters >2.5 micrometers (i.e., >$PM_{2.5}$) tend to be retained in the upper portions of the respiratory tract, whereas particles with diameters <2.5 micrometers (i.e., $PM_{2.5}$) are deposited in all areas, especially into the lower portions of the respiratory tract, including the deep lung. These fine and ultrafine particles have a very large surface area per gram mass (Chapter 2, Section 2.2.2), which enables them to adsorb and transport inorganic and organic compounds into the lung (Chapter 3, Section 3.3).

DPM is part of ambient particulate matter (PM). The EPA Emissions Trends Report (U.S. EPA, 2000) indicates that annual nationwide emissions of diesel $PM_{2.5}$ (on-road and nonroad) in 1998 were 77% of all mobile-source emissions in 1998, 23% of the total $PM_{2.5}$ inventory excluding natural and miscellaneous sources, and 6% if the natural and miscellaneous sources are included. Some geographic areas have a higher percentage of DPM in ambient $PM_{2.5}$ because of differences in the number and types of diesel engines present in the area (e.g., on-road engines as well as nonroad engines). For instance, in Manhattan, New York, on-road diesel PM was reported to contribute about 53% of ambient PM_{10} during 3 days in 1993, whereas 1996-1997 studies in the Phoenix and Denver areas showed diesel PM to be 10%-15% of total $PM_{2.5}$ mass (Chapter 2, Section 2.4.2.1).

DPM generally contains a high percentage of EC per unit mass, which can be used as a distinguishing feature from noncombustion sources of $PM_{2.5}$ and, to an extent, other combustion sources. The DPM EC content can range from more than 50% to approximately 75% of the DPM mass depending on age of engine, type of engine (heavy-duty versus light-duty), fuel characteristics, and driving conditions. The organic carbon portion of DPM can range approximately from 19% to 43%, though higher and lower values also have been reported. In comparison, gasoline engine exhaust generally has a reverse pattern of low EC content and a high percentage of organics on the particle mass (see Chapter 2, Table 2-13).

9.2.1.2. *Organic Compounds*

The organic compounds present in the gases and adsorbed onto the particles include a wide spectrum of compounds related to unburned diesel fuel, lube oil, low levels of partial combustion, and pyrolysis products (see Chapter 2, Table 2-19). The organic compounds present in the gaseous phase include alkanes, alkenes, aldehydes, monocyclic aromatic compounds, and polycyclic aromatic hydrocarbons (PAHs). Among the gaseous components of DE, the aldehydes are particularly important because of their potential carcinogenic effects and because they make up an important fraction of the gaseous emissions. Formaldehyde accounts for a majority of the aldehyde emissions (65%-80%) from diesel engines. Acetaldehyde and acrolein are the next most abundant aldehydes. Other gaseous components of DE that are notable for their carcinogenic effects include benzene, 1,3-butadiene, PAHs, and nitro-PAHs (including those with ≤4 rings and nitro-PAHs with 2 and 3 rings). A number of the gaseous compounds (e.g., aldehydes, alkanes, alkenes, NO_x, SO_x) also are known to induce respiratory tract irritation given sufficient exposure (see Chapter 2, Table 2-21). Very small amounts of dioxins have been measured in heavy-duty diesel truck exhaust. These emissions are estimated to represent about 1.2% of the 1995 national dioxin inventory; dioxin emissions from nonroad exhausts have not been estimated (Chapter 2, Section 2.2.7.2).

Organic substances adsorbed onto DPM include C_{14-35} hydrocarbon compounds, PAHs with ≥4 rings, and nitro-PAHs. PAHs and their derivatives comprise <1% of the DPM mass (Chapter 2, Section 2.2.8). Many of these hydrocarbons are known to have mutagenic and carcinogenic properties. California EPA (Cal EPA, 1998) identified at least 19 hydrocarbons present in DE that are known or suspected carcinogens, according to evaluations by the International Agency for Research on Cancer (IARC).

9.2.2. "Fresh" Versus "Aged" Diesel Exhaust

Newly emitted exhaust is termed "fresh," whereas exhaust that is more than 1 or 2 days old is referred to as "aged" because of alterations caused by sunlight and other chemical physical reactions that occur in the atmosphere. The overall toxicological consequence of DE aging is unclear because during aging some compounds in the DE mixture are altered to more toxic forms while others are made less toxic. For example, PAHs present in fresh emissions may be nitrated by atmospheric NO_3 to form nitro-PAHs, thus adding to the existing burden of toxic nitro-PAHs present in fresh exhaust. On the other hand, PAHs present in the gas phase can react with hydroxyl radicals present in the ambient air, leading to a reduced atmospheric lifetime of the original PAHs. Alkanes and alkenes may be converted to aldehydes, and oxides of nitrogen to nitric acid (Chapter 2, Section 2.3).

9.2.3. Changes in Diesel Exhaust Emissions and Composition Over Time

Chapter 2, with its Summary in Section 2.5, provides a full review of emissions trends and a complete characterization of the physical and chemical changes in DE over the years, taking into consideration the lack of consistent analytical and measurement techniques and the variability in emissions based on vehicle mix, driving cycles, engine deterioration, and other factors. Key findings and inferences relevant to the potential health effects of DE are discussed below.

As discussed in Chapter 2, Section 2.2.3, the EPA Emissions Trend Report estimates that DPM_{10} on-road emissions decreased 27% between 1980 and 1998. DPM emission factors (g/mile by model year) from new on-road diesel vehicles decreased on average by a factor of six from the mid-1970s to the mid-1990s. These significant reductions are largely attributable to reductions in three PM components: EC, organic carbon, and sulfate. Limited data are available to assess the changes in emission rates from locomotive, marine, or other nonroad diesel sources over time, although it is estimated that DPM_{10} (≤ 10 μm) emissions from nonroad diesel engines increased 17% between 1980 and 1998 (Chapter 2, Section 2.2.5).

Because of changes in engine technology and fuel composition, the chemical composition of DPM from on-road vehicles has also changed over time. The percentage of soluble organic material associated with DPM decreased by model year from the 1980s to the 1990s, and the proportion of EC is correspondingly higher. PAHs and nitro-PAHs are present in DPM from both new and older diesel engines. There are insufficient data to provide clear insight into the potential for changes in total PAH emissions over time or specific PAHs such as benzo[a]pyrene and 1-nitropyrene. It should be noted that the chemical composition of ambient DPM to which people are currently exposed is determined by a combination of exhaust from older and newer engines as well as on-road and nonroad applications of those engines. Consequently, the decrease in the soluble organic fraction of DPM by model year for on-road engines does not directly translate into a proportional decrease in DPM-associated organic material to which people are exposed. In addition, the contributions from high-emitting and/or smoking diesel engines have not been quantified (Chapter 2, Section 2.5.2).

Because of these uncertainties, the exposure impact of changes in DPM composition over time cannot be confidently characterized. Available data clearly indicate that toxicologically significant organic components of DE (e.g., PAHs, PAH derivatives, nitro-PAHs) were present in DPM and DE in the 1970s and are still present. Even though a significant fraction of ambient DPM (possibly more than 50%) is emitted by nonroad equipment, data are currently inadequate to characterize changes in the chemical composition of DPM from nonroad equipment over time. Given the variation in fuel, engine technology, and in-use operational factors over the years, caution should be exercised in presuming that a decrease in the amount of emissions or emission

constituents from older engines to present day in-use engines will result in a decrease in hazard/risk. In meeting the 2007 federal regulations for heavy-duty DE, the exhaust composition will be markedly changed with a consequence that health hazards are expected to be significantly reduced.

9.3. AMBIENT CONCENTRATIONS AND EXPOSURE TO DIESEL EXHAUST

Chapter 2, Section 2.4 provides information on occupational and environmental exposures to DE in order to provide a context for the hazard assessment and dose-response analysis. Highlights of the available information are discussed below.

DE is emitted from a variety of sources, both on-road (e.g., motor vehicles, construction equipment) and nonroad (e.g., farm equipment, railway locomotives, or marine uses). Environmental exposure to DE is generally higher in urban areas than in rural areas. The concentration of DE in the air will vary within any geographic area depending on the number and types of diesel engines in the area and the atmospheric patterns of dispersal. Some important factors that determine the difference between the ambient concentration of DE and the resultant exposure to an individual include the proximity of a person to the DE source and his/her pattern of activity which, for example, includes outdoor versus indoor activities as well as related breathing rates. Certain occupational populations (e.g., transportation and garage workers, heavy-equipment operators, and others who spend considerable time outdoors) can be exposed to much higher levels of DE than the general population. The amount or number of particles delivered and retained in the lung is one factor that could contribute to differential human susceptibility to DPM. For example, children have smaller lungs than adults and thus could have a higher lung burden of inhaled DPM per lung surface area if their activity pattern results in a high breathing frequency.

As DE is a complex mixture of many constituents, environmental concentration measurements and related human exposure is difficult to precisely measure. Even though levels of a number of DE constituents are generally known, it is difficult to quantify the portion that comes from DE since other types of emission sources also may emit the same constituent. Moreover, there is still incomplete knowledge about the relative roles of the relevant DE constituents in mediating the potential health effects of DE. Historically, exposure levels to DPM have been used as a surrogate marker/dosimeter for whole DE. Although uncertainty exists as to whether DPM mass (expressed as $\mu g/m^3$ of DPM) is the most appropriate dosimeter for health effect purposes, it is considered to be a reasonable choice until more definitive information is available about the mechanisms or mode(s) of toxicity action of DE.

Several techniques exist for estimating ambient concentrations of DPM, including chemical mass balance (CMB) source apportionment, dispersion modeling, and using EC as a

surrogate for DPM. DPM concentrations reported from CMB and dispersion modeling studies in the 1980s suggest that in urban and suburban areas (Phoenix and Southern California), the annual average DPM concentration ranged from 2 to 13 $\mu g/m^3$. In the 1990s, annual or seasonal average DPM concentrations in suburban or urban locations have ranged from 1.2 to 4.5 $\mu g/m^3$. DPM concentrations at a major bus stop in downtown Manhattan ranged from 13.2 to 46.7 $\mu g/m^3$ over a 3-day period in 1993. In nonurban and rural areas in the 1980s, DPM concentrations were reported to range from 1.4 to 5 $\mu g/m^3$. In the 1990s, nonurban air basins in California were reported to have DPM concentrations ranging from 0.2 to 2.6 $\mu g/m^3$ (Chapter 2, Section 2.4.2).

A comprehensive exposure assessment is not presented in this assessment, though EPA is developing this in an analysis called the National Air Toxics Assessment. Interim exposure estimation based on EPA's Hazardous Air Pollutant Exposure Model (HAPEM-MS3 model), for on-road sources only, suggests that in 1996 annual average DPM exposure in urban areas from only on-road engines was 0.7 $\mu g/m^3$, while in rural areas exposure was 0.3 $\mu g/m^3$. Among 10 urban areas, the 1996 annual average estimated exposure ranged from 0.5 to 1.2 $\mu g/m^3$. A high-end exposure estimate for 1996 is not yet available. Comparable 1990 exposure estimates for on-road sources ranged from 0.9 $\mu g/m^3$ for urban areas to 0.5 $\mu g/m^3$ for rural areas. In 1990 exposure estimates for the most highly exposed individuals (e.g., outdoor workers and children who spend large amounts of time outdoors) were estimated to be up to 4.0 $\mu g/m^3$ (Chapter 2, Section 2.4.3.2, Table 2-29). Nationwide level nonroad emission exposures are estimated to be nearly double those from on-road sources.

Estimates for occupational exposures to DE as DPM mass are generally higher than environmental exposures. Tables 2-27 and 2-28 provide historic exposure estimates for specific worker categories. For example, historic DPM exposure estimates range from 39–191 $\mu g/m^3$ for railroad workers, 4–748 $\mu g/m^3$ for firefighters, 7–98 $\mu g/m^3$ for public transit workers and airport crews, 5–61 $\mu g/m^3$ for mechanics and dock workers, and 2–7 $\mu g/m^3$ for long- and short-haul truck drivers. For a direct comparison of lifetime exposures between an occupational setting (8 hours per day, 5 days per week, for 45 years) and environmental exposure (continuous exposure for 70 years), the occupational estimates are converted to an equivalent environmental lifetime estimate,[1] which is also shown in Table 2-28. A conversion of EC-based measurements to total DPM also may be needed for some estimates. The estimated 70-year lifetime exposures equivalent to those for the occupational groups discussed above range from about 0.4–157 $\mu g/m^3$. These data indicate that some lower-end occupational estimates of DPM, when converted to environmental equivalents, overlap the range of estimated environmental exposures

[1]Environmental equivalent occupational exposure = 0.21 × occupational exposure.

to DPM from on-road emissions (national average in 1990 of 0.8 $\mu g/m^3$, with high-end exposures up to about 4 $\mu g/m^3$). The addition of nonroad emission exposures, when appropriate, makes the case for overlap of occupational and environmental exposure more prevalent.

9.4. HAZARD CHARACTERIZATION

The primary health effects of concern from environmental exposure to DE include effects associated with both acute and short-term exposures as well as chronic exposures. It is recognized that acute exposures may produce transitory physiological symptoms of varied severity as well as exacerbation of allergenic effects from acute and repeated exposures. On the basis of combined human and experimental evidence from chronic exposure studies, noncancer respiratory effects and lung cancer are observed.

The health effects data are based on DE from a variety of engines existing before the mid-1990s. There have been changes in the physical and chemical composition of some DE emissions (on-road vehicle emissions) over time, though there is no definitive information to show that the emission changes portend significant toxicological changes. The mode(s) of action for DE toxicity in humans is not understood, and hence knowledge is lacking about the role of exhaust mixture components in modulating the toxicity. Taken together, these considerations have lead to a judgment that the hazards identified from older technology-based exposures are applicable to current-day exposures. As new and cleaner diesel engines replace a substantial number of existing engines, the general applicability of the older data will need to be reevaluated.

As discussed in Chapter 6 (Section 6.4), it is also reasonable to expect that DPM, being a constituent of ambient fine PM ($PM_{2.5}$), would contribute to the wider spectrum of effects that have been associated with ambient $PM_{2.5}$. Community epidemiologic studies have shown that ambient $PM_{2.5}$ exposure is statistically associated with increased mortality (especially among people over 65 years of age with preexisting cardiopulmonary conditions) and morbidity as measured by increases in hospital admissions, respiratory symptom rates, decrements in lung function, and exacerbation of asthma, and possibly immunological effects in the respiratory system. There continues to be little epidemiologic evidence for an effect of ambient exposure to PM on cancer rates (U.S. EPA, 1996a,b), though U.S. EPA's Criteria Document for Ambient PM (expected to be released in 2002) will examine the question further.

9.4.1. Acute and Short-Term Exposures

The combined human and animal evidence indicates that DE can induce irritation to the eye, nose, and throat, as well as inflammatory responses in the airways and the lung following

acute and/or short-term exposure to high concentrations. There also is suggestive evidence for possible immunological and allergenic effects of DE.

9.4.1.1. *Acute Irritation*

DE contains various respiratory irritants in the gas phase and in the particulate phase (e.g., SO_x, NO_x, aldehydes). Acute exposure to DE has been associated with irritation of the eye, nose, and throat, respiratory symptoms (cough and phlegm), and neurophysiological symptoms such as headache, lightheadedness, nausea, vomiting, and numbness or tingling of the extremities. Such symptoms have been described mainly in reports of individuals exposed to DE in the workplace, or in clinical studies in humans exposed acutely to high concentrations of DE. Because of the general lack of validating exposure information in the reports, the role of DE in causing these effects is unknown. An exposure-response relationship for these acute irritation and respiratory symptoms has not been demonstrated (Chapter 5, Section 5.1.1.1).

9.4.1.2. *Respiratory Effects*

Available studies of occupational exposure to DE have not provided evidence for significant decrements of lung function in workers over a work shift or after a short-term exposure period. Short-term and subchronic inhalation studies of DE in animals (rats, mice, hamsters, cats, guinea pigs) showed inflammation of the airways and minimal or no lung function changes. These effects were associated with high DE exposures (up to 6 mg/m^3). Exposure-response relationships have not been established for these responses (Chapter 5, Sections 5.1.1, 5.1.2, and 5.1.3).

9.4.1.3. *Immunological Effects*

Recent human and animal studies show that acute DE exposure episodes can exacerbate immunological reactions to other allergens or initiate a DE-specific allergenic reaction. The effects seem to be associated with both the organic and carbon core fraction of DPM. In human subjects, intranasal administration of DPM has resulted in measurable increases of IgE antibody production and increased nasal mRNA for some proinflammatory cytokines. These types of responses also are markers typical of asthma, though for DE, evidence has not been produced in humans that DE exposure results in asthma. The ability of DPM to act as an adjuvant to other allergens also has been demonstrated in human subjects. For example, co-exposure to DPM and ragweed pollen was reported to significantly enhance the IgE antibody response and cytokine expression relative to ragweed pollen alone. Available animal studies also demonstrate the potential adjuvant effects of DPM with model allergens, e.g., in mouse studies the allergenic reaction to ovalbumin and Japanese cedar pollen (Chapter 5, Sections 5.1.1.1.3 and 5.1.1.1.4).

Additional research is needed to further characterize immunological effects of DE and to determine whether or not the immunological effects constitute a low-exposure hazard. This health endpoint is of considerable public health concern, given the increases in allergic hypersensitivity in the U.S. population (Chapter 5, Section 5.6.2.6).

9.4.2. Chronic Exposure

9.4.2.1. *Noncancer Effects*

Available long-term and cross-sectional human studies have provided evidence for an association between respiratory symptoms (cough and phlegm) and DE exposure, but there was no consistent effect on lung function. DE has been shown in many animal studies of several species to induce lung injury (chronic inflammation and histopathologic changes) following long-term inhalation exposure. DE also has been tested in laboratory animals for other health effects, but no significant effects have been found. Overall, available data lead to the conclusion of a potential chronic respiratory hazard to humans from long-term exposure to DE.

9.4.2.1.1. ***Respiratory effects.*** A few human studies in various diesel occupational settings suggest that DE exposure may impair pulmonary function, as evidenced by increases in respiratory symptoms and some reductions in baseline pulmonary function consistent with restrictive airway disease. Other studies found no particular effects. The methodologic limitations in available human studies limit their usefulness in drawing any firm conclusions about DE exposure and noncancer respiratory effects (Chapter 5, Section 5.1.1.2).

Available studies in animals, however, provide a large body of evidence demonstrating that prolonged inhalation exposure to high concentrations of DE can result in pulmonary injury. A number of long-term laboratory studies in rats, mice, hamsters, cats, and monkeys found varying degrees of adverse lung pathology including focal thickening of the alveolar walls, replacement of Type I alveolar cells by type II cells, and fibrosis. The rat is the most sensitive animal species to DE-induced pulmonary toxicity (Chapter 5, Sections 5.1.3 and 5.4).

Available mechanistic data, mainly in rats, indicates that the DPM fraction of DE is a controlling factor in the etiology of pulmonary toxicity, although a role for the adsorbed organic compounds on the particles and in the gaseous phase cannot be ruled out. The lung injury appears to be mediated by an invasion of alveolar macrophages that release chemotactic factors that attract neutrophils and additional alveolar macrophages, which in turn release mediators (e.g., cytokines, growth factors) and oxygen radicals. These mediators result in persistent inflammation, cytotoxicity, impaired phagocytosis, clearance of particles, and eventually deposition of collagen by activated fibroblasts. This mode of action seems to be operative for a variety of poorly soluble particles in addition to DPM (ILSI, 2000). Because long-term exposure

to DE has been shown to induce exposure-dependent chronic respiratory effects in a wide range of animal species, and the mode of action is deemed relevant to humans, there is a sufficient scientific basis to support a conclusion that humans also could be at hazard for these effects under a chronic exposure condition.

9.4.2.1.2. ***Other noncancer effects.*** The negative results from available studies in several animal species (rats, mice, hamsters, rabbits, monkeys) indicate that DE is not likely to pose a reproductive or developmental hazard to humans. There has been some evidence from animal studies indicating possible neurological and behavioral effects, as well as liver effects. These effects, however, are seen at exposures higher than the respiratory effects. Overall, there is insufficient evidence to conclude that a low-exposure hazard exists for these endpoints (Chapter 5, Section 5.1.3.3).

9.4.2.2. ***Carcinogenic Effects***

Many epidemiologic and toxicologic studies have been conducted to examine the potential for DE to cause or contribute to the development of cancer in humans and animals, respectively. In addition, there are some mode-of-action studies that seek to provide an improved understanding about the underlying carcinogenic process and thus contribute to a better understanding of the likelihood of hazard to humans. The available evidence indicates that chronic inhalation of DE is likely to pose a lung cancer hazard to humans. There is insufficient information for an evaluation of the potential cancer hazard of DE by oral and dermal routes of exposure.

9.4.2.2.1. ***Epidemiologic studies.*** Twenty-two epidemiologic studies about the carcinogenicity of workers exposed to DE in various occupations are reviewed in Chapter 7, Section 7.2. Exposure to DE has typically been inferred on the basis of job classification within an industry, with cumulative exposure based on duration of employment or age. Increased lung cancer risk, although not always statistically significant, has been observed in 8 out of 10 cohort studies and 10 of 12 case-control studies within several industries, including railroad workers, truck drivers, heavy-equipment operators, farm tractor operators, and professional diesel vehicle drivers. The increased lung cancer relative risks generally range from 1.2 to 1.5, although a few studies show relative risks as high as 2.6. Statistically significant increases in relative risk, 1.33 to 1.47, are also shown in two independent meta-analyses. The meta-analyses demonstrate the effect of pooling many studies and in this case show the positive relationship between DE exposure and lung cancer across a variety of DE-exposed occupations.

The generally small increases in lung cancer relative risk (1.2 to 1.5, i.e., less than 2) observed in the epidemiologic studies potentially weakens the evidence of causality. This is because with a relative risk of less than 2, if confounders (e.g., smoking, asbestos exposure) were having an effect on the observed risk increases, then it could be enough to account for the increased risk. With the strongest risk factor for lung cancer being smoking, there is a lingering uncertainty as to whether smoking effects may be influencing the magnitude of the observed increased relative risks, in spite of the fact that in key studies the investigating epidemiologists assert that they have effectively controlled for smoking. In studies in which the effects of smoking were controlled, increased relative risks for lung cancer prevailed. While some studies did not have information on smoking, confounding by smoking is judged unlikely to be significant if the comparison populations were from the same socioeconomic class.

As evaluated in Chapter 7 (Section 7.2.4.5), application of the criteria for causality provides a rational basis to conclude that the increased risks observed in available epidemiologic studies are consistent with a causal association between exposure to DE and occurrence of lung cancer. Overall, the human evidence for potential carcinogenicity for DE is judged to be strong but less than sufficient to satisfy the criteria for a "known" human carcinogen because of exposure uncertainties (lack of historical exposure of workers to DE) and residual uncertainty as to whether all confounders have been satisfactorily accounted for. The epidemiologic evidence is inconclusive for DE being associated with other forms of cancer.

9.4.2.2.2. ***Animal studies.*** DE and its organic constituents, both in the gaseous and particle phase, have been extensively tested for carcinogenicity in many experimental studies using several animal species and with different modes of administration. Several well-conducted studies have consistently demonstrated that chronic inhalation exposure to sufficiently high concentrations of DE produced dose-related increases in lung tumors (benign and malignant) in rats. In contrast, chronic inhalation studies of DE in mice showed equivocal results, whereas negative findings were consistently seen in hamsters. The gaseous phase of DE (filtered exhaust without particulate fraction), was found not to be carcinogenic in rats, mice, or hamsters. The available data indicate that among the traditional animal test species, the rat is the most sensitive species to DE. As reviewed in Chapter 7, Section 7.4, the lung cancer response in rats from high-concentration exposures to DE appears to be mediated by impairment of lung clearance mechanisms owing to particle overload, resulting in persistent chronic inflammation and subsequent pathologic and neoplastic changes (i.e., cancer) in the rat lung. Particle overload conditions in the human lung are not expected to occur as a result of environmental or most occupational exposures to DE. Thus, the increased lung tumors in the rat are not an appropriate

basis from which to judge the potential for a human hazard or perform a dose-response analysis to derive a cancer unit risk for humans.

In several intratracheal instillation studies, DPM, DPM organic extracts, and carbon black, which is virtually devoid of PAHs, have been found to produce increased lung tumors in rats. When directly implanted into the rat lung, DPM condensate containing mainly four- to seven-ring PAHs induced increases in lung tumors. DPM extracts also have been shown to cause skin tumors in several dermal studies in mice and sarcomas in mice following subcutaneous injection. Overall there are consistent findings of carcinogenic activity by the organic extracts of DPM in noninhalation studies (i.e., intratracheal instillation, lung implantation, skin painting). This contributes to the evidence for a potential human hazard.

9.4.2.2.3. ***Other key data.*** While not as extensive as the human and animal carcinogenicity data, other types of data are judged to be supportive of DE's potential carcinogenicity in humans. As mentioned previously, DE is a complex mixture of hundreds of constituents in either the gaseous phase or particle phase. Although present in small amounts, several organic compounds in the gaseous phase (e.g., PAHs, formaldehyde, acetaldehyde, benzene, 1,3-butadiene) are known to exhibit mutagenic and/or carcinogenic activities. PAHs and PAH derivatives, including nitro-PAHs present on the diesel particle, also are known to be mutagenic and carcinogenic. As reviewed in Chapter 4, DPM and DPM organic extracts have been shown to induce gene mutations in a variety of high-dose bacteria and mammalian cell test systems. DPM and DPM organic extracts also have been shown to induce chromosomal aberrations, aneuploidy, and sister chromatid exchange in both rodent and human in vitro tests.

There also is suggestive evidence for the bioavailability of organic compounds from the DE mixture. Elevated levels of DNA adducts in lymphocytes have been reported in workers exposed to DE. In addition, inhalation studies of animals using radio-labeled materials indicate some elution of organic compounds from DPM after deposition in the lung as measured by their presence in biological tissue and fluids (Chapter 3, Section 3.5).

9.4.2.2.4. ***Modes of carcinogenic action.*** The term "mode of action" refers to a series of key biological events and processes that are critical to the development of cancer. As discussed in Section 9.4.2.2.2, there is an understanding of the modes of action for the DE-induced lung tumors in the rat. However, the modes of action by which DE increases lung cancer risks in humans are unknown, and the evidence in rats is not applicable to environmentally exposed humans.

As discussed in Chapter 7, Section 7.4, it is hypothesized that multiple modes of action could be involved in mediating the carcinogenic effect of DE. These modes of action may

include: (a) mutagenic events (e.g., direct effects on DNA and effects on chromosomes) by organic compounds in the gas and particle phase, (b) indirect DNA damage via the production of reactive oxygen species (ROS) induced by particle-associated organics, and (c) particle-induced chronic inflammatory response leading to oxidative DNA damage through the release of cytokines, ROS, etc., and an increase in cell proliferation.

In rats, the particulate phase appears to have the greatest contribution to the carcinogenic effects, and both the particle core and the associated organic compounds have demonstrated carcinogenic properties in one or more test systems. While limited rat data and comparative potency calculations suggest that gas-phase components are not the primary factors in the development of lung cancer, a contributory role of the recognized toxic components cannot be dismissed. The relative importance of the various modes of action may be different at different exposure levels. Evidence from rat studies indicates the importance of the EC component of the DE particle in mediating lung tumor response at high exposure levels. As for the particle-absorbed organics, their inherent toxicity potential gives rise to a hypothesis that they may play a role in low or high exposures to DE.

9.4.2.2.5. ***Weight-of-evidence evaluation.*** Chapter 7, Section 7.5, provides an evaluation of the overall weight of evidence for human carcinogenicity in accordance with EPA's Guidelines for Carcinogen Risk Assessment (U.S. EPA, 1986, 1996a, 1999). The totality of evidence supports the conclusion that DE is a *probable human carcinogen (Group B1)* by inhalation exposure using the criteria in the 1986 guidelines. A cancer hazard narrative for DE also is provided in accordance with the revised draft 1996/1999 guidelines, which concludes that DE *is likely to be carcinogenic to humans* by inhalation from environmental exposures. The common bases for either conclusion include the following lines of evidence:

- strong but less than sufficient evidence for a causal association between DE exposure and increased lung cancer risk among workers in varied occupations where exposure to DE occurs;
- extensive supporting data including the demonstrated mutagenic and/or chromosomal effects of DE and its organic constituents, and knowledge of the known mutagenic and/or carcinogenic activity of a number of individual organic compounds present with particles and in the DE gases;
- evidence of carcinogenicity of DPM and the associated organic compounds in rats and mice by noninhalation routes of exposure; and
- suggestive evidence for the bioavailability of DE organics from DE in humans and animals.

A notable uncertainty in the characterization of the potential cancer hazard of DE at low levels of environmental exposure is the incomplete understanding of about its mode(s) of action for the induction of lung cancer in humans. Available data suggest that DE-induced lung carcinogenicity may be mediated by mutagenic and nonmutagenic events by both the particles and the associated organic compounds, and that a role for the organics in the gaseous phase cannot be ruled out. Given that there is some evidence for a mutagenic mode of action, a cancer hazard is presumed possible at environmental levels of exposure. This is consistent with EPA's science policy position that assumes a nonthreshold effect for carcinogens with a mutagenic component in the absence of definitive data demonstrating a threshold or nonlinear mechanism. Additional support for an environmental hazard also comes from a comparison of the estimated environmental levels to the estimated occupational exposure levels where risk is seen. Given that there is only a minimal margin between environmental and occupational exposure ranges, if not an overlap, the extrapolation of observable hazard from the occupational setting to the ambient environment is relatively confident. Because of insufficient information, the human carcinogenic potential of DE by oral and dermal exposures cannot be determined.

Several organizations previously have reviewed available relevant data and evaluated the potential human carcinogenicity of DE or the particulate component (DPM) of DE. Similar conclusions were reached by various organizations (see Table 7-9). For example, some organizations have concluded that DE is probably carcinogenic to humans (IARC, 1989; IPCS, 1996), or reasonably is anticipated to be a carcinogen (NTP, 2000).

Overall, the weight of evidence for potential human carcinogenicity for DE is considered strong, even though inferences are involved. Uncertainties are present, however, and include the following unresolved issues.

First, there has been a considerable scientific debate about the significance of the available human evidence for a causal association between occupational exposure and increased lung cancer risk. Some experts view the evidence as weak and/or inconsistent while others consider the evidence compelling. This is due to a lack of consensus about whether the effects of smoking and other potential confounders have been adequately accounted for in key studies, and the lack of agreed-upon historical DE exposure data for the available studies.

Second, while the mode of action for DE-induced lung tumors in rats from high exposure is sufficiently understood, the mode of action for the DE lung cancer risk in humans is not known. To date, available evidence for the role of both the adsorbed organics and the carbon core particle has only been shown under high-exposure experimental animal test conditions. There is virtually no information about the relative role of DE constituents in mediating carcinogenic effects at the low-exposure levels.

Additional research is needed to address these issues to reduce the uncertainty associated with the potential cancer hazard of exposure to DE.

The relevance of this hazard characterization to current ambient DE exposures hinges on recognizing that the health effects data are derived from engine technologies and fuels that existed in the past, and that some changes in the DE exhaust mixture have occurred and can be expected in the future. Although decreases in amount and changes in composition of DE emissions have occurred over time for on-road engines, a change is slow to manifest in the environment because, for example, vehicular fleet turnover is slow and the change is slow to dominate across an engine fleet. Available studies have not focused on the potential toxicological effect of the emission changes. There is no compelling evidence at present to show that past and present exhaust characteristics are so toxicologically dissimilar as to render the current use of the assessment's findings outdated.

9.5. DOSE-RESPONSE ASSESSMENT

In assessments of estimated human health risks, human data from environmental exposures are always preferred over animal data, if available, as their use obviates the need for extrapolation across species, e.g., from animals to humans. However, for most environmental agents, available health effects information is generally limited to occupational exposures in studies of humans (e.g., workers) or high experimental exposures to laboratory animals. For the agents with high-exposure data compared to environmental exposure levels of interest, dose-response assessment is performed in two steps: assessment of data in the observable range to derive a point of departure (which usually is the lowest exposure or dose that induces some, minimal, or no apparent effects), followed by extrapolation to lower exposures to the extent necessary. Extrapolation to low exposures is ideally based on the understanding of mode(s) of toxic action of the agent which allows the development and use of a mode of action specific exposure-response model. In the absence of sufficient data, default methods and models are used to extrapolate to the lower exposure levels.

For DE, there is sufficient evidence to conclude that acute or short-term inhalation exposure at relatively high levels can cause irritant effects to the eye, nose, and throat, respiratory symptoms, and neurophysiological symptoms such as headache, nausea, etc., however, no quantitative data are available to derive an estimate of human exposure that is not likely to elicit irritant and inflammatory effects in humans.

There is also sufficient evidence to support the conclusion that DE has the potential to cause cancer and noncancer effects of the lung from long-term inhalation exposure. Chapters 6 and 8 provide dose-response analyses related to the noncancer and cancer hazards to humans, respectively, from lifetime exposure to DE. A dose-response analysis to estimate the expected

response at environmental exposure levels has less uncertainty the closer the animal test or estimated human epidemiologic-related exposures are to the environmental levels of interest. With increasing exposure margins (EM), and thus a greater range of extrapolation, the uncertainty about the shape of the dose-response curve in the region of low-dose extrapolation increases and the possibility of a zero risk cannot be ruled out.

9.5.1. Evaluation of Risk for Noncancer Health Effects

As discussed previously (Section 9.4.2.1), the evidence for potential chronic noncancer health effects of DE is based primarily on findings from chronic animal inhalation studies showing a spectrum of dose-dependent chronic inflammation and histopathological changes in the lung in several animal species including rats, mice, hamsters, and monkeys. A limited number of epidemiologic investigations of workers exposed to DE have not provided consistently clear evidence of significant chronic respiratory effects associated with DE exposure. On the other hand, the relatively large epidemiologic database for ambient PM shows a clear relationship between respiratory effects and ambient fine PM that is partially composed of DPM. The specific role of DPM or any other source-related constituent of ambient PM in causing the observed respiratory effects has not been defined.

The approach taken in this assessment to estimate a level of DE in the air to which humans may be exposed throughout their lifetime without an appreciable risk of deleterious effects is to derive a reference concentration (RfC) for DE based on the consistent data for respiratory inflammation in the rat studies. This approach assumes that humans would respond to DE similarly to the tested animals under similar exposure conditions. An uncertainty of this approach stems from the circumstance that animal studies have used high DE exposures, and the animal results must be translated to humans as well as to lower exposure levels since the potential chronic health effects of DE in humans at environmental exposure levels cannot be ascertained from the available DE human data.

It also is relevant to recognize that DPM is a component of ambient fine PM and that there is a relative wealth of human effects data for ambient PM showing a similarity of certain adverse health effects for DPM and ambient fine PM. This allows one to reasonably expect that the $PM_{2.5}$ National Ambient Air Quality Standard (NAAQS) would provide a measure of protection from DPM, reflecting DPM's current and approximate proportion to $PM_{2.5}$. Ambient $PM_{2.5}$ has been shown to be statistically associated with increased mortality (especially among people over 65 years of age with preexisting cardiopulmonary conditions) and morbidity, as measured by increases in hospital admissions, respiratory symptom rates, and decrements in lung function with both long- and short-term changes in ambient $PM_{2.5}$ concentrations.

9.5.1.1. *Chronic Reference Concentrations for Diesel Exhaust*

An inhalation Reference Concentration (RfC) is based upon long-term data, i.e., chronic exposure, and can be derived from either human or animal data. An RfC is correctly defined as "an estimate of a continuous inhalation exposure to the human population, including sensitive subgroups, with uncertainty spanning perhaps an order of magnitude, that is likely to be without appreciable risks of deleterious noncancer effects during a lifetime." The RfC methodology assumes that there is an exposure threshold below which effects will not occur. The RfC is not a bright line; rather, as the long-term human exposure increases above the RfC, the margin of protection decreases.

With the absence of DE exposure-response data in humans, this assessment derives an RfC for DE based on dose-response data from four chronic inhalation studies in rats (Mauderly et al., 1987; Ishinishi et al., 1988; Heinrich et al., 1995; Nikula et al., 1995). All of these studies used DPM (expressed as $\mu g/m^3$) as a measure of DE exposure. The pulmonary effects, including inflamation and histopathologic lesions, were considered to be the critical noncancer effects. As shown in Table 6-2, the no-observable-adverse-effects levels (NOAELs), the lowest-observable-adverse-effects levels (LOAELs), and the adverse effects levels (AELs) for lung inflammation and histopathologic changes were identified for the first three studies. For the Nikula et al. study, lower 95% confidence estimates of the concentrations of DPM associated with a 10% incidence ($BMCL_{10}$) of chronic pulmonary inflammation and fibrosis were derived since NOAEL's were not observed. For all four studies, human equivalent concentrations (HECs) corresponding to the animal NOAEL, LOAEL, AEL, and $BMCL_{10}$ were then computed using a dosimetry model developed by Yu et al. (1991) as described in Chapter 6, Section 6.5.2, and Appendix A. The dosimetry model accounts for species differences (rat to human) in respiratory exchange rates, particle deposition efficiency, differences in particle clearance rates at high and low doses, and transport of particles to lymph nodes. The purpose is to identify the highest HEC value with no apparent effect, i.e., $NOAEL_{HEC}$.

The highest $NOAEL_{HEC}$ associated with no apparent effect is 144 $\mu g/m^3$ from the Ishinishi et al. (1988) study; this then becomes the point of departure for deriving an RfC. To obtain the RfC, this point of departure was divided by two types of uncertainty factors (UF): a factor of 3 recognizes interspecies (i.e., rat to human) extrapolation uncertainties, and a factor of 10 reflects uncertainties about interindividual human variation in sensitivity. An evaluation of the interspecies extrapolation issues for dosimeteric and pharmacodynamic equivalence between rats and humans showed that although some adjustments could be accounted for, there remained a residual uncertainty, and thus an uncertainty of 3 out of a possible factor of 10 is used. In the absence of mechanistic or specific data, a default value of 10 is considered appropriate to account for possible human variability in sensitivity, particularly for children and people with

preexisting respiratory conditions. The spectrum of the population that may have a greater susceptibility cannot be better characterized until there is additional knowledge about mode of action. The resulting RfC for DE is 5 $\mu g/m^3$ of DPM.

Overall, the confidence level in the RfC is considered medium in a range of low to high confidence. A principal uncertainty of the RfC analysis is the reliance on animal data to predict human risk. The critical effects, chronic inflammation, and pathologic changes, which are well characterized in four animal species, are considered relevant to humans. Collective evidence for all poorly soluble particles, including DPM, indicates that the rat is the most sensitive laboratory animal species tested to date. Although in general the rat is thought to be more sensitive to lung injury than humans to poorly soluble particles (ILSI, 2000), it is not clear that this is the case specifically for diesel. We must recall that DE is a mixture of not just carbon particles but also various organics, both on the particles and in gases. In addition, differences in particle deposition, retention, and clearance mechanisms have been largely but perhaps not completely addressed by the use of the rat-to-human dosimetry model. The use of rat data is not likely to grossly underestimate the human risk for pulmonary noncancer health effects. In terms of the potential for other critical health effects, there is growing evidence suggesting that DE can exacerbate allergenic effects to known sensitizers, while also evoking production of biochemical markers typically associated with asthma. Some work in this area indicates that humans may be as sensitive as rats and mice to the immunologic effects (Chapter 6, Section 6.3.4). This database is currently lacking key exposure-response data, but may in the future provide an alternative basis for RfC derivation. It also should be noted that the ambient PM health effects data show a broader array of adverse human health concerns (e.g., cardiovascular effects, as well as acute exposure effects). With DPM being a ubiquitous component of ambient PM, there is an uncertainty about the adequacy of the existing DE noncancer database to identify all of the pertinent DE-caused noncancer health hazards.

9.5.1.2. *Risks Based on Ambient $PM_{2.5}$*

As discussed in Chapter 6 (Section 6.4), in 1997 EPA established an annual NAAQS for $PM_{2.5}$, at a level of 15 $\mu g/m^3$ to provide protection against adverse health effects associated with both long- and short-term exposures to ambient fine PM. DPM is a typical constituent of ambient fine PM (generally about 10% of $PM_{2.5}$ with some examples up to 36%).[2] Given the

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[2]"A qualitative comparison of adverse effects of exposure to DPM and ambient fine PM shows that the respiratory system is adversely affected in both cases, though a wider spectrum of adverse effects has been identified for ambient fine PM. In contrast to the diesel PM database, there is a wealth of human data for fine PM noncancer effects which indicates that the health effects from fine PM do not have a discernable threshold at this time."

similarity of health concerns for respiratory inflammation and pulmonary health effects from both DPM and fine particles, it is reasonable to expect that DPM contributes to some of the health effects associated with $PM_{2.5}$. Current knowledge is insufficient, however, to describe the relative potencies of DPM and the other components of $PM_{2.5}$. As long as the percentage of DPM to total ambient $PM_{2.5}$ remains in similar proportion, protective levels for $PM_{2.5}$ would be expected to offer a measure of protection from effects associated with DPM.

9.5.1.3. *Conclusions*

This assessment estimates an exposure air level of DE (as measured by DPM) to which humans may be exposed throughout their lifetime without experiencing any adverse noncancer health effects. The approach taken applies the RfC method using data specific to DE to produce an RfC of 5 $\mu g/m^3$ of DPM on the basis of four chronic inhalation studies of DE in rats and a composite uncertainty factor of 30. In addition, this assessment also recognizes the relative wealth of data regarding health effects associated with ambient PM and presumes that a health protective level for $PM_{2.5}$ also would be expected to provide a measure of protection from DPM, a constituent part of $PM_{2.5}$. The $PM_{2.5}$ standard of 15 $\mu g/m^3$ as an annual average thus is expected to provide a measure of protection from DPM noncancer health effects, reflecting DPM's current approximate proportion to $PM_{2.5}$.

9.5.2. Evaluation of Cancer Risks

As discussed in Section 9.4.3, the combined weight of evidence indicates that DE has the potential to pose a cancer hazard to humans at anticipated levels of environmental exposure. The target organ of DE-induced carcinogenicity is the lung. Strong evidence exists for a causal relationship between risk for lung cancer and occupational exposure to DE in certain occupational workers such as railroad workers, truck drivers, heavy-equipment operators (e.g., shipyard, diesel farm equipment, and construction), and transit workers. The evidence, however, was less than sufficient to confidently characterize DE as carcinogenic to humans, and instead the assessment concludes that DE is likely to be a human carcinogen. It also has been shown unequivocally in several studies that DE can cause benign and malignant lung tumors in rats in a dose-related manner following chronic inhalation exposure to high concentrations; however, this response is not thought applicable to predict a hazard to humans exposed at lower environmental levels. The mechanism(s) by which DE would induce lung cancer in humans has not been established, but available data suggest that mutagenic and nonmutagenic modes of action are possible. Hence, for estimating DE cancer risk at low environmental exposures, linear low-dose extrapolation would be considered an appropriate default assumption, which is consistent with EPA's science policy position that in the absence of an understanding of modes of carcinogenic

action, a nonthreshold effect is to be presumed (U.S. EPA, 1986, 1996a). This same assumption has been used by other organizations/risk assessors who have previously used either linear risk extrapolation models or mechanistically based models to estimate cancer risk from environmental exposure to DE (e.g., WHO-IPCS, 1996; Cal EPA, 1998; also see Appendix C).

Dose-response assessment is based on either human or animal data, although human data are always preferred if available. Several quantitative assessments have been conducted by organizations and investigators on the basis of both occupational data and rat data (see Appendix C). However, more recent evidence indicates that DE causes tumors in the rat lung via a mode of action that involves impairment of lung clearance mechanisms (referred to as "lung overload response") associated with high exposures. This lung overload response is not expected in humans exposed to environmental levels (nor is it expected to occur in many occupational exposures), and thus the rat lung tumor dose-response data are not considered suitable for predicting human risk at low environmental exposures. Given that the rat data are not appropriate for estimating cancer risk to humans, this assessment focuses on using the occupational epidemiologic data for estimating environmental risk of DE to humans.

Even though occupational data are considered most relevant for use in dose-response assessment, uncertainties exist, including the following issues:

- the use of DPM (expressed as $\mu g/m^3$) as a surrogate dosimeter for DE exposure, given that the relative roles of various constituents in mediating carcinogenic effects and the mode of carcinogenic action are still unknown;
- the representativeness of occupational populations for the general population and vulnerable subgroups, including infants and children and individuals with preexisting diseases, particularly respiratory conditions;
- the lack of actual DE exposure data for workers in the available epidemiologic studies;
- possible confounders (smoking and asbestos exposure) that could contribute to the observed lung cancer risk in occupational studies of DE if the control for these confounders is not adequate; and
- whether or not an exposure-response relationship for occupational lung cancer risk can be estimated for DE.

Chapter 8, Section 8.3, provides a discussion of these uncertainties, along with an evaluation of the suitability of available occupational studies for a derivation of a cancer unit risk estimate for DE. Unit risk is defined as the estimated upper-bound cancer risk at a specific exposure or dose

from a continuous average lifetime exposure of 70 years (in this case, cancer risk per $\mu g/m^3$ of DPM).

Among the occupational studies, the railroad worker studies (Garshick et al., 1987, 1988) and the Teamsters Union truck driver studies (Steenland et al., 1990, 1998) are considered to have the best available exposure data for possible use in establishing exposure-response relationships and deriving a cancer unit risk. There have been different views on the suitability of these studies for estimating environmental cancer risks (e.g., Cal EPA, 1998; HEI, 1995, 1999). Given the equivocal evidence for the presence or absence of an exposure-response relationship for the study of railroad workers, and exposure uncertainties for the study of truck drivers, it is judged that available data are too uncertain at this time for the development of a confident quantitative dose-response analysis and subsequent derivation of cancer unit risk for DE.

In the absence of a cancer unit risk to assess population cancer risk, this assessment provides a "perspective" about the possible magnitude of risk in the population from environmental exposure to DE. One approach to estimating the possible magnitude of risk involves simply noting that risks to the general public would be low in comparison with occupational risk if the differences in the lower environmental exposures compared to the higher occupational exposures are large. If the differences are small, the environmental risks would approach the workers' risk observed in studies of past occupational exposures. A comparison of environmental equivalent occupational and ambient environmental exposures showed that for certain occupations, there is a potential for overlap between environmental exposure and the estimated environmental equivalent occupational exposure, while in other cases the environmental exposures could be up to about 100-fold lower than the occupational levels (see Table 8-1). For the exposure overlap case, one can infer that the environmental risk could be the same as, or approach, the risk magnitudes observed in the occupational studies. In the 100-fold lower case, the environmental risk could be about 100-fold lower than the observed risk magnitudes in the occupational studies. Risks to the general public are of potential concern when a significant risk is seen in the occupational setting and the difference between occupational and ambient exposure may overlap or is relatively small (within one to two orders of magnitude).

A second approach, which is related to the first approach but more quantitative, is to estimate possible ranges of lung cancer risk from occupational exposures to DE, and then use a proportional relationship of exposure differences (e.g., EMs) to scale the occupational risk to the environmental exposure setting. Given the range of observed relative risks or odds ratios of lung cancer in a number of occupational studies, a relative risk increase of 1.4 was selected as a reasonable estimate of occupational risk for the purpose of this analysis. The relative risk of 1.4

means that the workers faced an extra risk that is 40% higher than the approximate 5% background lifetime lung cancer risk in the U.S. population. Using the relationship [*excess risk = (relative risk-1) × background risk*], 2% of these DE-exposed workers (i.e., 10^{-2} risk) would have been at risk (and developed lung cancer) attributable to occupational exposure to DE.

Using a nationwide average environmental exposure (0.8 $\mu g/m^3$ DPM), and assuming (a) the excess lung cancer risk from occupational exposure is about 10^{-2}; and (b) the past occupational exposures were no higher than about 1,200 $\mu g/m^3$ (equivalent to an environmental equivalent EM of 315, connoting a relatively large EM), the environmental cancer risk would fall between 10^{-4} and 10^{-5}. The selection of 1,200 $\mu g/m^3$ is a very high value intentionally selected to illustrate a high-end exposure boundary and thus a lower bounding of risk calculated by this exploratory approach. On the other hand, if occupational exposures for some groups were lower, for example, closer to 100 $\mu g/m^3$ (equivalent to an environmental equivalent EM of 26, connoting a smaller EM), the environmental risk would be higher and approach 10^{-3}. The selection of 100 $\mu g/m^3$ is purposefully toward the lower end of the reported occupational exposure range which spans 7–403 $\mu g/m^3$ in Table 8-1. The risk estimates are attended by numerous uncertainties; their inclusion in this document does not constitute Agency endorsement of their validity as a surrogate for cancer unit risk; the range of values is not useful for estimating numbers of cancer cases; and the range of possible risk from environmental exposures also could be lower and a zero risk cannot be ruled out.

These types of exploratory analyses are not intended to be precise or provide a definitive characterization of cancer risk but are useful in illustrating and gauging the possible range of risk based on applying reasonable judgment. The analyses provides a sense of where an upper limit (or "upper bound") of the risk may be. These analyses are subject to uncertainties, particularly the lack of actual exposure information for the occupational epidemiologic studies and the use of public-health-conservative risk assessment assumptions. The possible risks also could be lower and a zero risk cannot be ruled out because (a) some individuals in the population may have a high tolerance to exposure from DE and therefore not be susceptible to cancer from environmental exposure, and (b) although not reported, there could be a threshold of exposure below which there is no cancer risk. Given these circumstances, we refer to this risk analysis as a "perspective" on possible risks. Best scientific judgment guided the selection of assumptions and other elements of this analysis which are deemed reasonable and appropriate for identifying possible risks based on the information currently available. Further research is needed to more accurately assess and characterize environmental cancer risks from DE.

9.6. SUMMARY AND CONCLUSIONS

The available health effects data show that acute (short-term episodic exposure) and chronic (long-term) exposure to DE can pose hazards to humans and that environmental exposures, in some cases, may have a risk.

At relatively high acute exposures, DE can cause acute irritation to the eye and upper respiratory airways and symptoms of respiratory irritation which may be temporarily debilitating. Evidence also shows that DE has immunological toxicity that can induce allergic responses (some of which are also typical of asthma) and/or exacerbate existing respiratory allergies. While the hazard potential is important for these acute and short exposure-related effects, quantitative dose-response estimates for these effects could not be developed because of the lack of exposure-response information.

It is concluded that long-term exposure to low levels of DE poses a hazard for chronic inflammation and pathological changes in the human lung. A level of human lifetime exposure thought to be without appreciable risk for lung damage is estimated to be 5 $\mu g/m^3$ of DPM, this being a calculated RfC value for DE. Because DPM is a constituent of ambient $PM_{2.5}$ and there is some similarity in potential adverse effects from DE and $PM_{2.5}$, it is expected that a measure of protection from health effects associated with DE is provided by the 1997 annual $PM_{2.5}$ NAAQS, set at a level of 15 $\mu g/m^3$.

DE is considered to pose a human lung carcinogenicity hazard, which is expressed in a weight-of-evidence conclusion that DE is judged to be a "probable" human carcinogen, or is "likely to be carcinogenic in humans by inhalation" at environmental or higher exposure conditions. Because of uncertainty in the available exposure-response data, a cancer unit risk/cancer potency for DE has not been derived. One should note that the closeness of the high-end environmental exposures and low-end estimates of occupational exposure suggest less uncertainty in the extrapolation of hazard and possible risk to the environmental setting. Exploratory analyses using public health conservative assumptions provides a perspective on the possible range of lung cancer risk from environmental exposure to DE. Best scientific judgment guided the selection of assumptions and other elements of this analysis which are deemed reasonable and appropriate for identifying possible risks based on the information currently available. These analyses indicate that lifetime cancer risk may exceed 10^{-5} and could be as high as 10^{-3} or nearly so, though considering the assumptions used and the uncertainties, lower risk is possible and a zero risk cannot be ruled out. This range of values is attended by numerous uncertainties, the inclusion of the range in this assessment does not constitute Agency endorsement of their validity as surrogates for cancer unit risk values, and the range is not suitable for estimating numbers of cancer cases. These risk findings should not be viewed as a definitive characterization of risk.

Even though the evidence for potential human health hazards for DE is convincing and persuasive, uncertainties exist because of the use of assumptions to bridge data and knowledge gaps about human exposures to DE and the underlying mechanisms by which DE may cause the observed toxicities in humans and animals. A notable uncertainty of this assessment is how the physical and chemical nature of DE emissions has changed over the years because the toxicological and epidemiologic observations are based on older engines and their emissions, yet the desire is to focus on the potential health hazards related to exposure from present-day or future emissions. There have been changes in the physical and chemical composition of some DE emissions (on-road vehicle emissions) over time, though there is no definitive information to show that the emission changes portend significant toxicological changes. The mode(s) of action for DE toxicity in humans is not understood, and hence knowledge is lacking about the role of exhaust mixture components in modulating the toxicity. Taken together, these considerations have lead to a judgment that the hazards identified from older technology-based exposures are applicable to current-day exposures. As new and cleaner diesel engines replace a substantial number of existing engines, the general applicability of the conclusions in this assessment will need to be reevaluated.

Other uncertainties include the assumptions that health effects observed at high doses may be applicable to low doses, and that toxicologic findings in laboratory animals are predictive of human responses. Also, the available data are not sufficient to demonstrate the absence or presence of an exposure/dose-response threshold in humans for DE toxicity at environmental exposures. Again, this is due in part to the lack of understanding of how DE may cause adverse health effects in exposed humans and laboratory animals. Although there are hypotheses about the specific mechanisms by which DE might cause cancer and other toxicities, no specific biological pathways or specific constituents of DE have been firmly established as responsible for low-dose effects. The assumptions used in this assessment, i.e., the presence of a biological threshold for chronic respiratory effects based on cumulative dosage and the absence of a threshold for lung cancer stemming from subtle and irreversible effects, are considered prudent and reasonable default choices.

The characterization of health hazards and risks contained in this document assumes that the potential DE health hazards are relevant for long-term exposures, up to and including lifetime exposures, and would apply to a wide spectrum of individuals but not necessary those that would have significant differential susceptibility. There is no DE-specific information that provides direct insight into the question of differential susceptibility within the general human population or vulnerable subgroups, for example, children or the elderly. Although default approaches to account for interindividual variation have been included in the derivation of the noncancer effects RfC (i.e., use of an uncertainty factor of 10), this may or may not adequately

protect certain subgroups that could be more vulnerable. Differential susceptibility to DPM among individuals in the population would be due to differences in dosimetry (i.e., differences in retained particle mass or number in the lung) and/or differences in respiratory system tissue response sensitivity. From the dosimetry perspective, we understand that age, gender, and disease status can influence deposition in the lung and other areas of the respiratory tract (U.S. EPA, 1996b, Section 10.7.7). For example, given that DE chronic toxicity is focused on the respiratory system, vulnerable subgroups might include those individuals who predispose their lungs to increased particle retention (e.g., smoking, high particulate burdens from nondiesel sources) or those having existing respiratory or lung inflammation, repeated respiratory infections, or chronic bronchitis or asthma. For children, there is also the hypothesis of possible increased sensitivity to exposure, given the ongoing processes of development from birth to maturation, of the respiratory and immune systems.

Despite the uncertainties regarding intraspecies variability, the default approach of using an uncertainty factor of 10 in the derivation of the noncancer effects RfC to account for possible interindividual variation in the toxic response to DE exposure is appropriate and reasonable given the lack of DE-specific data.

Variation in DE exposure is another source of uncertainty. Because of variation in human activity patterns and their proximity to DE sources of emissions, different population subgroups could potentially receive higher or lower exposure to DE. The highest exposed are clearly occupational subgroups whose job brings them very close to DE sources, such as diesel engine vehicle drivers and workers, diesel powered machinery operators, some underground miners, etc. High exposures in the general population would be to those living very near or having time outdoors in proximity to DE sources as well as those engaged in activities that cause high breathing rates where DE is present. Accordingly, where appropriate, analyses in this assessment have included possible high-end DE exposures in addition to the lower nationwide average exposure estimates.

Lastly, this assessment considers only potential heath effects from exposures to DE alone. DE exposure could be additive or synergistic to concurrent exposures to other air pollutants. For example, there is evidence that DPM that has been altered by being in the presence of ambient ozone significantly increases the rat lung inflammatory effect compared to DPM that was not subjected to ozone (Madden et al., 2000). This observation suggests a hypothesis that inflammation-related noncancer hazards of airborne DPM may be worsened by the increasing presence of ozone in the ambient air. Other concerns include the possible impacts for children and adults on the exacerbation of existing allergens resulting from DE exposure. However, in the absence of more definitive data demonstrating interactive effects

from combined exposures to DE and other pollutants, it is not possible to further address these issues at this time.

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Appendix A

Calculation of Human Equivalent Continuous Exposure Concentrations (HECs)

A.1. INTRODUCTION

As discussed in Chapter 3, the lung burden of diesel particulate matter (DPM) during exposure is determined by both the amount and site of particle deposition in the lung and, subsequently, by rates of translocation and clearance from the deposition sites. Mathematical models have often been used to complement experimental studies in estimating the lung burdens of inhaled particles in different species under different exposure conditions. This appendix presents a mathematical model that simulates the deposition and clearance of DPM in the lungs of rats and humans of Yu et al.(1991) also published as Yu and Yoon (1990).

Diesel particles are aggregates formed from primary spheres 15-30 nm in diameter. The aggregates are irregularly shaped and range in size from a few molecular diameters to tens of microns. The mass median aerodynamic diameter (MMAD) of the aggregates is typically 0.2 μm and is polydisperse with a geometric standard deviation of around 2.3. The organics adsorbed onto the aggregates normally account for 10% to 30% of the particle mass. However, the exact size distribution of DPM and the specific composition of the adsorbed organics depend upon many factors, including engine design, fuels used, engine operating conditions, and the thermodynamic process of exhaust. The physical and chemical characteristics of DPM have been reviewed extensively by Amann and Siegla (1982) and Schuetzle (1983).

Four mechanisms deposit DPM within the respiratory tract during exposure: impaction, sedimentation, interception, and diffusion. The contribution from each mechanism to deposition, however, depends upon lung structure and size, the breathing condition of the subject, and particle size distribution. Under normal breathing conditions, diffusion is the most dominant mechanism and the other three mechanisms play minor roles.

Once DPM is deposited in the respiratory tract, both the carbonaceous core and the adsorbed organics will be removed from the deposition sites by mechanical clearance, provided by mucociliary transport in the ciliated conducting airways as well as macrophage phagocytosis and migration in the nonciliated airways, and dissolution. As the carbonaceous core or soot of DPM is insoluble, it is removed from the lung primarily by mechanical clearance, whereas the adsorbed organics are removed principally by dissolution (Chapter 3).

A.2. PARTICLE MODEL

To develop a mathematical model that simulates the deposition and clearance of DPM in the lung, an appropriate model for diesel particles must be introduced. For the deposition study, an equivalent sphere model developed by Yu and Xu (1987) was used to simulate the dynamics and deposition of DPM in the respiratory tract by various mechanisms. For the clearance study, a diesel particle is assumed to be composed of three different material components according to their characteristic clearance rates: (1) a carbonaceous core of approximately 80% of the particle

mass; (2) absorbed organics of about 10% of particle mass, which are slowly cleared from the lung; and (3) adsorbed organics quickly cleared from the lung, accounting for the remaining 10% of particle mass. The presence of two discrete organic phases in the particle model is suggested by observations that the removal of particle-associated organics from the lung exhibits a biphasic clearance curve (Sun et al., 1984; Bond et al., 1986), as discussed in Chapter 3. This curve represents two major kinetic clearance phenomena: a fast- phase organic washout with a half-time of a few hours, and a slow phase with a half-time that is a few hundred times longer. The detailed components involved in each phase are not known. It is possible that the fast phase consists of organics that are leached out primarily by diffusion mechanisms while the slow phase might include any or all of the following components: (a) organics that are "loosened" before they are released, (b) organics that have become intercalated in the carbon core and whose release is thus impeded, (c) organics that are associated for longer periods of time because of hydrophobic interaction with other organic-phase materials, (d) organics that have been ingested by macrophages and as a result effectively remain in the lung for a longer period of time because of metabolism by the macrophage (metabolites formed may interact with other cellular components), and (e) organics that have directly acted on cellular components, such as the formation of covalent bonds with DNA and other biological macromolecules to form adducts.

The above distinction of the organic components is general and made to account for the biphasic clearance of DPM; it does not specifically imply the actual nature of the adsorbed organics. For aerosols made of pure organics, such as benzo(*a*)pyrene (BaP) and nitropyrene (NP) in the same size range of DPM, Sun et al. (1984) and Bond et al. (1986) observed a nearly monophasic clearance curve. This might be explained by the absence of intercalative phenomena (a) and of hydrophobic interaction imposed by a heterogeneous mixture of organics (b). The measurement of a pure organic might also neglect that quantity which has become intracellularly (c) or covalently bound (d).

A.3. COMPARTMENTAL LUNG MODEL

The model of Yu et al. (1991) comprises three principal compartments involved in deposition and clearance: tracheobronchial (T or TB), alveolar (A), and lung-associated lymph node (L), as shown in Figure A-1. The outside compartments blood (B) and GI tract (G) and nasopharyngeal or head (H) are also represented. The alveolar compartment in the model is obviously the most important for long-term retention studies. However, for short-term consideration, retentions in other lung compartments may also be significant. The presence of these lung compartments and the two outside compartments in the model therefore provides a complete description of all clearance processes involved.

In Figure A-1, $r_H^{(i)}$, $r_T^{(i)}$ and $r_A^{(i)}$ are, respectively, the mass deposition rates of DE material component i (i=1 [core], 2 [slowly cleared organics], and 3 [rapidly cleared organics]) in the head, tracheobronchial, and alveolar compartments; and $\lambda_{XY}^{(i)}$ represents the transport rate of material component i from any compartment X to any compartment Y. Let the mass fraction of material component i of a diesel particle be f_i. Then

$$r_H^{(i)} = f_i \, r_H \, , \tag{A-1}$$

$$r_T^{(i)} = f_i \, r_T \, , \tag{A-2}$$

$$r_A^{(i)} = f_i \, r_A \, , \tag{A-3}$$

where r_H, r_T, and r_A are, respectively, the total mass deposition rates of DPM in the H, T, and A compartments, determined from the equations:

$$r_H = c(TV)(RF)(DF)_H \, , \tag{A-4}$$

$$r_T = c(TV)(RF)(DF)_T \, , \tag{A-5}$$

$$r_A = c(TV)(RF)(DF)_A \, . \tag{A-6}$$

In Equations A-4 to A-6, c is the mass concentration of DPM in the air, TV is the tidal volume, RF is the respiratory frequency, and $(DF)_H$, $(DF)_T$, and $(DF)_A$ are, respectively, the deposition fractions of DPM in the H, T, and A compartments over a respiratory cycle. The

values of $(DF)_H$, $(DF)_T$, and $(DF)_A$, which vary with the particle size, breathing conditions, and lung architecture, were determined from the deposition model of Yu and Xu (1987).

The differential equations for $m_{XY}^{(i)}$, the mass of material component i in compartment X as a function of exposure time t, can be written as

Head (H)

$$\frac{dm_H^{(i)}}{dt} = r_H^{(i)} - \lambda_{HG}^{(i)} m_H^{(i)} - \lambda_{HB}^{(i)} m_H^{(i)} , \tag{A-7}$$

Tracheobronchial (T)

$$\frac{dm_T^{(i)}}{dt} = r_T^{(i)} + \lambda_{AT}^{(i)} m_A^{(i)} - \lambda_{TG}^{(i)} m_T^{(i)} - \lambda_{TB}^{(i)} m_T^{(i)} , \tag{A-8}$$

Alveolar (A)

$$\frac{dm_A^{(i)}}{dt} = r_A^{(i)} - \lambda_{AT}^{(i)} m_A^{(i)} - \lambda_{AL}^{(i)} m_A^{(i)} - \lambda_{AB}^{(i)} m_A^{(i)} , \tag{A-9}$$

Lymph nodes (L)

$$\frac{dm_L^{(i)}}{dt} = \lambda_{AL}^{(i)} m_A^{(i)} - \lambda_{LB}^{(i)} m_L^{(i)} . \tag{A-10}$$

Equation A-9 may also be written as

$$\frac{dm_A^{(i)}}{dt} = r_A^{(i)} - \lambda_A^{(i)} m_A^{(i)} , \tag{A-11}$$

where

$$\lambda_A^{(i)} = \lambda_{AT}^{(i)} + \lambda_{AL}^{(i)} + \lambda_{AB}^{(i)} . \tag{A-12}$$

is the total clearance rate of material component i from the alveolar compartment. In Equations A-7 to A-10, we have assumed vanishing material concentration in the blood compartment to calculate diffusion transport.

The total mass of the particle-associated organics in compartment X is the sum of $m_X^{(2)}$ and $m_X^{(3)}$ the total mass of DPM in compartment X is equal to

$$m_X = m_X^{(1)} + m_X^{(2)} + m_X^{(3)} \tag{A-13}$$

The lung burdens of diesel soot (core) and organics are defined, respectively, as

$$m_{Lung}^{(1)} = m_T^{(1)} + m_A^{(1)} , \tag{A-14}$$

and

$$m_{Lung}^{(2)+(3)} = m_T^{(2)} + m_A^{(2)} + m_T^{(3)} + m_A^{(3)} . \tag{A-15}$$

Because the clearance of diesel soot from compartment T is much faster than from compartment A, $m_T^{(1)} < m_A^{(1)}$ a short time after exposure, Equation A-14 leads to

$$m_{Lung}^{(1)} \cong m_A^{(1)} . \tag{A-16}$$

Solution to Equations A-7 to A-10 can be obtained once all the transport rates $\lambda_{XY}^{(i)}$ are known. When $\lambda_{XY}^{(i)}$ are constant, which is the case in linear kinetics, Equations A-7 to A-10 will have a solution that increases with time at the beginning of exposure but eventually saturates and reaches a steady-state value. This is the classical retention model developed by the International Commission of Radiological Protection (ICRP, 1979). However, as discussed in Chapter 3, data have shown that when rats are exposed to DPM at high concentration for a prolonged period, long-termed clearance is impaired. This is the so-called overload effect, observed also for other insoluble particles. The overload effect cannot be predicted by the classical ICRP model. Soderholm (1981) and Strom et al. (1987, 1988) have proposed a model to simulate this effect by adding a separate sequestering compartment in the alveolar region. In the present approach, a single compartment for the alveolar region of the lung is used and the overload effect is accounted for by a set of variable transport rates $\lambda_{AT}^{(i)}$, $\lambda_{AL}^{(i)}$, and $\lambda_A^{(i)}$ which are functions of m_A. The transport rates $\lambda_A^{(i)}$ and $\lambda_{AL}^{(i)}$ in Equations A-7 to A-10 can be determined directly from experimental data on lung and lymph node burdens, and $\lambda_{AT}^{(i)}$ and $\lambda_{AB}^{(i)}$ from Equation A-12.

A.4. SOLUTIONS TO KINETIC EQUATIONS

Equation A-11 is a nonlinear differential equation of $m_A^{(i)}$ with known function of $\lambda_A^{(i)}$. For diesel soot, this equation becomes

$$\frac{dm_A^{(1)}}{dt} = r_A^{(1)} - \lambda_A^{(1)}(m_A)m_A^{(1)} \ . \qquad \text{(A-17)}$$

Because clearance of the particle-associated organics is much faster than diesel soot, $m_A^{(2)}$ and $m_A^{(3)}$ constitute only a very small fraction of the total particle mass (less than 1%) after a long exposure, and we may consider $\lambda_A^{(1)}$ as a function of $m_A^{(1)}$ alone. Equation A-17 is then reduced to a differential equation with $m_A^{(1)}$ the only dependent variable.

The general solution to Equation A-17 for constant $r_A^{(1)}$ at any time, t, can be obtained by the separation of variables to give

$$\int_0^{m_A^{(1)}} \frac{dm_A^{(1)}}{r_A^{(1)} - \lambda_A^{(1)} m_A^{(1)}} = t \ . \qquad \text{(A-18)}$$

If $r_A^{(1)}$ is an arbitrary function of t, Equation A-17 needs to be solved numerically such as by a Runge-Kutta method. Once $m_A^{(1)}$ is found, the other kinetic equations A-7 to A-10 for both diesel soot and the particle-associated organics can be solved readily, as they are linear equations. The solutions to these equations for constant $r_H^{(i)}$, $r_T^{(i)}$ and $r_A^{(i)}$ are given below:
Head (H)

$$m_H^{(i)} = r_H^{(i)}/\lambda_H^{(i)} + (m_{H0}^{(i)} - r_H^{(i)})/\lambda_H^{(i)}) \exp\ (-\lambda_H^{(i)}\ t) \qquad \text{(A-19)}$$

$$\textit{where} \quad \lambda_H^{(i)} = \lambda_{HG}^{(i)} + \lambda_{HB}^{(i)} \qquad \text{(A-20)}$$

Tracheobronchial (T)

$$m_T^{(i)} = \exp\,(-\lambda_T^{(i)}\,t\,)\int_0^t (\,r_T^{(i)} + \lambda_{AT}^{(i)}\;\; m_A^{(i)}\,)\,\exp\,(\lambda_T^{(i)}\,t\,)\,dt + m_{T0}^{(i)} \qquad \text{(A-21)}$$

$$where\;\; \lambda_T^{(i)} = \lambda_{TG}^{(i)} + \lambda_{TB}^{(i)} \qquad \text{(A-22)}$$

Lymph nodes (L)

$$m_L^{(i)} = \exp(-\lambda_{LB}^{(i)}\,t)\int_0^t \lambda_{AL}^{(i)} m_A^{(i)} \exp(\lambda_{LB}^{(i)}\,t\,)\,dt + m_{L0}^{(i)}) \qquad \text{(A-23)}$$

In Equations A-19 to A-23, $m_{XO}^{(i)}$ represents the value of $m_X^{(i)}$ at t = 0.

In the sections to follow, the methods of determining $r_H^{(i)}$, $r_T^{(i)}$ and $r_A^{(i)}$ or $(DF)_H$, $(DF)_T$, and $(DF)_A$ $r_H^{(DF)}$, $r_T^{(DF)}$ and $r_A^{(DF)}$ as well as the values of $\lambda_{XY}^{(i)}$ in the compartmental lung model are presented.

A.5. DETERMINATION OF DEPOSITION FRACTIONS

The mathematical models for determining the deposition fractions of DPM in various regions of the respiratory tract have been developed by Yu and Xu (1986, 1987) and are adopted in this report. Yu and Xu consider DPM as a polydisperse aerosol with a specified mass median aerodynamic diameter (MMAD) and geometrical standard deviation σ_g. Each diesel particle is represented by a cluster-shaped aggregate within a spherical envelope of diameter d_e. The envelope diameter d_e is related to the aerodynamic diameter of the particle by the relation

$$\frac{d_e}{d_a} = \varphi^{-1/2}\left(\frac{C_a}{C_e}\right)^{1/2)}\left(\frac{\zeta}{\zeta_o}\right)^{1/2} \qquad \text{(A-24)}$$

where ζ is the bulk density of the particle in g/cm^3, ζ_0 = 1 g/cm^3; φ is the packing density, which is the ratio of the space actually occupied by primary particles in the envelope to the overall envelope volume; and C_x is the slip factor given by the expression:

$$C_x = 1 + 2\frac{\lambda}{d_x}\,[1.257 + 0.4\ \exp -(\frac{0.55d_x}{\lambda})] \qquad \text{(A-25)}$$

in which $\lambda \cong 8 \times 10^{-6}\text{cm}^3$ is the mean free path of air molecules at standard conditions. In the diesel particle model of Yu and Xu (1986), ζ has a value of 1.5 g/cm^3 and a φ value of 0.3 is chosen based upon the best experimental estimates. As a result, Equation A-24 gives d_e/d_a = 1.35. In determining the deposition fraction of DPM, d_e is used for diffusion and interception according to the particle model.

A.5.1. Deposition in the Head

Particle deposition in the naso- or oropharyngeal region is referred to as head or extrathoracic deposition. The amount of particles that enters the lung depends upon the breathing mode. Normally, more particles are collected via the nasal route than by the oral route because of the nasal hairs and the more complex air passages of the nose. Since the residence time of diesel particles in the head region during inhalation is very small (about 0.1 s for human adults at normal breathing), diffusional deposition is insignificant and the major deposition mechanism is impaction. The following empirical formulas derived by Yu et al. (1981) for human adults are adopted for deposition prediction of DPM:

For mouth breathing:

$$(DF)_{H,\ in} = 0,\ for\ d_a^2 \leq 3000 \qquad \text{(A-26)}$$

$$(DF)_{H,\ in} = -1.117 + 0.324\ \log(d_a^2 Q),\ for\ d_a^2 Q > 3000 \qquad \text{(A-27)}$$

$$(DF)_{H,\ ex} = 0, \qquad \text{(A-28)}$$

and for nose breathing:

$$(DF)_{H,\ in} = -0.014 + 0.023\ \log(d_a^2 Q),\ for\ d_a^2 Q \leq 337 \qquad \text{(A-29)}$$

$$(DF)_{H,\ in} = -0.959 + 0.397 \log(d_a^2 Q),\ for\ d_a^2 Q > 337 \qquad \text{(A-30)}$$

$$(DF)_{H,\ ex} = 0.003 + 0.033 \log(d_a^2 Q),\ for\ d_a^2 Q \leq 215 \qquad \text{(A-31)}$$

$$(DF)_{H,\ ex} = -0.851 + 0.399 \log(d_a^2 Q),\ for\ d_a^2 Q > 215 \qquad \text{(A-32)}$$

where $(DF)_H$ is the deposition efficiency in the head, the subscripts in and ex denote inspiration and expiration, respectively, d_a is the particle aerodynamic diameter in μm, and Q is the air flowrate in cm^3/sec.

Formulas to calculate deposition of diesel particles in the head region of children are derived from those for adults using the theory of similarity, which assumes that the air passage in the head region is geometrically similar for all ages and that the deposition process is characterized by the Stokes number of the particle. Thus, the set of empirical equations from A-26 through A-32 are transformed into the following form:

For mouth breathing:

$$(DF)_{H,\ in} = 0,\ for\ d_a^2 Q \leq 3000 \qquad \text{(A-33)}$$

and for nose breathing:

$$(DF)_{H,\ in} = -1.117 + 0.972\ logK + 0.324 \log(d_a^2 Q),\ for\ d_a^2 Q > 3000 \qquad \text{(A-34)}$$

$$(DF)_{H,\ ex} = 0. \qquad \text{(A-35)}$$

$$(DF)_{H,\ in} = -\ 0.014 + 0.690 \log K + 0.023 \log(d_a^2 Q),\ for\ d_a^2 Q \leq 337 \qquad \text{(A-36)}$$

$$(DF)_{H,\ in} = -0.959 + 1.191 \log K + 0.397 \log (d_a^2 Q),\ \text{for}\ d_a^2 Q > 337 \qquad \text{(A-37)}$$

$$(DF)_{H,\ ex} = 0.003 + 0.099 \log K + 0.033 \log(d_a^2 Q),\ \text{for}\ d_a^2 Q \leq 215 \qquad \text{(A-38)}$$

where K is the ratio of the linear dimension of the air passages in the head region of adults to that of children, which is assumed to be the same as the ratio of adult/child tracheal diameters.

$$(DF)_{H,\ ex} = 0.851 + 1.197 \log K + 0.399 \log(d_a^2 Q), \text{ for } d_a^2 Q > 215 \qquad \text{(A-39)}$$

For rats, the following empirical equations are used for deposition prediction of DPM in the nose:

$$(DF)_{H,\ in} = (DF)_{H,\ ex} = 0.046 + 0.009 \log(d_a^2 Q), \text{ for } d_a^2 Q \leq 13.33 \qquad \text{(A-40)}$$

A.5.2. Deposition in the Tracheobronchial and Alveolar Regions

The deposition model adopted for DPM is the one previously developed for monodisperse (Yu, 1978) and polydisperse spherical aerosols (Diu and Yu, 1983). In the model,

$$(DF)_{H,\ in} = (DF)_{H,\ ex} = -0.522 + 0.514 \log(d_a^2 Q), \text{ for } d_a^2 Q > 13.33 \qquad \text{(A-41)}$$

the branching airways are viewed as a chamber model shaped like a trumpet (Figure A-2). The cross-sectional area of the chamber varies with airway depth, x, measured from the beginning of the trachea. At the last portion of the trumpet, additional cross-sectional area is present to account for the alveolar volume per unit length of the airways. Inhaled diesel particles that escape capture in the head during inspiration will enter the trachea and subsequently the bronchial airways (compartment T) and alveolar spaces (compartment A).

Assuming that the airways expand and contract uniformly during breathing, the equation for the conservation of particles takes the form:

$$\beta(A_1 + A_2)\frac{\partial c}{\partial x} + Q\frac{\partial c}{\partial x} = -Qc\eta \qquad \text{(A-42)}$$

where c is the mean particle concentration at a given x and time t; A_1 and A_2 are, respectively, the summed cross-sectional area (or volume per unit length) of the airways and alveoli at rest; η is the particle uptake efficiency per unit length of the airway; β is an expansion factor, given by:

$$\beta = 1 + \frac{V_t}{V_l} \qquad \text{(A-43)}$$

and Q is the air flow rate, varying with x and t according to the relation

$$\frac{Q}{Q_o} = 1 - \frac{V_x}{V_l} \tag{A-44}$$

where Q_0 is the air flow rate at x = 0. In Equations A-43 and A-44, V_t is the volume of new air in the lungs and V_x and V_ℓ are, respectively, the accumulated airway volume from x = 0 to x, and total airway volume at rest.

Equation A-42 is solved using the method of characteristics with appropriate initial and boundary conditions. The amount of particles deposited between location x_1 and x_2 from time t_1 to t_2 can then be found from the expression

$$DF = \int_{t_1}^{t_2}\int_{x_1}^{x_2} Qc\eta\, dx dt \tag{A-45}$$

For diesel particles, η is the sum of those due to the individual deposition mechanisms described above, i.e.,

where η_I, η_S, η_P, and η_D are, respectively, the deposition efficiencies per unit length of the

$$\eta = \eta_I + \eta_S + \eta_P + \eta_D \tag{A-46}$$

airway due to impaction, sedimentation, interception, and diffusion. On the basis of the particle model described above, the expressions for η_I, η_S, η_P, and η_D are obtained in the following form:

$$\eta_I = \frac{0.768}{L}(St)\theta. \tag{A-47}$$

$$\eta_S = \frac{2}{\pi L}[2\epsilon\sqrt{1 - \epsilon^{(2/3)}} - \epsilon^{1/3}\sqrt{1 - \epsilon^{2/3}} + \sin^{-1}\epsilon^{1/3}] \tag{A-48}$$

$$\eta_P = \frac{4}{3\pi L}(\Gamma - \frac{\Gamma^3}{32}) \tag{A-49}$$

$$\eta_D = \frac{1}{L}[1-0.819\exp(-14.63\Delta) - 0.0976\ \exp(-89.22\Delta) - 0.0325\ \exp(-228\Delta) - 0.0509\ \exp(-125\Delta^{2/3})] \quad \text{(A-50)}$$

$$\eta_D = \frac{4}{L}\Delta^{1/2}\ (1 - 0.444\Delta^{1/2}) \quad \text{(A-51)}$$

for Reynolds numbers of the flow smaller than 2000, and for Reynolds numbers greater than or equal to 2000, where $ST=d_a^2u/(18\mu R)$ is the particle Stokes number, $\theta = L/(8R)$, $\epsilon = 3\mu u_s L/(32uR)$, $\Gamma = d_e/R$, and $\Delta = DL/(4R^2u)$. In the above definitions u is the air velocity in the airway; μ is the air viscosity; L and R are, respectively, the length and radius of the airway; $u_s = C_a d_a^2/(18\mu)$ is the particle settling velocity; and $D = C_e kT(3\pi\mu d_e)$ is the diffusion coefficient with k denoting the Boltzmann constant and T the absolute temperature. In the deposition model, it is also assumed that η_I and $\eta_P = 0$ for expiration, while η_D and η_S have the same expressions for both inspiration and expiration.

During the pause, only diffusion and sedimentation are present. The combined deposition efficiency in the airway, E, is equal to:

$$E = 1 - (1 - E_S)\ (1 - E_D)\ . \quad \text{(A-52)}$$

where E_D and E_S are, respectively, the deposition efficiencies due to the individual mechanisms of diffusion and sedimentation over the pause period. The expression for E_D and E_S are given by

$$E_D = 1 - \sum_{i=1}^{3} \frac{4}{\alpha_i} \exp(-\alpha_i^2\tau_D)(1 - \sum_{i=1}^{3} \frac{4}{\alpha_i^2}) \exp\left[- \frac{4\tau_D^{1/2}}{\pi^{1/2}(1 - \sum_{i=1}^{3} \frac{4}{\alpha_i^2})} \right] \quad \text{(A-53)}$$

where $\tau_D = D\tau/R^2$ in which τ is the pause time and α_1, α_2, and α_3 are the first three roots of the equation:

$$J_o(\alpha) = 0\ . \quad \text{(A-54)}$$

in which J_o is the Bessel function of the zero$_{th}$ order, and:

$$E_S = 1.1094\tau_S - 0.1604\tau_S^2,\ for\ 0 < \tau_S \le 1. \quad \text{(A-55)}$$

and

$$E_S = 1 - 0.0069\tau_S^{-1} - 0.0859\tau_S^{-2} - 0.0582\tau_S^{-3}, \quad for\ \tau_S > 1, \tag{A-56}$$

where $\tau_S = u_S\tau/2R$.

The values of $(DF)_T$ and $(DF)_A$ over a breathing cycle are calculated by superimposing DF for inspiration, deposition efficiency E during pause, and DF for expiration in the tracheobronchial airways and alveolar space. It is assumed that the breathing cycle consists of a constant flow inspiration, a pause, and a constant flow expiration, each with a respective duration fraction of 0.435, 0.05, and 0.515 of a breathing period.

A.5.3. Lung Models

Lung architecture affects particle deposition in several ways: the linear dimension of the airway is related to the distance the particle travels before it contacts the airway surface; the air flow velocity by which the particles are transported is determined by the cross-section of the airway for a given volumetric flowrate; and flow characteristics in the airways are influenced by the airway diameter and branching patterns. Thus, theoretical prediction of particle deposition depends, to a large extent, on the lung model chosen.

A.5.3.1. *Lung Model for Rats*

Morphometric data on the lung airways of rats were reported by Schum and Yeh (1979). Table A-1 shows the lung model data for Long Evans rats with a total lung capacity of 13.784 cm^3. Application of this model to Fischer rats is accomplished by assuming that the rat has the same lung structure regardless of its strain and that the total lung capacity is proportional to the body weight. In addition, it is also assumed that the lung volume at rest is about 40% of the total lung capacity and that any linear dimension of the lung is proportional to the cubic root of the lung volume.

A.5.3.2. *Lung Model for Human Adults*

The lung model of mature human adults used in the deposition calculation of DPM is the symmetric lung model developed by Weibel (1963). In Weibel's model, the airways are assumed to be a dichotomous branching system with 24 generations. Beginning with the 18th generation, increasing numbers of alveoli are present on the wall of the airways, and the last three generations are completely aleveolated. Thus, the alveolar region in this model consists of

all the airways in the last seven generations. Table A-2 presents the morphometric data of the airways of Weibel's model adjusted to a total lung volume of 3000 cm^3.

A.5.3.3. *Lung Model for Children*

The lung model for children in the diesel study was developed by Yu and Xu (1987) on the basis of available morphometric measurements. The model assumes a lung structure with dichotomous branching of airways, and it matches Weibel's model for a subject when evaluated at the age of 25 years, the age at which the lung is considered to be mature. The number and size of airways as functions of age t (years) are determined by the following equations.

A.5.3.3.1. ***Number of airways and alveoli.*** The number of airways $N_i(t)$ at generation i for age t is given by

$$N_i(t) = 2^i, \qquad \text{for } 0 \le i \le 20 \tag{A-57}$$

$$\begin{cases} N_{21}(t) = N_r(t), \\ N_{22}(t) = N_{23}(t) = 0. \end{cases} \qquad \text{for } N_r(t) \le 2^{21} \tag{A-58}$$

$$\begin{cases} N_{21}(t) = 2^{21}, \\ N_{22}(t) = N_r(t) - 2^{21}, \\ N_{23}(t) = 0, \end{cases} \qquad \text{for } 2^{21} < N_r(t) \le 2^{22} \tag{A-59}$$

$$\begin{cases} N_{21}(t) = 2^{21}, \\ N_{22}(t) = 2^{22}, \\ N_{23}(t) = N_r(t) - 2^{21} - 2^{22} \end{cases} \qquad \textit{for } N_r(t) > 2^{21} + 2^{22}, \tag{A-60}$$

where $N_r(t)$ is the total number of airways in the last three airway generations. The empirical equation for N_r which best fits the available data is

Thus, $N_r(t)$ increases from approximately 1.5 million at birth to 15 million at 8 years of age and

$$N_r(t) = \begin{cases} 2.036 \times 10^7(1 - 0.926e^{-0.15}t), & t \le 8 \\ 1.468 \times 10^7, & t > 8 \end{cases} \tag{A-61}$$

remains nearly constant thereafter. Equations A-58 to A-60 also imply that in the last three

generations, the airways in the subsequent generation begin to appear only when those in the preceding generation have completed development.

The number of alveoli as a function of age can be represented by the following equation according to the observed data:

$$N_A(t) = 2.985 \times 10^8(1 - 0.919e^{-0.45}t) \qquad \text{(A-62)}$$

The number of alveoli distributed in the unciliated airways at the airway generation level is determined by assuming that alveolization of airways takes place sequentially in a proximal direction. For each generation, alveolization is considered to be complete when the number of alveoli in that generation reaches the number determined by Weibel's model.

A.5.3.3.2. ***Airway size.*** Four sets of data are used to determine airway size during postnatal growth: (a) total lung volume as a function of age; (b) airway size as given by Weibel's model; (c) the growth pattern of the bronchial airways; and (d) variation in alveolar size with age. From these data, it is found that the lung volume, LV(t) at age t, normalized to Weibel's model at 4800 cm^3 for an adult (25 years old), follows the equation

$$LV(t) = 0.959 \times 10^5(1 - 0.998e^{-0.002}t) \quad (cm^3). \qquad \text{(A-63)}$$

The growth patterns of the bronchial airways are determined by the following equations

$$D_i(t) - D_{iw} = \alpha_i[H(t) - H(25)], \qquad \text{(A-64)}$$

$$L_i(t) - L_{iw} = \beta_i[H(t) - H(25)], \qquad \text{(A-65)}$$

where $D_i(t)$ and $L_i(t)$ are, respectively, the airway diameter and length at generation i and age t, D_{iw} and L_{iw} the corresponding values for Weibel's model, α_i and β_i are coefficients given by

$$\alpha_i = 3.26 \times 10^{-2}\exp[-1.183\ (i+1)^{0.5}] \qquad \text{(A-66)}$$

$$\beta_i = 1.05 \times 10^{-6} \exp\ [10.1]\ (i+1)^{-0.2}] \qquad \text{(A-67)}$$

and H(t) is the body height, which varies with age t in the form

$$H(t) = 1.82 \times 10^2(1 - 0.725e^{-0.14}t)\ (cm). \tag{A-68}$$

For the growth patterns of the airways in the alveolar region, it is assumed that

$$\frac{D_i}{D_{iw}} = \frac{L_i}{L_{iw}} = \frac{D_a}{D_{aw}} = f(t), \qquad for\ 17 \le i \le 23 \tag{A-69}$$

where D_a is the diameter of an alveolus at age t, D_{aw} = 0.0288 cm is the alveolar diameter for adults in accordance with Weibel's model, and f(t) is a function determined from

$$f(t) = \sqrt[3]{\frac{\{LV(t) - \sum_{i=0}^{16} \frac{\pi}{4} D_i^2(t)\ L_i(t)N_i(t)\}}{\{\sum_{i=17}^{23} \frac{\pi}{4} D_{iw}^2 L_{iw} N_i(t) + \frac{5\pi}{36} D_{aw}^3 N_A(t)\}}} \tag{A-70}$$

A.6. TRANSPORT RATES

The values of transport rates $\lambda_{XY}^{(i)}$ for rats have been derived from the experimental data of clearance for diesel soot (Chan et al., 1981; Strom et al., 1987, 1988) and for the particle-associated organics (Sun et al., 1984; Bond et al., 1986; Yu et al., 1991). These values are used in the present model of lung burden calculation and are listed below:

$$\lambda_{HG}^{(i)} = 1.73\ (i = 1,2,3) \tag{A-71}$$

$$\lambda_{HB}^{(1)} = \lambda_{TB}^{(1)} = \lambda_{LB}^{(1)} = \lambda_{AB}^{(i)} = 0.00018 \tag{A-72}$$

$$\lambda_{HB}^{(2)} = \lambda_{TB}^{(2)} = \lambda_{LB}^{(2)} = \lambda_{AB}^{(2)} = 0.0129 \tag{A-73}$$

$$\lambda_{HB}^{(3)} = \lambda_{TB}^{(3)} = \lambda_{LB}^{(3)} = \lambda_{AB}^{(3)} = 12.55 \tag{A-74}$$

$$\lambda_{TG}^{(i)} = 0.693 \qquad (i = 1,2,3) \tag{A-75}$$

$$\lambda_{AL}^{(1)} = 0.00068\ [1 - \exp(-0.046 m_A^{1.62})] \tag{A-76}$$

$$\lambda_{AL}^{(i)} = \frac{1}{4}\lambda_{AB}^{(i)} \qquad (i = 2,3) \tag{A-77}$$

$$\begin{aligned} \lambda_{AT}^{(i)} &= 0.012\ \exp(-0.11 m_A^{1.76}) + \\ &0.00068\ \exp(-0.046 m_A^{1.62}) \quad (i = 1,2,3) \end{aligned} \tag{A-78}$$

$$\begin{aligned} \lambda_A^{(1)} &= \lambda_{AL}^{(1)} + \lambda_{AT}^{(1)} + \lambda_{AB}^{(1)} = \\ &0.012\ \exp(-0.11 m_A^{1.76}) + 0.00086 \end{aligned} \tag{A-79}$$

$$\begin{aligned} \lambda_A^{(2)} &= \lambda_{AL}^{(2)} + \lambda_{AT}^{(2)} + \lambda_{AB}^{(2)} = 0.012\ \exp(-0.11 m_A^{1.76}) + \\ &0.00068\ \exp(-0.046 m_a^{1.62}) + 0.0161 \end{aligned} \tag{A-80}$$

$$\begin{aligned} \lambda_A^{(3)} &= \lambda_{AL}^{(3)} + \lambda_{AT}^{(3)} + \lambda_{AB}^{(3)} = 0.012\ \exp(-0.11 m_A^{1.76}) + \\ &0.00068\ \exp(-0.046 m_A^{1.62}) + 15.7 \end{aligned} \tag{A-81}$$

where $\lambda_{XY}^{(i)}$ is the unit of day^{-1}, and $m_A \cong m_A^{(1)}$ is the particle burden (in mg) in the alveolar compartment.

Experimental data on the deposition and clearance of DPM in humans are not available. To estimate the lung burden of DPM for human exposure, it is necessary to extrapolate the transport rates $\lambda_{XY}^{(i)}$ from rats to humans. For organics, it is assumed that the transport rates are the same for rats and humans. This assumption is based upon the observation of Schanker et al. (1986) that the lung clearance of inhaled lipophilic compounds appears to depend only on their lipid/water partition coefficients and is independent of species. In contrast, the transport rates of diesel soot in humans should be different from those of rats, since the alveolar clearance rate, λ_A,

of insoluble particles at low lung burdens for human adults is approximately seven times that of rats (Bailey et al., 1982).

No data are available on the change of the alveolar clearance rate of insoluble particles in humans due to excessive lung burdens. It is seen from Equation A-79 that $\lambda_A^{(1)}$ for rats can be written in the form

$$\lambda_A^{(1)} = a \exp(-bm_A^c) + d \tag{A-82}$$

where a, b, c, and d are constants. The right-hand side of Equation A-82 consists of two terms, representing, respectively, macrophage-mediated mechanical clearance and clearance by dissolution. The first term depends upon the lung burden, whereas the second term does not. To extrapolate this relationship to humans, we assume that the dissolution clearance term is independent of species and that the mechanical clearance term for humans varies in the same proportion as in rats under the same unit surface particulate dose. This assumption results in the following expression for $\lambda_A^{(1)}$ in humans

$$\lambda_A^{(1)} = \frac{a}{P} \exp[-b(m_A/S)^c] + d \tag{A-83}$$

where P is a constant derived from the human/rat ratio of the alveolar clearance rate at low lung burdens and S is the ratio of the pulmonary surface area between humans and rats. Equation A-83 implies that rats and humans have equivalent amounts of biological response in the lung to the same specific surface dose of inhaled DPM.

From the data of Bailey et al. (1982), a value of $\lambda_A^{(1)} = 0.00169$ day^{-1} is obtained for humans at low lung burdens leading to P = 14.4. A value for S of 148 is reported from the data of the anatomical lung model of Schum and Yeh (1979) for rats and Weibel's model for human adults. For humans less than 25 years old, the model assumes the same value for P, but S is computed from the data of the lung model for young humans (Yu and Xu 1987). The value of S for different ages is shown in Table A-3.

The equations for other transport rates that have a lung-burden-dependent component are extrapolated from rats to humans in a similar manner. The following lists the values of $\lambda_{XY}^{(i)}$ (in day^{-1}) for humans used in the present model calculation:

$$\lambda_{HG}^{(1)} = 1.73 \quad (i = 1,2,3) \tag{A-84}$$

$$\lambda_{HB}^{(1)} = \lambda_{TB}^{(1)} = \lambda_{LB}^{(1)} = \lambda_{AB}^{(1)} = 0.00018 \tag{A-85}$$

$$\lambda_{HB}^{(2)} = \lambda_{TB}^{(2)} = \lambda_{LB}^{(2)} = \lambda_{AB}^{(2)} = 0.0129 \tag{A-86}$$

$$\lambda_{HB}^{(3)} = \lambda_{TB}^{(3)} = \lambda_{LB}^{(3)} = \lambda_{AB}^{(3)} = 12.55 \tag{A-87}$$

$$\lambda_{TG}^{(i)} = 0.693 \qquad (i = 1,2,3) \tag{A-88}$$

$$\lambda_{AL}^{(1)} = 0.00068\ \{1 - 0.0694\ \exp[-0.046(m_A/S)^{1.62}]\} \tag{A-89}$$

$$\lambda_{AL}^{(i)} = \frac{1}{4}\lambda_{AB}^{(i)} \qquad (i = 2,\ 3) \tag{A-90}$$

$$\lambda_{AT}^{(i)} = 0.0694\ \{0.012\ \exp[-0.11(m_A/S)^{1.76}] + 0.00068\ \exp[-0.046(m_A/S)^{1.76}]\}\ (i = 1,\ 2,\ 3) \tag{A-91}$$

$$\lambda_{A}^{(1)} = \lambda_{AL}^{(1)} + \lambda_{AB}^{(1)} + \lambda_{AT}^{(1)} = 0.0694\ \{0.012\ \exp[-0.11(m_A/S)^{1.76}]\} + 0.00086 \tag{A-92}$$

$$\lambda_{A}^{(2)} = \lambda_{AL}^{(2)} + \lambda_{AT}^{(2)} + \lambda_{AB}^{(2)} = \tag{A-93}$$

$$0.0694\{0.012\ \exp[-0.11(m_A/A)^{1.76}] +$$

$$0.00068\ \exp[-0.046(m_A/S)^{1.76}]\} + 0.016 \tag{A-94}$$

A.7. RESULTS

A.7.1. Simulation of Rat Experiments

To test the accuracy of the model, simulation results are obtained on the retention of DPM in the rat lung and compared with the data of lung burden and lymph node burden obtained by Strom et al. (1988). A particle size of 0.19 μm MMAD and a standard geometric deviation, σ_g, of 2.3 (as used in Strom's experiment) are used in the calculation.

The respiratory parameters for rats are based on their weight and calculated using the following correlations of minute volume, respiratory frequency, and growth curve data.

$$\text{Minute volume} = 0.9W\ (\text{cm}^3/\text{min}) \tag{A-95}$$

$$\text{Respiratory frequency} = 475W^{-0.3}\ (1/\text{min}) \tag{A-96}$$

where W is the body weight (in grams) as determined from the equation

$$W = 5+537T/(100+T),\ \text{for } T \geq 56 \text{ days} \tag{A-97}$$

in which T is the age of the rat measured in days.

Equation A-95 was obtained from the data of Mauderly (1986) for rats ranging in age from 3 mo to 2 years old; Equation A-96 was obtained from the data of Strom et al. (1988); and Equation A-97 was determined from the best fit of the experimental deposition data. Figures A-3 and A-4 show the calculated lung burden of diesel soot ($m_A^{(1)} + m_D^{(1)}$) and lymph node burden, respectively, for the experiment by Strom et al. (1988) using animals exposed to DPM at 6 mg/m^3 for 1, 3, 6, and 12 weeks; exposure in all cases was 7 days/week and 20 h daily. The solid lines represent the calculated accumulation of particles during the continuous exposure phase and the dashed lines indicate calculated post-exposure retention. The agreement between the calculated and the experimental data for both lung and lymph node burdens during and after the exposure periods was very good.

Comparison of the model calculation and the retention data of particle-associated BaP in rats obtained by Sun et al. (1984) is shown in Figure A-5. The calculated retention is shown by the solid line. The experiment of Sun et al. consisted of a 30-min exposure to diesel particles coated with [^3H] benzo[a]pyrene *([^3H] - BaP)* at a concentration of 4 to 6 μg/m^3 of air and followed by a post-exposure period of over 25 days. The fast and slow phase of *([^3H] - BaP)* clearance half-times were found to be 0.03 day and 18 days, respectively. These correspond to $\lambda_{AO}^{2} = 0.0385$ day^{-1} and $\lambda_{AO}^{(3)} = 23.1$ day^{-1} in our model, where $\lambda_{AO}^{(i)}$ is the value of $\lambda_{XY}^{(i)}$ at $m_A \to 0$. Figure A-5 shows that the calculated retention is in excellent agreement with the experimental data obtained by Sun et al. (1984).

A.7.2. Predicted Burdens in Humans

Selected results of lung burden predictions in humans are shown in Figures A-6 to A-9. The particle conditions used in the calculation are 0.2 μm MMAD with $\sigma_g = 2.3$, and the mass fractions of the rapidly and slowly cleared organics are each 10% $(f_1 = f_2 = 0.1)$. Figures A-6 and A-7 show, respectively, the lung burdens per unit concentration of diesel soot and the associated organics in human adults for different exposure patterns at two soot concentrations, 0.1 and 1 mg/m^3. The exposure patterns used in the calculation are (a) 24 h/day and 7 days week; (b) 12 h/day and 7 days/week; and (c) 8 h/day and 5 days/week, simulating environmental and occupational exposure conditions. The results show that the lung burdens of both diesel soot and the associated organics reached a steady-state value during exposure. Because of differences in the amount of particle intake, the steady-state lung burdens per unit concentration were highest for exposure pattern (a) and lowest for exposure pattern (b). Also, increasing soot concentration from 0.1 to 1 mg/m^3 increased the lung burden per unit concentration. However, the increase was not noticeable for exposure pattern (c). The dependence of lung burden on the soot concentration is caused by the reduction of the alveolar clearance rate at high lung burdens discussed above.

Figures A-8 and A-9 show the effect of age on lung burden, where the lung burdens per unit concentration per unit weight are plotted versus age. The data of lung weight at different ages are those reported by Snyder (1975). The exposure pattern used in the calculation is 24 h/day and 7 days/week for a period of 1 year at the two soot concentrations, 0.1 and 1 mg/m^3. The results show that, on a unit lung weight basis, the lung burdens of both soot and organics are functions of age, and the maximum lung burdens occur at approximately 5 years of age. Again, for any given age, the lung burden per unit concentration is slightly higher at 1 mg/m^3 than at 0.1 mg/m^3.

A.8. PARAMETRIC STUDY OF THE MODEL

The deposition and clearance model of DPM in humans, presented above, consists of a large number of parameters that characterize the size and composition of diesel particles, the structure and dimension of the respiratory tract, the ventilation conditions of the subject, and the clearance half-times of the diesel soot and the particle-associated organics. Any single or combined changes of these parameters from their normal values in the model would result in a change in the predicted lung burden. A parametric study has been conducted to investigate the effects of each individual parameter on calculated lung burden in human adults. The exposure pattern chosen for this study is 24 h/day and 7 days/week for a period of 10 years at a constant soot concentration of 0.1 mg/m^3. The following presents two important results from the parametric study.

A.8.1. Effect of Ventilation Conditions

The changes in lung burden due to variations in tidal volume and respiratory frequency are depicted in Figures A-10 and A-11. Increasing any one of these ventilation parameters increased the lung burden, but the increase was much smaller with respect to respiratory frequency than to tidal volume. This small increase in lung burden was a result of the decrease in deposition efficiency as respiratory frequency increased, despite a higher total amount of DPM inhaled. The mode of breathing has only a minor effect on lung burden because switching from nose breathing does not produce any appreciable change in the amount of particle intake into the lung (Yu and Xu, 1987). All lung burden results presented in this report are for nose breathing.

A.8.2. Effect of Transport Rates

Transport rates have an obvious effect on the retention of DPM in the lung after deposition. Because we are mainly concerned with the long-term clearance of diesel soot and the associated organics, only the effects of two transport rates, $\lambda_A^{(1)}$ and $\lambda_A^{(2)}$, are studied. Experimental data of $\lambda_A^{(1)}$ from various diesel studies in rats have shown that $\lambda_A^{(1)}$ can vary by a factor of two or higher. We use a multiple of 0.5 to 2 for the uncertainty in $\lambda_A^{(1)}$ and $\lambda_A^{(2)}$ to examine the effect on lung burden. Figures A-12 and A-13 show respectively, the lung burden results for diesel soot and the associated organics versus the multiples of $\lambda_A^{(1)}$ and $\lambda_A^{(2)}$ used in the calculation. As expected, increasing the multiple of $\lambda_A^{(1)}$ reduced the lung burden of diesel soot with practically no change in the organics burden (Figure A-12), while just the opposite occurred when the multiple of $\lambda_A^{(2)}$ was increased (Figure A-13).

A.9. OPERATIONAL DERIVATION OF HUMAN EQUIVALENT CONCENTRATIONS (HECs)

The model of Yu et al. (1991) is ordered into two parts; one part parameterized on the physiology and anatomy of a 300 g rat and the other part parameterized on the physiology and anatomy of a 25 year old human male. The sequence of steps taken to calculate the human equivalent continuous concentrations (the HECs), outlined in Table A-4, were as follows:

- The exposure scenario of the rats was entered into the rat portion of the model and the model ran to obtain the output of lung burden in mg DPM/ rat lung at the time of the sacrifice of the rats.
- The output of mg DPM/ rat lung was normalized to mg DPM/ cm^2 of rat lung tissue based on a total pulmonary surface area of 4090 cm^2.

- The normalized rat lung burdens were used to calculate the corresponding lung burden based on the pulmonary surface area of 627,000 cm^2. This operation yielded mg DPM / lung of a 25 year old human male.
- Various air concentrations were run in an iterative fashion with the human portion of the model under a continuous exposure scenario of 24 hrs/day, 7d/wk for 70 years with ventilatory parameters set at 0.926 L for tidal volume and 15 breaths per minute as the respiratory frequency to yield a total daily pulmonary volume of 20 m^3. This was continued until the output (mg DPM/lung) was matched to the mg DPM /human lung obtained from the normalized rat lung burden; the concentration from the model that matched this lung burden was termed the human equivalent continuous concentration, the HEC. The human modeling runs did not consider the preadult status of airway and alveoli number discussed above but rather were ran for 1 to 70 years with adult (25 years of age) parameters mentioned above.

These HEC values address kinetic issues of DPM deposition and retention in the lung by humans. As noted above, these values do not reflect the kinetic variability that may exist in the human population exposed to DPM which includes men and women, young and old. However, the limited parametric analysis of the model clearly shows variability of those parameters most determinative in humans (e.g., tidal volume, respiration rate, and rates of clearance of particles from the airways) were mirrored in the corresponding output of the model (lung burden of DPM). One interpretation of this parallel in parameter-output is that the variability in the physiological characteristics of humans reflects the variability in the model such that, for example, a small tidal volume would be reflected with a decreased lung burden of DPM. Variability among humans of these key parameters such as tidal volume do vary but within an order of magnitude. This would mean that the DPM dose received by different individuals in the population from the same concentration would indeed vary within the extremes of these determinative parameters.

Table A-1. Lung model for rats at total lung capacity

Generation number	Number of airways	Length (cm)	Diameter (cm)	Accumulative volume[a] (cm)
1	1	2.680	0.340	0.243
2	2	0.715	0.290	0.338
3	3	0.400	0.263	0.403
4	5	0.176	0.203	0.431
5	8	0.208	0.163	0.466
6	14	0.117	0.134	0.486
7	23	0.114	0.123	0.520
8	38	0.130	0.112	0.569
9	65	0.099	0.095	0.615
10	109	0.091	0.087	0.674
11	184	0.096	0.078	0.758
12	309	0.073	0.070	0.845
13	521	0.075	0.058	0.948
14	877	0.060	0.049	1.047
15	1,477	0.055	0.036	1.414
16[b]	2,487	0.035	0.020	1.185
17	4,974	0.029	0.017	1.254
18	9,948	0.025	0.016	1.375
19	19,896	0.022	0.015	1.595
21	39,792	0.020	0.014	2.003
22	79,584	0.019	0.014	2.607
25	318,336	0.017	0.014	7.554
24	636,672	0.017	0.014	13.784

[a]Including the attached alveoli volume (number of alveoli = 3×10^7, alveolar diameter = 0.0086 cm).
[b]Terminal bronchioles.

Table A-2. Lung model by Weibel (1963) adjusted to 3000 cm^3 lung volume

Generation number	Number of airways	Length (cm)	Diameter (cm)	Accumulative volume[a] (cm)
0	1	10.260	1.539	19.06
2	2	4.070	1.043	25.63
2	4	1.624	0.710	28.63
3	8	0.650	0.479	29.50
4	16	1.086	0.385	31.69
5	32	0.915	0.299	33.75
6	64	0.769	0.239	35.94
7	128	0.650	0.197	38.38
8	256	0.547	0.159	41.13
9	512	0.462	0.132	44.38
10	1,024	0.393	0.111	48.25
11	2,048	0.333	0.093	53.00
12	4,096	0.282	0.081	59.13
13	8,192	0.231	0.070	66.25
14	16,384	0.197	0.063	77.13
15	32,768	0.171	0.056	90.69
16[b]	65,536	0.141	0.051	109.25
17	131,072	0.121	0.046	139.31
18	262,144	0.100	0.043	190.60
19	524,283	0.085	0.040	288.16
20	1,048,579	0.071	0.038	512.94
21	2,097,152	0.060	0.037	925.04
22	4,194,304	0.050	0.035	1,694.16
23	8,388,608	0.043	0.035	3,000.00

Table A-3. Ratio of pulmonary surface areas between humansand rats as a function of human age

Age (year)	Surface area
0	4.99
1	17.3
2	27.6
3	36.7
4	44.7
5	51.9
6	58.5
7	64.6
8	70.4
9	76.0
10	81.4
11	86.6
12	91.6
13	96.4
14	101
15	106
16	110
27	115
28	119
19	123
20	128
21	132
22	136
23	140
24	144
25	148

Table A-4. Human equivalent continuous concentrations (HECs) calculated with the model of Yu et al. (1991) from long-term repeated exposure rat studies of DPM exposure

Study	Exposure conditions[a]	Rat exposure concs (mg/m^3)	mg DPM/ rat lung (modeled)[b]	mg DPM/cm^2 rat&human lung[b,c]	mg DPM/ human lung[c]	HEC (mg/m^3)[c]
Mauderly et al., 1987a	7 h/day, 5 days/wk, 130 wk[d]	0.35	0.28	6.85E-5	43	0.038
Mauderly et al., 1987a	7 h/day, 5 days/wk, 130 wk	3.47	20.23	4.95E-3	3101	1.375
Mauderly et al., 1987a	7 h/day, 5 days/wk, 130 wk	7.08	44.52	1.09E-2	6825	3.05
Ishinishi et al., 1988 (LD[c])	16 h/day, 6 days/wk, 130 wk	0.11	0.24	5.87E-5	37	0.032
Ishinishi et al., 1988 (LD)	16 h/day, 6 days/wk, 130 wk	0.41	1.00	2.45E-4	153	0.128
Ishinishi et al., 1988 (LD)	16 h/day, 6 days/wk, 130 wk	1.18	18.45	4.51E-3	2828	1.25
Ishinishi et al., 1988 (LD)	16 h/day, 6 days/wk, 130 wk	2.32	39.89	9.75E-3	6115	2.75
Ishinishi et al., 1988 (HD)	16 h/day, 6 days/wk, 130 wk	0.46	1.15	2.81E-4	176	0.144
Ishinishi et al., 1988 (HD)	16 h/day, 6 days/wk, 130 wk	0.96	12.94	3.16E-3	1984	0.883
Ishinishi et al., 1988 (HD)	16 h/day, 6 days/wk, 130 wk	1.84	31.22	7.63E-3	4786	2.15
Ishinishi et al., 1988 (HD)	16 h/day, 6 days/wk, 130 wk	3.72	64.67	1.58E-2	9914	4.4
Nikula et al., 1995	16 h/day, 5 days/wk, 100 wk	2.44	28.64	7.00E-3	4391	1.95
Nikula et al., 1995	16 h/day, 5 days/wk, 100 wk	6.3	76.15	1.86E-2	11674	5.1
Heinrich et al., 1995	18 h/day, 5 days/wk, 104 wk	0.84	3.83	9.4E-4	587	0.33
Heinrich et al., 1995	18 h/day, 5 days/wk, 104 wk	2.5	34.4	8.4E-3	5274	2.35
Heinrich et al., 1995	18 h/day, 5 days/wk, 104 wk	6.98	97.8	2.4E-2	14993	6.7

[a] These are entered into the program as hrs/day, days/week for the total number of weeks exposed and the last week of exposure before evaluation (as this would affect clearance). The parameters for the rat were based on a body weight which was set in the program at 300g.
[b] These values were obtained with the rat portion of the model and are noted as lung burden, in mg DPM /lung of a 300 g rat, at the final week of the exposure scenario. These outputs were then normalized to cm^2 of the rat lung, at 4090 cm^2 total (Xu and Yu, 1987).
[c] Preparatory to using the human portion of the model, the mg DPM/cm^2 value from above was used to project the mg DPM that would be present in the adult human lung based on a total lung surface area of 627,000 cm^2 (Xu and Yu, 1987). Various air concentrations were then entered into the human model as 70 years continuous exposure scenarios and ran iteratively until the output (in mg DPM / lung at age 70) matched this mg DPM/human lung, i.e., the total lung burden. This matching air concentration is, by definition, the human equivalent continuous concentration (HEC).
[d] weeks = (months of exposure) × 4.33.

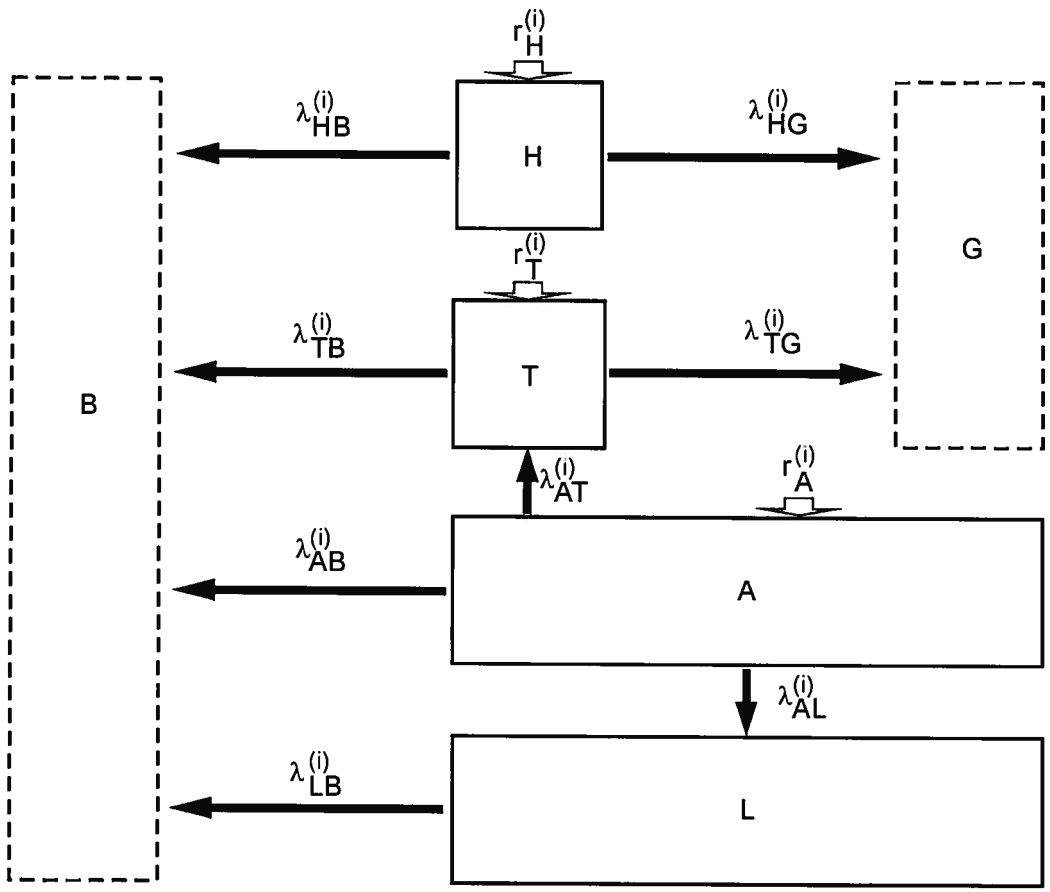

Figure A-1. Compartmental model of DPM retention.

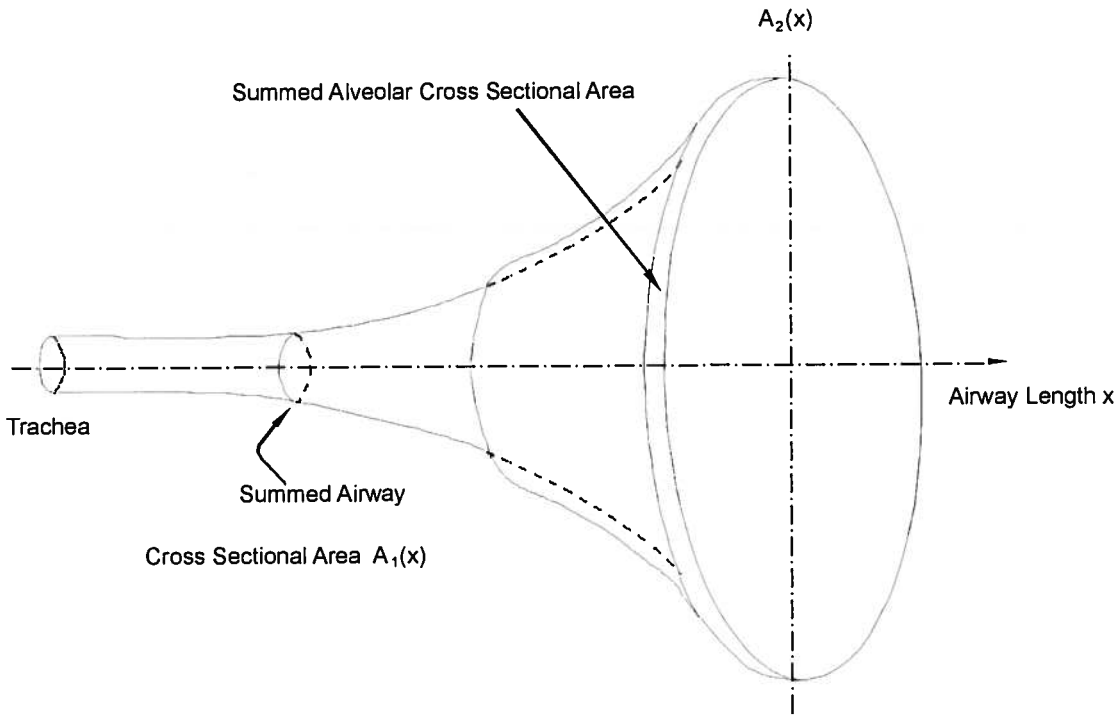

Figure A-2. Trumpet model of lung airways.

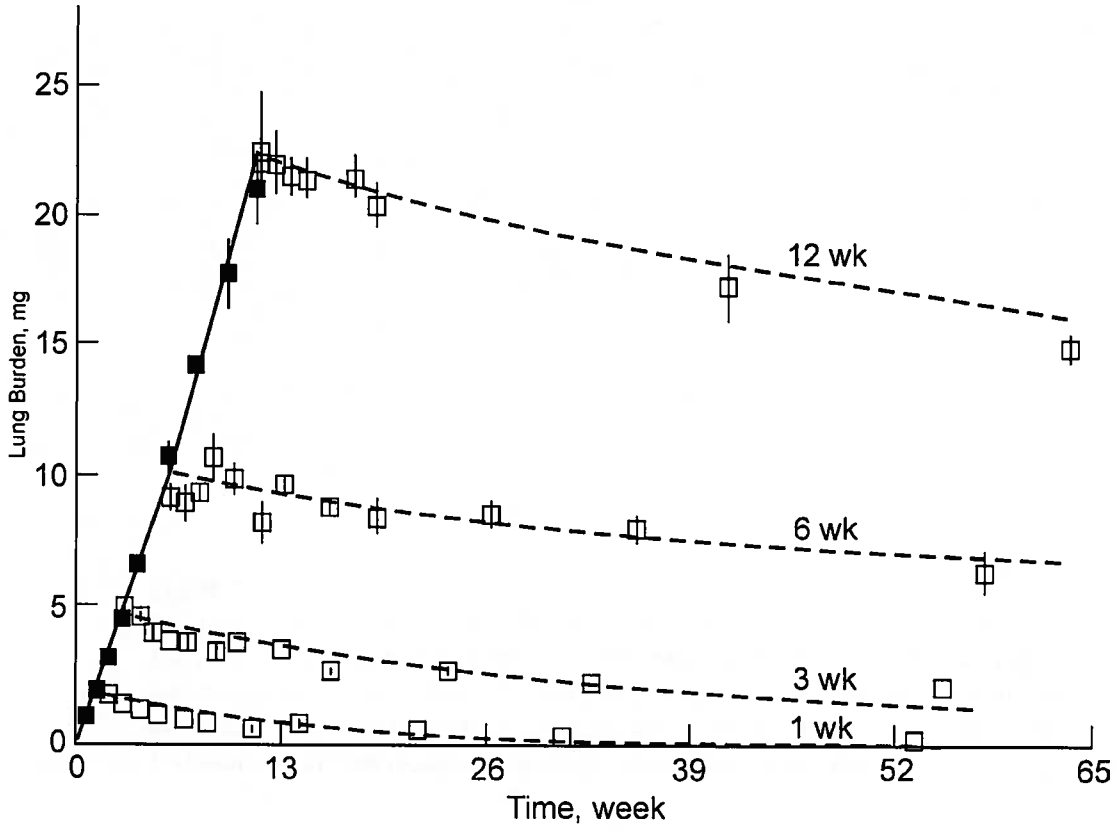

Figure A-3. The experimental and predicted lung burdens of rats to DPM at a solid and dashed concentration of 0.6 mg/m^3 for different exposure spans. Lines are, respectively, the predicted burdens during exposure and post-exposure. Particle characteristics and exposure pattern are explained in the text. The symbols represent the experimental data from Strom et al. (1988).

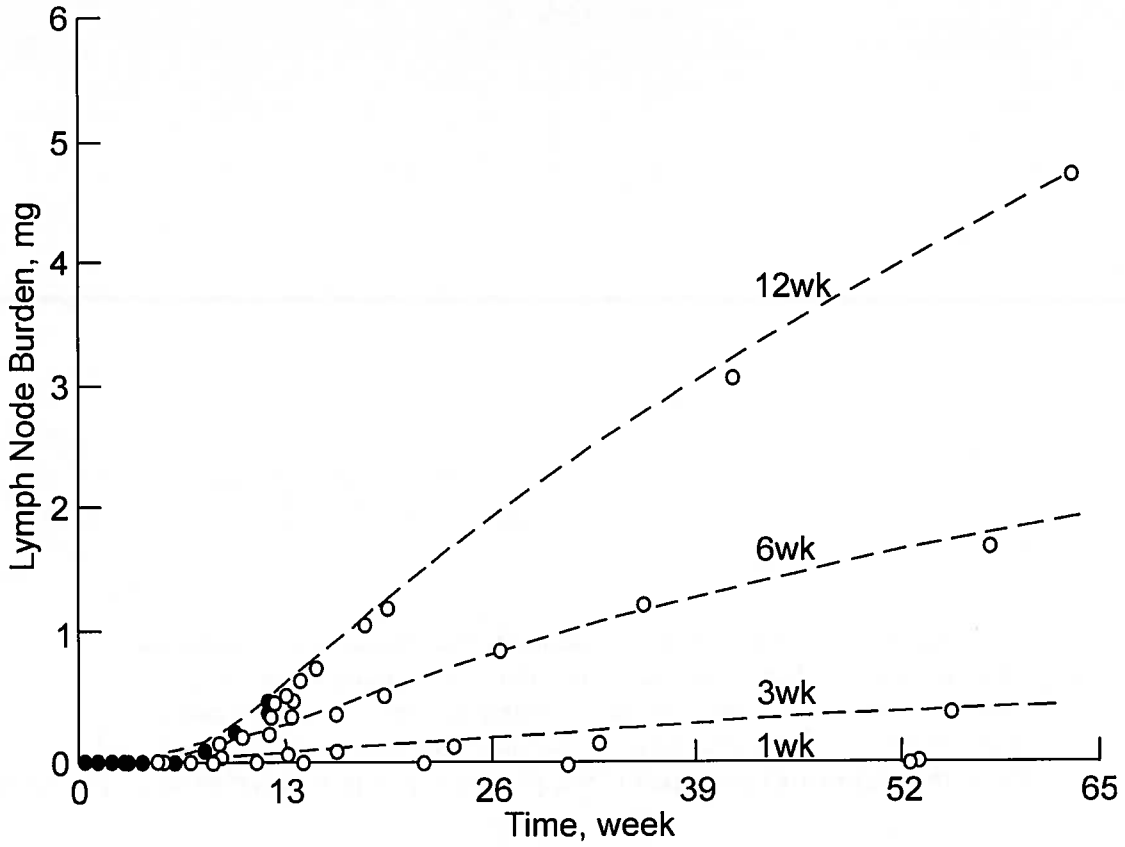

Figure A-4. Experimental and predicted lymph node burdens of rats exposed to CEPs at a concentration of 6.0 mg/m^3 for different exposure spans. The solid and dashed lines are, respectively, the predicted burdens during exposure and post-exposure. Particle characteristics and exposure pattern are explained in the text. The symbols represent the experimental data from Strom et al. (1988).

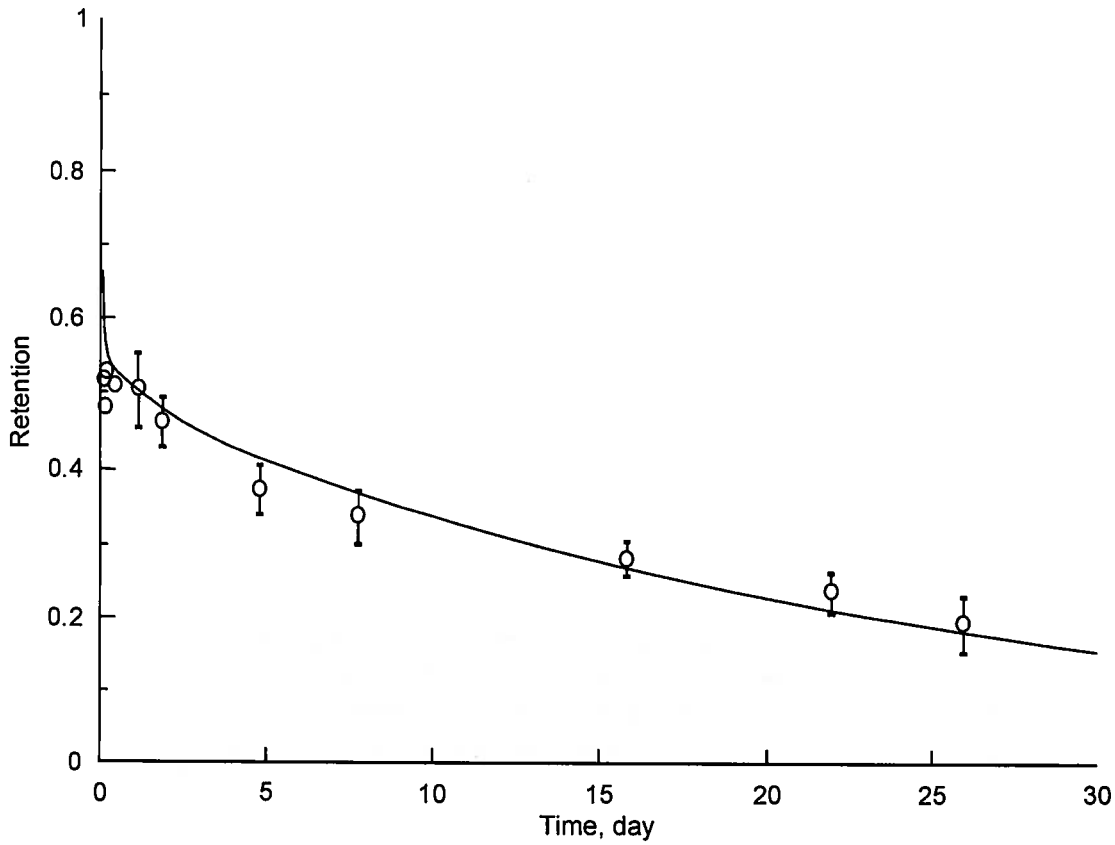

Figure A-5. Comparison between the calculated lung retention (solid line) and the experimental data obtained by Sun et al. (1984) for the particle-associated BaP in rats.

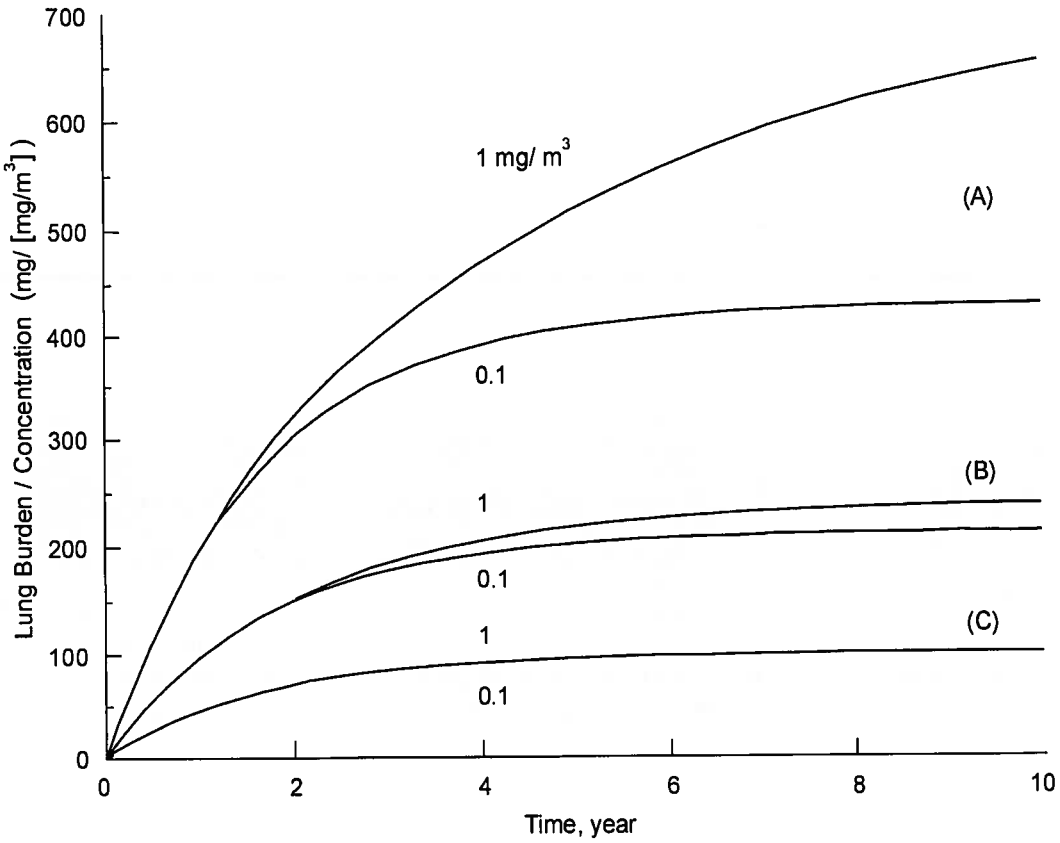

Figure A-6. Calculated lung burdens of diesel soot per unit exposure concentration in human adults exposed continuously to DPM at two different concentrations of 0.1 and 1.0 mg/m^3. Exposure patterns are (a) 24 h/day and 7 days/week, (b) 12 h/day and 7 days/week, and (c) 8 h/day and 5 days/week.

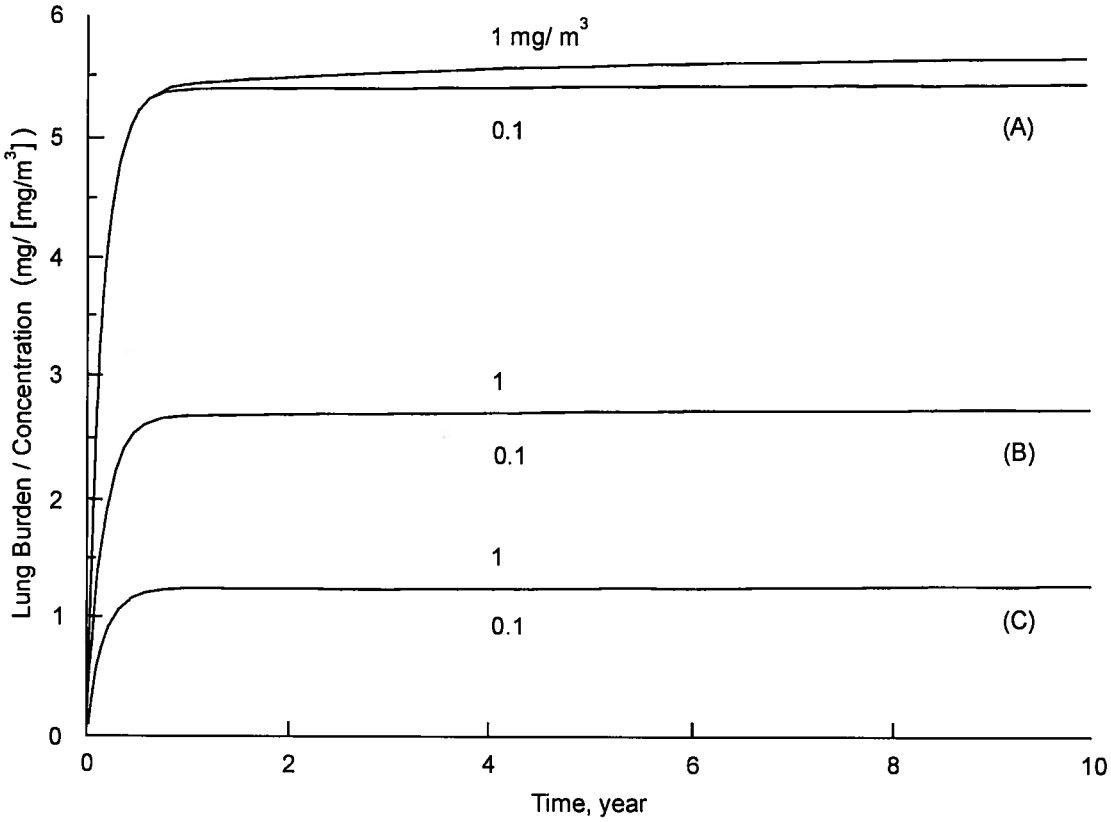

Figure A-7. Calculated lung burdens of the particle-associated organics per unit exposure concentration in human adults exposed continuously to DPM at two different concentrations of 0.1 and 1.0 mg/m^3. Exposure patterns are (a) 24 h/day and 7 days/week, (b) 12 h/day and 7 days/week, and (c) 8 h/day and 5 days/week.

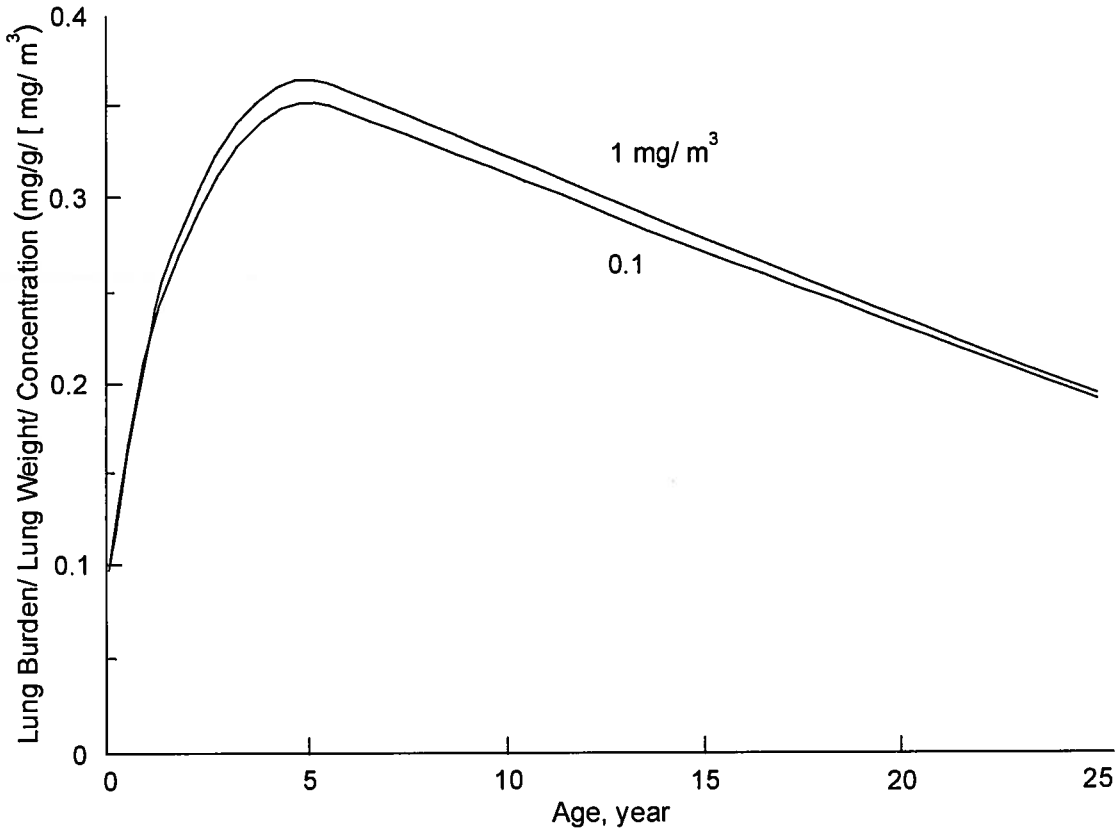

Figure A-8. Calculated lung burdens of diesel soot per gram of lung per unit exposure concentration in humans of different ages exposed continuously for 1 year to DPM of two different concentrations of 0.1 and 1.0 mg/m^3 for 7 days/week and 24 h daily.

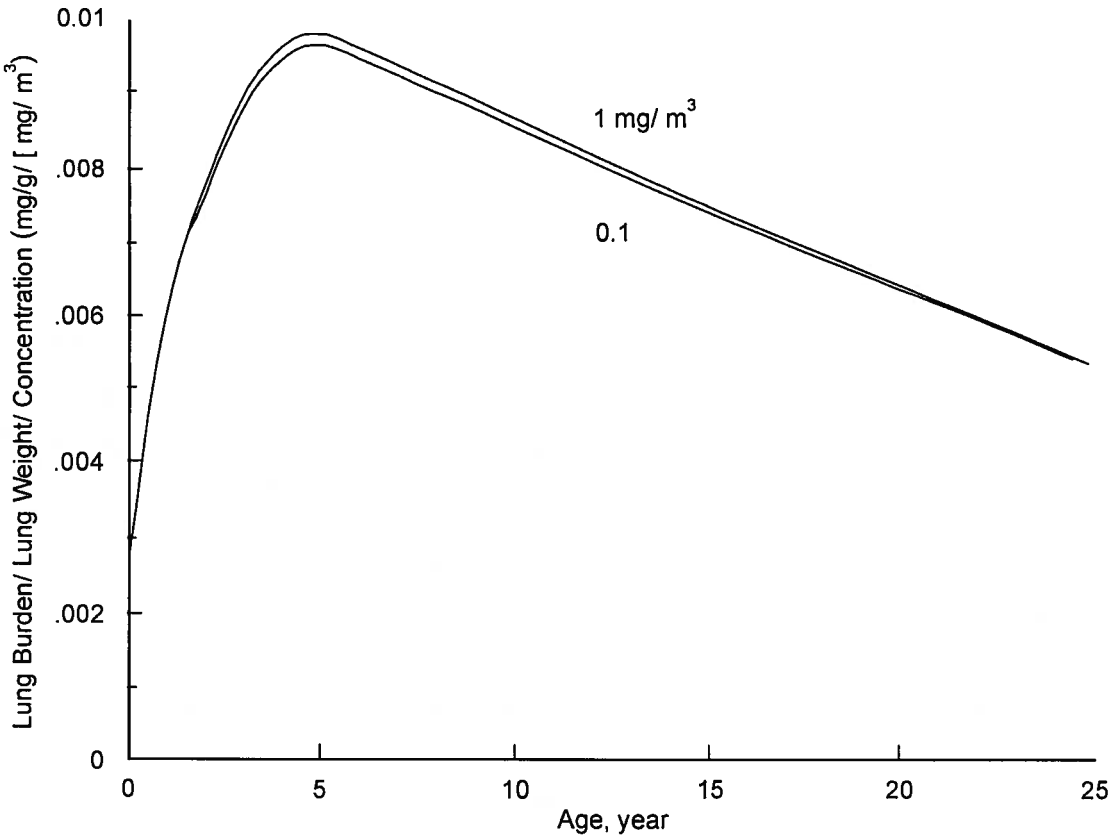

Figure A-9. Calculated burdens of the particle-associated organics per gram of lung per unit exposure concentration in humans of different ages exposed continuously for 1 year to DPM of two different concentrations of 0.1 and 1.0 mg/m^3 for 7 days/week and 24 h daily.

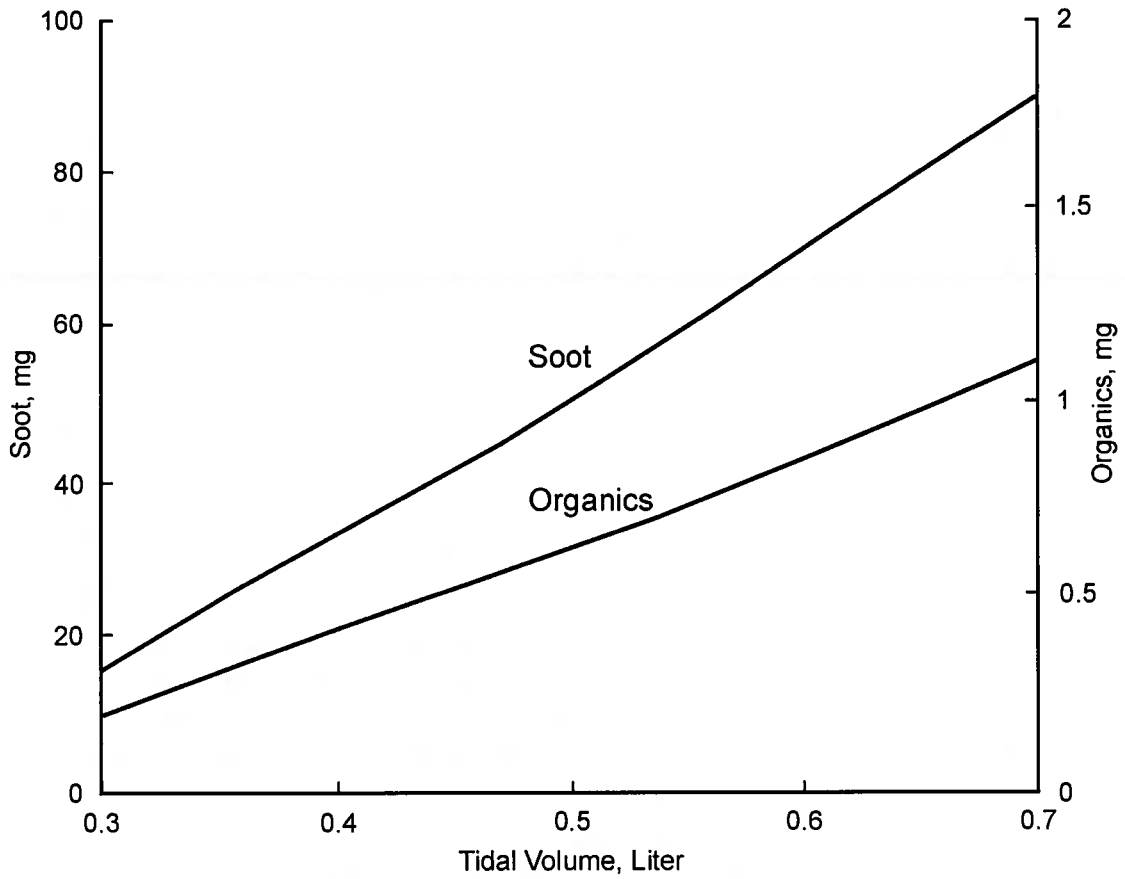

Figure A-10. Calculated lung burdens in human adults versus tidal volume in liters for exposure to DPM at 0.1 mg/m^3 for 10 years at 7 days/week and 24 h daily. Parameters used in the calculation are: (a) MMAD=0.2 µm, σ_g=2.3, f_2=0.1, f_3=0.1; (b) respiratory frequency = 14 min^{-1}; and (c) lung volume = 3000 cm^3.

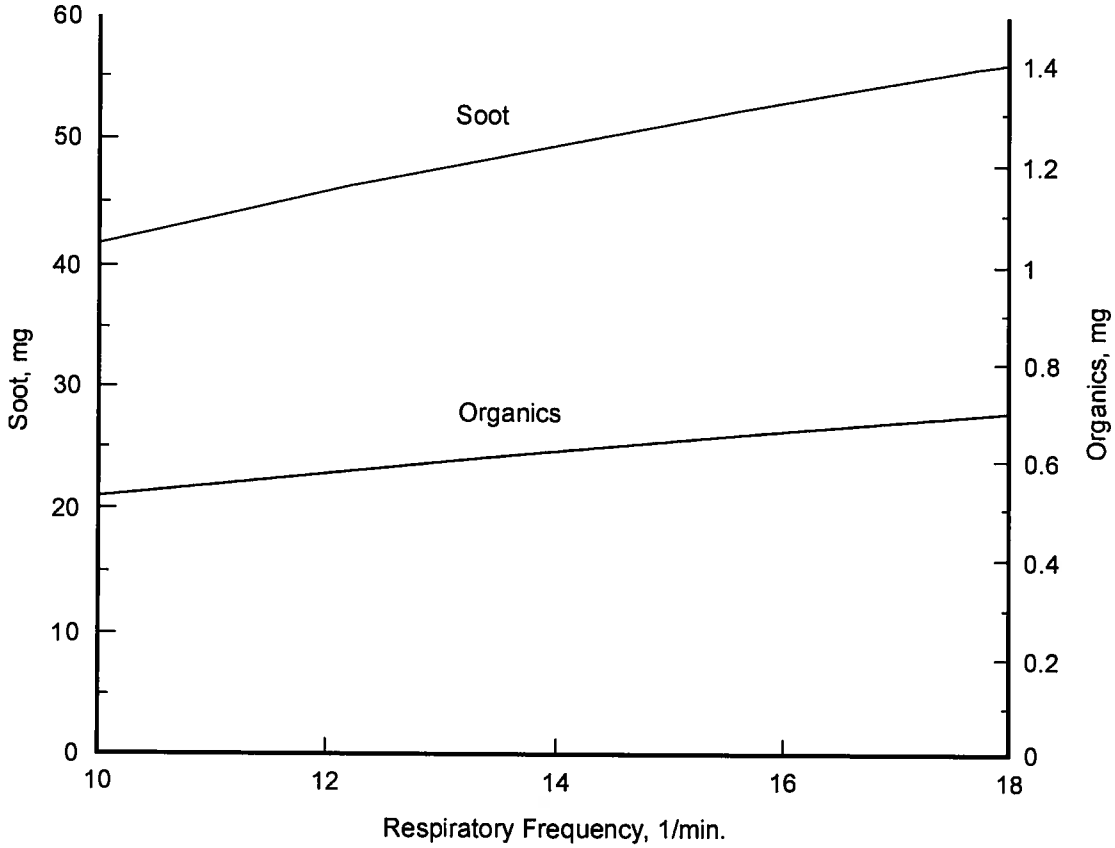

Figure A-11. Calculated lung burdens in human adults versus respiratory frequency in *bpm* for exposure to DPM at 0.1 mg/m^3 for 10 years at 7 days/week and 24 h daily. Parameters used in the calculation are: (a) MMAD=0.2 µm, σ_g=2.3, f_2=0.1, f_3=0.1; (b) tidal volume = 500 cm^3, and (c) lung volume = 3200 cm^3.

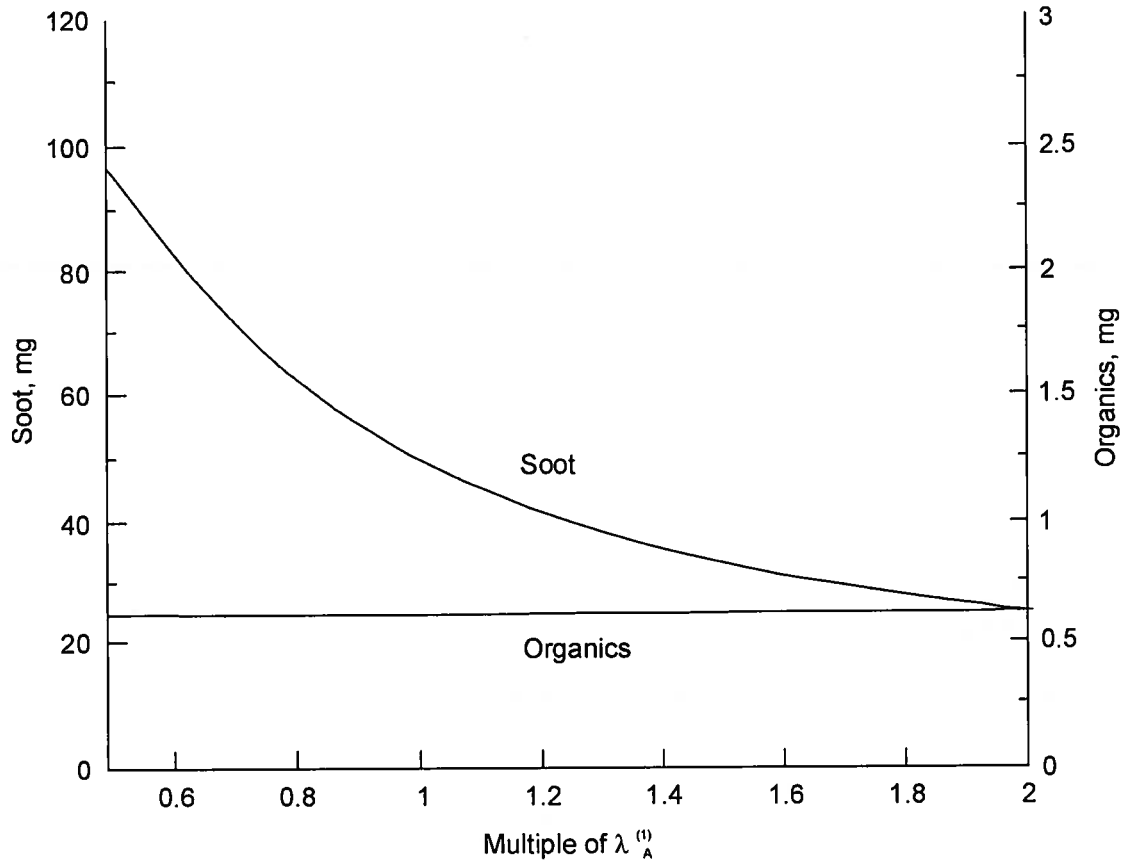

Figure A-12. Calculated lung burdens in human adults versus multiple of $\lambda_A^{(1)}$ for exposure to DPM at 0.1 mg/m$_3$ for 10 years at 7 days/week and 24 h daily. Parameters used in the calculation are: (a) MMAD=0.2 μm, σ_g=2.3, f_2=0.1, f_3=0.1; (b) tidal volume = 500 cm^3, respiratory frequency = 14 min^{-1}; and (c) lung volume = 3200 cm^3.

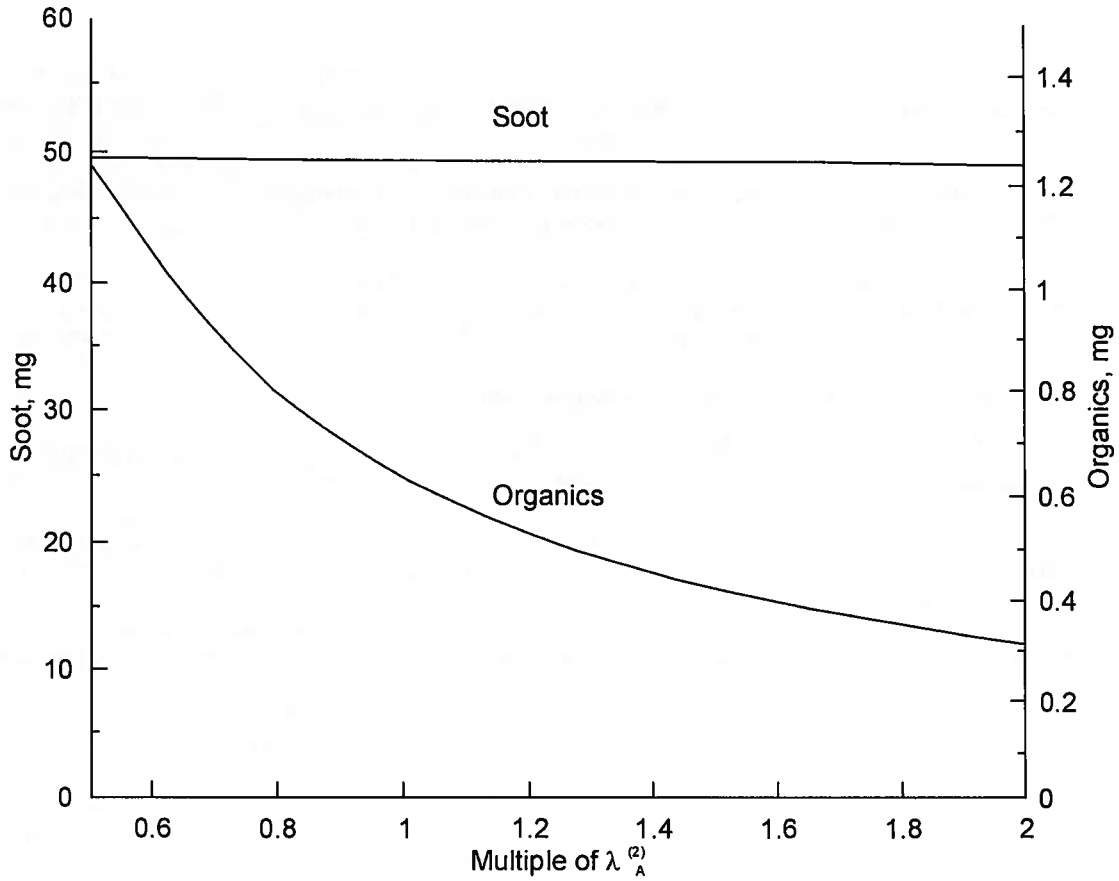

Figure A-13. Calculated lung burdens in human adults versus multiple of $\lambda_A^{(1)}$ for exposure to DPM at 0.1 mg/m^3 for 10 years at 7 days/week and 24 h daily. Parameters used in the calculation are: (a) MMAD=0.2 μm σ_g=2.3, f_2=0.1, f_3=0.1; (b) tidal volume = 500 cm^3, respiratory frequency = 14 min^{-1}; and (c) lung volume = 3200 cm^3.

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Appendix B

Benchmark Concentration Analysis of Diesel Data

B-1. INTRODUCTION TO BENCHMARK

The benchmark dose or benchmark concentration approach, hereafter referred to as the BMC approach, is an alternate to the N/LOAEL option for deriving effect levels. The BMC is currently undergoing extensive consideration by the Agency with promulgation of software and guidelines for application of this methodology (U.S. EPA, 2000). The BMC approach involves fitting a dose-response function to dose and effect information from a single study to derive the best fit of those data. This "best fit"is statistically termed the maximum likelihood estimate but is referred to in the benchmark terminology as the BMC curve. The curve defining the corresponding lower 95% confidence limit of this "best fit"estimate is termed the BMCL curve. This BMCL curve is used to predict the dose that will result in a level of response that is defined *a priori* as the benchmark response "x", $BMCL_x$. In the analyses below, for example, the benchmark response for a 10% increase in incidence[1] of chronic inflammation is defined as a $BMCL_{10}$; the corresponding 10% increase as determined from the BMC curve would be termed the BMC_{10}. This $BMCL_{10}$ would be derived by first using the data and the programs to determine the BMC and BMCL curves. The concentration corresponding to a 10% increase in incidence would then be determined directly from the BMCL. The $BMCL_{10}$ then would be used as the representative value for the effect level or point of departure in the dose-response assessment.

The latest version of the Agency Benchmark Dose Software (BMDS Version 1.2; U.S. EPA, 2000) was used to analyze data on chronic inflammation and pulmonary histopathology present in the chronic studies that were amenable to benchmark analysis. At this time, the Agency BMDS offers sixteen different models total that are appropriate for the analysis of dichotomous data (gamma, logistic, probit, Weibull, log-logistic, multistage, log-probit, quantal-linear, quantal-quadratic), continuous data (linear, polynomial, power, Hill) and nested developmental toxicology data (NLogistic, NCTR, Rai & Van Ryzin). Results from all models include a reiteration of the model formula and model run options chosen by the user, goodness-of-fit information, a graphical presentation for visual inspection and the concentration estimate for the response at the designated $BMCL_x$, as well as the corresponding BMC_x. More details on the modeling results are described and presented in the analysis on dichotomous data following.

The U.S. EPA benchmark dose (BMD/C) methods guidance has not been finalized at this time to provide definitive procedures and criteria (U.S. EPA 1995). Therefore, in this document provisional criteria for minimum data to perform a benchmark analysis are designated such that (1) complete quantitative information on the response of interest should be available (e.g.,

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[1]For increases in incidence "extra risk" is used which is response incidence (inc) normalized to the background (BG) incidence; response – BG/1-BG.

incidence as number affected / total, means with variability) and that (2) at least two exposure levels with responses that differ from those of the controls are provided, and (3) a benchmark response of 10% is employed such that outcomes are $BMCL_{10}$s. A response of 10% is at or near the limit of sensitivity in most long-term bioassays as determined from both the typical number of animals used in bioassays and a low spontaneous background rate (e.g., 0.1%) for a given effect (Haseman, 1984; Haseman et al., 1989).

B-2. DIESEL DATA FOR BENCHMARK ANALYSIS

Using the criteria set forth in Section B-1 and the information about the critical effects that have been identified (pulmonary inflammation, pulmonary histopathology including indicators of fibrotic changes such as increases in alveolar-capillary wall thickness) the following rat chronic studies identified in Chapter 6 were analyzed for information suitable for BMC analysis: Ishinishi et al. (1986, 1988), Mauderly et al. (1987a,b; 1988); Heinrich et al. (1986, 1995), and Nikula et al. (1995).

Results from this analysis yielded only a few data sets from a single study, that of Nikula et al. (1995), that could be used for BMC analysis. The basis for not including data from the other studies varied. Information on pulmonary histopathology in the studies of Ishinishi et al. (1986, 1988), for example, was supplied only in narrative form with no quantitative information given. A similar situation was found for those reports of the ITRI study; Wolff et al. (1987) reports on clearance alterations due to DPM exposure; Henderson et al. (1988) does give information on hydroxyproline but only in graphical form; the 1988 study of Mauderly et al. deals with pulmonary function as a function of DPM lung loading; the 1987a reference of Mauderly et al. discusses tumor prevalence only and the Mauderly 1987b reference reports on diesel exhaust in developing lung to a single exposure concentration of DPM with no dose-response information available. Those reports on the General Motor study contain extensive information relating not to the critical effects, but mostly to precursors of inflammation such as levels of polymorphonuclear neutrophils and lymphocytes in bronchoalveolar lavage from DPM exposed rats (Strom, 1984) and guinea pigs (Barnhart et al., 1981) as well as information on collagen biosynthesis (Misiorowski et al., 1980) all of which is presented in graphical rather than tabular form amenable for benchmark analysis. The information on noncancer histopathology reported by Heinrich et al. (1995) is in text form only and this author's 1986 study deals primarily with clearance and mortality. Nikula et al. (1995), however, do present extensive quantitative dose-response information (incidence / dichotomous data) on several measures of the critical effect including chronic inflamation (presence of focal aggregates of neutrophils), focal fibrosis with epithelial hyperplasia (nodular fibrosis rimmed by hyperplasia), and septal fibrosis (interstitial fibrosis within alveolar septa) although the study had but 2 exposure

concentrations both of which are different from the controls, a minimal number on which benchmark analysis should be performed.

B-3. BENCHMARK ANALYSIS OF DIESEL DATA

These data from Nikula et al. (1995) were extracted, HEC concentrations calculated using the model of Yu et al. (1991; Appendix A), and analyzed using all 9 applicable models for dichotomous data. Because the benchmark models were ran with the HEC, general from the model of Yu et al. (1991), the $BMCL_{10s}$ are also HECs. The results and data are presented in Table B-1. Results were evaluated based on the nature of the data set, visual inspection of the graphical output, and on the goodness-of-fit parameters, including p values and the AIC. When p values were generated for model fits, values for p that were less than 0.1 were considered to reflect a minimal fit to the data and were disqualified from further consideration. However, the small set of only 3 data points was often matched by the number of parameters fitted in several of the models such that the outcome of the model exactly fit the data and thus no p value is generated; these model fits are often referred to as being overparameterized, and are indicated as "NA" in Table B-1. Values for p that were less than 0.1 were considered to reflect a minimal fit to the data. The AIC (Akaike Information Coefficient; Akaike, 1973; Stone, 1998) is a parameter generated for the models in U.S. EPA (2000) that allows for a general comparison among models run on the same data set. The AIC is defined as $-2 \log L + 2 p$ where log L is the log likelihood of the fitted model, and p is the number of parameters estimated; smaller values indicate better fits.

The overall results of this mathematical analysis is reasonable in a biologically mechanistic sense in that chronic inflammation is more prevalent and apparently occurs at lower concentrations (i.e., has lower $BMCL_{10}$ values) than does focal fibrosis. The information on septal fibrosis were not interpretable as the data were not amenable (no or zero background and then total incidence) to any meaningful benchmark or other dose-response analysis. The most sensitive endpoint, chronic inflammation, is therefore the most sensitive benchmark concentration followed by focal fibrosis.

The choice for the most appropriate $BMCL_{10}$ from among the various modeled values for chronic inflammation requires analysis of both the statistical and graphical outputs of the data. The shape of the dose-response curve from information given in Chapter 6 (Table 6-2) gives evidence of considerable "S" character, e.g., several low HECs without any reported effects up to about 0.2 mg/m^3. The shape of the dose-response curves generated by several of the models, including gamma-hit, Weibull, multistage, and quantal linear were all a uniformly upward sloping arc from the origin (graphs not shown) with minimal evidence of any "S" character, a shape not concordant with the data array in Table 6.2. Models that did generate curves with "S"

character included log-logistic, logistic, probit, quantal-quadratic, and log-probit. Because of their concordance with this independent data array on dose-response, the latter outputs are further analyzes.

The results for both chronic inflammation and focal fibrosis for those models with outputs having appreciable "S" character suggest that females may be more sensitive than males for these endpoints as the incidences are higher and the $BMCL_{10}$ values are generally lower for females than for males. However, the model fits of the $BMCL_{10}$s to the chronic inflammation data segregated by sex were generally inadequate as judged from the p values (most being far less than 0.1) or from visual inspection of the fits to the data, several of which (e.g., log-logistic and log-probit) were lacking any appreciable "S" character. However, combining female and male data improved data fitting as judged by the increased p values to where nearly all were >0.1 and to where the visual fits were concordant with the independent information on dose-response. Too, most of the combined $BMCL_{10}$s were either intermediate between the female and male values or somewhat closer to the female values such that the combined $BMCL_{10}$ values were not much different from the females $BMCL_{10}$s.

From among the combined male and female model outputs in Table B-1, the logistic, probit, and quantal quadratic results were all excluded based on the high AIC value relative to the log-logistic and log-probit results. The log-logistic results were excluded based on the shape of the lower portion of the dose-response curve which was upward sloping near the origin (graph not shown) and not as concordant with the independent dose-response information in Table 6-2 as was the fit of the log-probit model (Figure B-1). This leaves the fit of the log-probit model as being most reflective of the information in Table 6-2. The $BMCL_{10}$ of the log-probit curve at 0.37 mg/m^3 remains and, by elimination, appears to be the most defensible choice from among the $BMCL_{10}$s arrayed in Table B-1. Figure B-1 shows the graphical representation of the log-probit model fit to the data and the origin of the $BMCL_{10}$. This graph also shows the relationship of the $BMCL_{10}$ of 0.37 mg/m^3 to the variability that exists around the control value and that the value of 0.37 mg/m^3 is not far removed from the outer range of this variability. The log-probit $BMCL_{10}$ for focal fibrosis (combined) of 1.3 mg/m^3 noted as being representative of this lesion from the BMC analysis in Table B-1.

Characterization of this benchmark value indicates that it may not be a suitable candidate for use as a point of departure for development of a dose-response assessment such as the RfC. An attribute of the benchmark method is that the response (such as the 10% as used here) is near the range of the actual experimental values, such that extrapolation is not far below the observed experimental range. However, due to the paucity of data points overall and lack of any values below an HEC of nearly 2 mg/m^3 in the Nikula et al. (1995) study, the extrapolation of this BMC to the 10% response level is considerable, the $BMLC_{10}$ of 0.37 mg/m^3 being > 5-fold below the

nearest observed value of 1.95 mg/m^3. Also, the high experimental exposures used in this study are in the range of those resulting in pulmonary overload conditions in rats and therefore in the range of the model assumptions of Yu et al. (1991) about this phenomenon in humans for calculation of the HECs (Chapter 3). The $BMCL_{10}$ of 0.37 mg/m^3 is considerably greater than other NOAELs in the DPM data base of 0.144 mg/m^3 and 0.128 mg/m^3 (Table 6-2 in Chapter 6), possibly indicating that these NOAELs represent actual incidence levels that are considerably less than10%; from the same log-probit model the corresponding $BMCL_{05}$ was 0.21 mg/m^3 (near the range of these NOAELs) and the corresponding $BMCL_{01}$ was 0.07 mg/m^3 (below the range of these NOAELs). These limitations on this $BMCL_{10}$ make it a less than optimal candidate for consideration as a point of departure in the development of dose-response assessments.

B-4. SUMMARY

The recently developed EPA Benchmark dose software (U.S. EPA, 2000) and preliminary guidance was utilized to analyze diesel data by the benchmark approach. Data from only one of the array of principal studies identified elsewhere (Chapter 6) was found to contain data amenable to benchmark analysis. The data from this study, that of Nikula et al. (1995) on pulmonary inflammation and histopathology, was extracted and analyzed as dichotomous data using all available models and designating a 10% response level such that $BMCL_{10}$s were calculated; as the models were ran with HECs, the $BMCL_{10s}$ were also HECs.

The analysis resulted in an array of $BMCL_{10}$s from 3 different effects in two sexes (both separate and combined) with 9 different models. These $BMCL_{10}$s were each considered from a perspective of biological relevance, known dose-response character, and from the individual fit to the data by the models from statistical parameters and visual judgments. The $BMCL_{10}$ that emerged after the above considerations was 0.37 mg/m^3 for the combined male plus female incidence of chronic active pulmonary inflammation. A $BMCL_{10}$ of 1.3 mg/m^3 for pulmonary focal fibrosis was also noted in this analysis. Characterization of these benchmark values indicates that neither may be a suitable candidate for use as a point of departure in development of a dose-response assessment such as the RfC but that they are concordant with other quantitative dose-response aspects of the DPM database.

Table B-1. BMC analysis of pathology incidence data in male and female F344 rats from the study of Nikula et al. (1995) using the different models available from U. S. EPA benchmark dose project (U.S. EPA, 2000) for dichotomous data based on 10% extra risk (i.e., a 10% increase relative to a total that has been adjusted for background) and no threshold term. The concentrations used in the analysis are human continuous equivalent concentrations (HECs) obtained from the interspecies extrapolation model of Yu et al. (1991). The table listings include the $BMCL_{10}$ (the benchmark response level of 10% obtained from the lower 95% limit of the benchmark curve in mg/m^3), the BMC_{10} (the corresponding estimate at 10% response from the best fit benchmark curve, also in mg/m^3), P = goodness-of-fit values. NA indicates a G-O-F value was not available, usually due to the lack of degrees of freedom. AIC = Akaike Information Coefficient (see U.S. EPA, 2000 and below) which may be used for model comparison on the same data set.

Effect (from Table 5 and 6, p 86, Nikula et al., 1995)	Inc @ 0 mg/m^3	Inc @ 1.95 mg/m^3 HEC	Inc @ 5.1 mg/m^3 HEC	$BMCL_{10}$ (BMC_{10}) log-logistic	$BMCL_{10}$ (BMC_{10}) log-probit	$BMCL_{10}$ (BMC_{10}) multi-stage	$BMCL_{10}$ (BMC_{10}) - Weibull	$BMCL_{10}$ (BMC_{10}) - gamma	$BMCL_{10}$ (BMC_{10}) - quantal linear	$BMCL_{10}$ (BMC_{10}) - probit	$BMCL_{10}$ (BMC_{10}) - logistic	$BMCL_{10}$ (BMC_{10}) quantal quadratic
Chronic active inflammation >18 mos, grades 1-3, male + female combined	5/177	59/162	118/174	0.32(0.64) P= NA AIC= 483	0.37(.70) P=NA AIC = 483	0.43(.49) P= 0.982 AIC= 481	0.43(.49) P= 0.982 AIC= 481	0.43(.49) P=0.98 AIC= 480	0.43(.49) P= .982 AIC= 481	1.06(1.19) P= 0.000 AIC= 499	1.12(1.26) P=0.000 AIC= 502	1.34(1.45) P= 0.000 AIC = 505
Chronic active inflammation >18 mos, grades 1-3 in males	1/86	19/81	54/85	0.67(1.16) P= NA AIC= 217	0.74(1.22) P = NA AIC = 217	0.56(.95) undefined AIC= 217	.56(1.04) P= NA AIC= 216	.56(1.09) P= NA AIC= 217	0.50(.61) P= 0.15 AIC= 216	1.31(1.55) P= 0.05 AIC= 219	0.67(1.16) P= NA AIC= 217	1.42(1.57) P= 0.055 AIC = 218
Chronic active inflammation >18 mos, grades 1-3 in females	4/91	40/81	64/89	0.18(0.26) P= NA AIC= 257	.016(.30) P = NA AIC = 257	0.33(.40) P= 0.173 AIC= 257	0.33(.40) P= 0.173 AIC= 257	0.33(.40) P= 0.17 AIC= 257	0.33(.40) P= 0.173 AIC= 257	0.83(.96) P= 0.0001 AIC= 272	0.85(1.0) P= 0.000 AIC= 273	1.21(1.35) P= 0.000 AIC = 279
Focal fibrosis with epithelial hyperplasia, grades 1-4 in males and females combined	0/177	18/162	63/174	1.25(1.8) P= 1.000 AIC= 345	1.3(1.8) P = 1.000 AIC = 345	1.21(1.8) P= 1.000 AIC= 345	1.21(1.8) P= 1.000 AIC= 345	1.21(1.8) P= 1.0 AIC= 345	1.1(1.3) P= 0.363 AIC= 345	2.32(2.61) P= 0.013 AIC= 353	2.50(2.8) P= 0.006 AIC= 356	2.14(2.34) P= 0.091 AIC = 347
Focal fibrosis with epithelial hyperplasia, grades 1-4 in males	0/86	5/81	19/85	1.72(2.7) P= 1.00 AIC= 132	1.6(2.7) P = 1.000 AIC = 132	1.79(2.8) undefined AIC= 134	1.79(2.8) P= 1.00 AIC= 132	1.79(2.75 P= 1.0 AIC= 132	1.7(2.4) P= 0.70 AIC= 131	2.98(3.5) P= 0.199 AIC= 134	3.17(3.69) P= 0.153 AIC= 135	2.68(3.1) P=0.552 AIC = 131
Focal fibrosis with epithelial hyperplasia, grades 1-4 in females	0/91	13/81	44/89	0.80(1.4) P= 1.00 AIC= 199	0.87(1.47) P = 1.000 AIC = 199	0.77 P= 0.99 AIC= 199	0.77(1.4) P=1.0 AIC=199	0.71(1.4) P= 1.00 AIC= 199	0.71(.88) P= 0.445 AIC= 198	1.76 P= 0.037 AIC= 205	1.89(2.2) P= 0.02 AIC= 207	1.7(1.9) P= 0.21 AIC = 200
Septal fibrosis, >18 mos, grades 1-4 in males	1/86	79/81	83/85	.003(.008) P= 0.35 AIC= 53	(failed)	0.07(.08) P= 0.000 AIC= 65	0.07(.08) P= 0.000 AIC= 65	0.07(.08) P= 0.000 AIC= 65	0.07(.08) P= 0.000 AIC= 65	0.29(.37) P= 0.000 AIC= 114	0.32(.44) P= 0.000 AIC= 86	0.42(0.47) P= 0.000 AIC = 100
Septal fibrosis, >18 mos, grades 1- 4 in females	2/91	75/81	87/89	0.009 (.05) P= NA AIC= 87	(failed)	0.08(.10) P= 0.003 AIC= 91	0.08(.10) P= 0.000 AIC= 91	0.08(.10) P= 0.003 AIC= 91	0.08(.10) P= 0.003 AIC= 91	0.32(.40) P= 0.000 AIC= 131	0.34(.45) P= 0.000 AIC= 109	0.46(.51) P= 0.000 AIC = 119

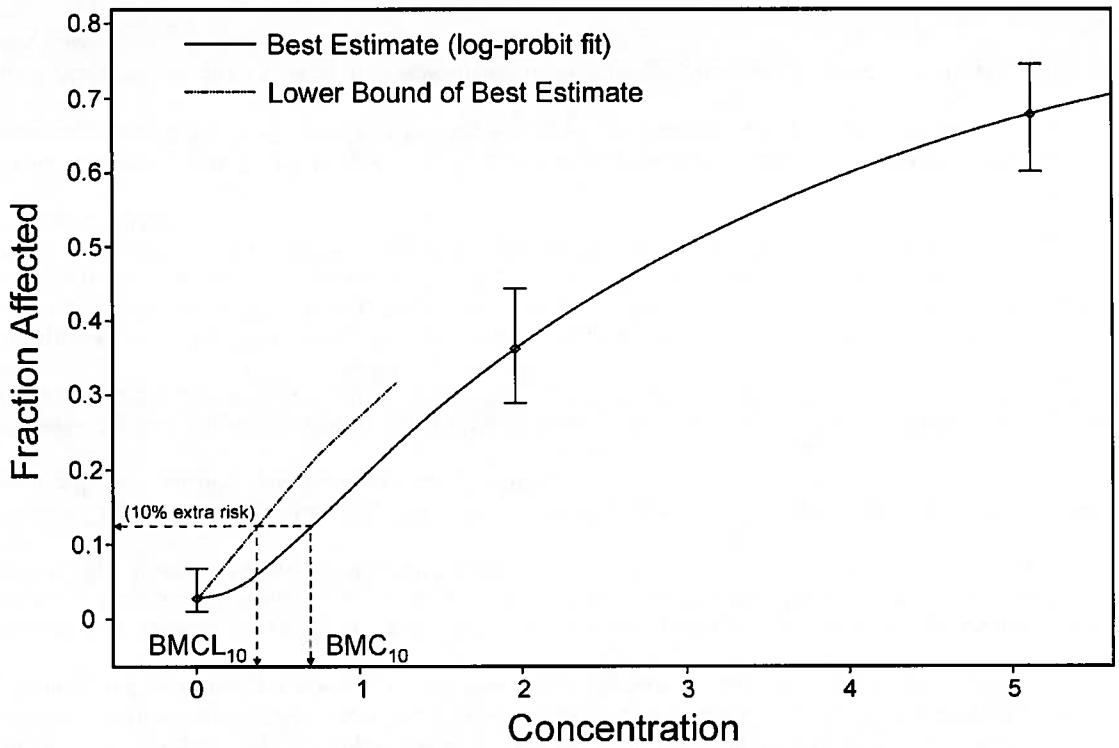

Figure B-1. Benchmark concentration analysis (log-probit) of chronic pulmonary inflammation in rats exposed to DPM from Nikula et al. (1995). $BMCL_{10}$, the lower confidence estimate of the concentration of DPM associated with a 10% incidence (extra risk); BMC_{10}, the corresponding estimate from the best (log-probit) fit. (◊) data with 95% error bounds.

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Appendix C

A Summary Review of Cancer Dose-response Analyses on Diesel Exhaust

C.1. INTRODUCTION

Several individuals and organizations have previously conducted dose-response assessments to estimate quantitatively the cancer risk from exposures to DE. Estimations were performed on the basis of either epidemiologic and/or experimental data. As concluded in Section 8.5, EPA finds that available epidemiologic data are too uncertain to confidently derive a unit risk estimate for DE-induced lung cancer, and that rat data are not suitable for estimating human risk. Nevertheless, a review of historical dose-response evaluations is provided here as background information. This information is not intended to constitute endorsement or a recommendation for use in quantitative risk assessment.

Early analyses to quantitatively assess the carcinogenicity of DE were hindered by a lack of positive epidemiologic studies and long-term animal studies. One means of overcoming these obstacles was the use of comparative potency methods based on combined epidemiologic and experimental data. By the late 1980s, the availability of dose-response data from animal bioassays and epidemiologic studies provided an opportunity for the derivation of both animal and human data-based estimates, although considerable uncertainties were generally acknowledged by the authors of these assessments.

C.2. COMPARATIVE POTENCY METHODS

In this method, the potency of diesel particulate matter (DPM) extract is compared with other combustion or pyrolysis products for which epidemiology-based unit risk estimates have been developed. Comparisons are made using short-term tests such as skin painting, mutations, and mammalian cell transformation. The ratio of the potency of DPM extract to each of these agents is then multiplied by their individual unit risk estimates to obtain the unit risk for DE. If epidemiology-based estimates from more than one pollutant are used, the derived potencies are generally averaged to obtain an overall mean. Major uncertainties of this method include the assumptions that (1) the cancer potency of DE can be determined on the basis of the relative effectiveness of the organic fraction alone; (2) the relative potency in short-term tests is an accurate predictor of lung cancer potency; and (3) DPM extracts are similar in chemical composition and proportion as combustion or pyrolysis products.

In the study by Albert et al. (1983), epidemiology-based unit cancer risk estimates for coke oven emissions, cigarette smoke condensate, and roofing tar were used. Samples of DPM were collected from three light-duty engines (a Nissan 220 C, an Oldsmobile 350, and a Volkswagen turbocharged Rabbit), all run on a highway fuel economy test cycle, and from a heavy-duty engine (Caterpillar 3304) run under steady-state, low-load conditions. The DPM extracts were tested in a variety of assays. Dose/concentration-dependent increases in response were obtained for the four assays listed below:

- Ames *Salmonella typhimurium* (TA98) reverse mutation,
- Gene mutation in L5178Y mouse lymphoma cells,
- Sencar mouse skin tumor initiation test, and
- Viral enhancement of chemical transformation in Syrian hamster embryo cells.

Only the first three assays were used to develop comparative potency estimates because of variability of responses in the enhancement of the viral transformation assay. The in vitro studies were carried out both in the presence and absence of metabolic activators. The potency, defined as the slope of the dose-response curve, was measured for each sample in each short-term assay.

The skin tumor initiation test was positive for all the engines tested except the Caterpillar engine. Only the Nissan engine, however, resulted in strong dose-response data. Because skin tumor initiation was considered to be the most biologically relevant test, it was used to derive potency estimates for the Nissan engine. An estimate for the Nissan engine was then derived by multiplying the epidemiology-based potency estimates for each of the three agents (coke oven emissions, roofing tar, and cigarette smoke condensate) by the ratios of their potencies in the skin
tumor initiation test to that of the Nissan diesel engine. According to this method, three 95% upper-bound estimates of lifetime cancer risk per microgram per cubic meter of extractable organic matter were derived for the Nissan diesel, based on potency comparisons with each of the three agents. These values are: coke oven emissions, 2.6×10^{-4}; roofing tar, 5.2×10^{-4}; and cigarette smoke condensate, 5.4×10^{-4}. The average of the three equals 4.4×10^{-4}.

The potency of the other diesel emission samples was not estimated directly because of the weak response in the skin tumor initiation test. Instead, their potency relative to the Nissan engine was estimated as the arithmetic mean of their potency relative to the Nissan in the Salmonella assay in strain TA98, the sister chromatid exchange assay in Chinese hamster ovary cells, and the mutation assay in mouse lymphoma cells. The estimated lifetime cancer risk per microgram per cubic meter of extractable organic matter for extracts from these engines are as follows: Volkswagen, 1.3×10^{-4}; Oldsmobile, 1.2×10^{-4}; and Caterpillar, 6.6×10^{-6}.

Harris (1983) developed comparative potency estimates for the same four engines used by Albert et al. (1983) but used only two epidemiology-based potency estimates: those for coke oven emissions and for roofing tar. He employed preliminary data from three of the same assays used by Albert et al. (1983): the Sencar mouse skin tumor initiation assay, enhancement of viral transformation in Syrian hamster embryo cells, and the L5178 mouse lymphoma test. The DE cancer potency estimates were then derived by multiplying the epidemiology-based cancer potency estimates for both coke oven emissions and roofing tar by the ratio of their potencies compared with DPM extract in each of the three bioassays. Harris (1983) derived an overall

mean relative risk value of 3.5×10^{-5} per $\mu g/m^3$ for the three light-duty engines with a 95% upper confidence limit of 2.5×10^{-4}. Individual mean values for each engine were not reported.

McClellan (1986), Cuddihy et al. (1981, 1984), and Cuddihy and McClellan (1983) estimated a risk of about 7.0×10^{-5} per $\mu g/m^3$ DPM using a comparative potency method similar to those reported in the preceding paragraph. The database was similar to that used by Albert et al. (1983) and Harris (1983).

C.3. EPIDEMIOLOGY-BASED ESTIMATION OF CANCER RISK

The first lung cancer risk estimates based on epidemiologic data were derived by Harris (1983). He assessed the risk of exposure to DE using data from the London Transport Worker Study reported by Waller (1981). Five groups of employees from the London Transport Authority (LTA) were used: bus garage engineers, bus drivers, bus conductors, engineers in central works, and motormen and guards. The first group was considered to have received the highest exposure; the next two, intermediate; and the last two groups, none. When cancer death rates for the high-exposure group were compared with those of London males, there was no increase in the observed-to-expected (O/E) ratios. The author, in fact, considered the results to be negative. However, because the low rate of lung cancer in all the LTA exposure groups may have been the result of a "healthy worker" effect, Harris (1983) compared the exposed groups with internal controls. He merged the three exposed groups and compared them with the two groups considered to be unexposed. An adjustment was made for the estimated greater exposure levels of garage engineers compared with bus drivers and conductors. Using this method, the relative risk of the exposed groups was greater than 1 but was statistically significant only for garage engineers exposed from 1950 to 1960. In that case, the O/E ratio was 29% greater than the presumed unexposed controls.

Harris (1983) identified a variety of uncertainties relative to potency assessment based on this study. These included:

- small unobserved differences in smoking incidences among groups, which could have a significant effect on lung cancer rates;
- uncertainty about the magnitude of exposure in the exposed groups;
- uncertainty regarding the extent of change in exposure conditions over time;
- random effects arising from the stochastic nature of the cancer incidence; and
- uncertainty in the mathematical specification of the model.

Taking the uncertainties into account, he derived a maximum likelihood excess relative risk estimate of 1.23×10^{-4}, with a 95% upper confidence limit of 5×10^{-4} per $\mu g/m^3$ DPM per year.

McClellan et al. (1989) reported risk estimates based on the Garshick et al. (1987) case-control study in which lung cancer in railroad workers was evaluated. Using a logistic regression, the expected relative risk of lung cancer death was estimated to rise 0.016 per year of exposure to DE. Adjustments were made to convert to continuous exposure (168 vs. 40 hours) for 70 years. Because exposure levels could not be defined exactly, two sets of calculations were made, assuming inhaled DPM concentrations of either 500 or 125 $\mu g/m^3$ DPM. The number of excess cancer deaths per year in the United States was estimated to be 3,800 (95% C.I. 400-7400 when an exposure of 125 $\mu g/m^3$ was used, and 950 (95% C.I. 100-1,900) when 500 $\mu g/m^3$ DPM was used.

The California EPA (Cal-EPA, 1998) derived unit risk estimates for lung cancer based upon the Garshick et al. (1987) case-control study and the Garshick et al. (1988) cohort study of U.S. railroad workers. A variety of exposure patterns were considered, characterized by two components: the average exposure concentration for the workers as measured by Woskie et al. (1988) and the extent of change in exposure from 1959 to 1980. The lowest lifetime risk estimate derived was 1.3×10^{-4} per $\mu g/m^3$ and the highest was 2.4×10^{-3} per $\mu g/m^3$. The geometric mean was 6×10^{-4} per $\mu g/m^3$.

Steenland et al. (1998) estimated lung cancer risk of truck drivers on the basis of a case-control study of decedents in the Teamsters Union (Steenland et al., 1990). Retrospective exposure estimates were made starting with a set of 1990 exposure measurements for different job categories and then retrospectively estimating from 1982 to about 1950 using various factors, including diesel vehicle miles traveled and engine emission rates per mile. The 1990 job category estimates came from an extensive industrial hygiene survey of elemental carbon (EC) exposures in the trucking industry by Zaebst et al. (1991). Lifetime (through age 75) excess risk of lung cancer death for male truck drivers was calculated with the aid of a cumulative exposure model. Assuming a most likely emissions scenario of 4.5 g/mile in 1970, and a 45-year exposure to 5 $\mu g/m^3$ of EC beginning at age 20 and ending at age 65, the estimated excess lung cancer risk was determined to be 1.6% (95% CI 0.4%-3.1%). Using the same data base, Stayner et al (1998) presented an estimate of excess lifetime risk of 4.5E-4 for a worker exposed to 1 $\mu g/m^3$ of DE for 45 years.

C.4. ANIMAL BIOASSAY-BASED CANCER POTENCY ESTIMATES

With the availability of chronic cancer bioassays, a considerable number of potency estimates were derived using lung tumor induction in rats. A high degree of uncertainty exists in the use of the rat data to predict human risk. Major uncertainties include: (1) differences in particle deposition patterns between rats and humans, (2) differences in sensitivity between rats and humans to the carcinogenic action of DE, and (3) extrapolation of rat lung tumor responses

at high concentrations to ambient concentrations without a clear understanding of the mode of action of DE. It is now widely recognized that the rat lung tumor response associated with any insoluble particles at high concentrations is mediated by a particle-overload mechanism (ILSI, 2000), suggesting that rat data for DE are not suitable for estimating human risk at low environmental concentrations.

The first risk estimate was reported by Albert and Chen (1986), based on the chronic rat bioassay conducted by Mauderly et al. (1987). Using a multistage model and assuming equivalent deposition efficiency in humans and rats, they derived a 95% upper confidence limit of 1.6×10^{-5} for lifetime risk of exposure to 1 $\mu g/m^3$. Pott and Heinrich (1987) also used a linear model and data reported by Brightwell et al. (1989), Heinrich et al. (1986), and Mauderly et al. (1987). They reported risk estimates ranging from 6×10^{-5} to 12×10^{-5} per $\mu g/m^3$. Smith and Stayner (1990), using time-to-tumor models based on the data of Mauderly et al. (1987), derived point (MLE) estimates ranging from 1.0×10^{-4} to 2.1×10^{-4} per $\mu g/m^3$ after converting from occupational to environmental exposure scenario.

Pepelko and Chen (1993) developed unit risk estimates based on the data of Brightwell et al. (1989), Ishinishi et al. (1986), and Mauderly et al. (1987) using a detailed dosimetry model to extrapolate dose to humans and a linearized multistage (LMS) model. Taking the geometric mean of individual estimates from the three bioassays, they derived unit risk estimates of 1.4×10^{-5} per $\mu g/m^3$ when dose was based on carbon particulate matter per unit lung surface area rather than whole DPM, and 1.2×10^{-4} per $\mu g/m^3$ when based on lung burden per unit body weight.

Hattis and Silver (1994) derived a maximum likelihood estimate for occupational exposure of 5.2×10^{-5} per $\mu g/m^3$ based on lung burden and bioassay data reported by Mauderly et al. (1987) and use of a five-stage Armitage-Doll low-dose extrapolation model. California EPA (CAL-EPA, 1998) derived a geometric mean estimate of 6×10^{-5} per $\mu g/m^3$ from five bioassays using an LMS model.

To demonstrate the possible influence of particle effects as well as particle-associated organics, an additional modeling approach was conducted by Chen and Oberdorster (1996). Employing a biologically based two-stage model and using malignant tumor data from Mauderly et al. (1987), the upper-bound risk estimate for exposure to 1 $\mu g/m^3$ was estimated to be 1.7×10^{-5}. This estimate is virtually identical to that using the LMS model, assuming nonthreshold effect of particles. If a threshold of particle effect is assumed, however, the estimated risk decreases about fivefold. The results also show that the mechanism of DE-induced lung tumor at high exposure concentrations may differ from that at low exposure concentrations, with the organics and particles playing primary roles of tumorigenesis, respectively, at low and high concentrations. Overall, the potency estimates on the basis of

animal bioassays are in the range of 10^{-6} to 10^{-4} per 1 $\mu g/m^3$ of DPM.

Valberg and Crouch (1999) conducted a meta-analysis of rat bioassays by pooling together data of low-dose groups from different bioassays. There are eight bioassays used in the meta-analysis; half of them had duration of 24 months, and the remaining studies had duration of 30 months or more. Animals with continuous lifetime exposure of less than 600 $\mu g/m^3$ of DE were included in the analysis. Continuous lifetime exposure is calculated by protracting actual DE exposure to 30 months (24 hours per day, 7 days per week). The researchers concluded that exposure of rats to DE at concentrations not associated with lung overload is consistent with no tumorigenic effect.

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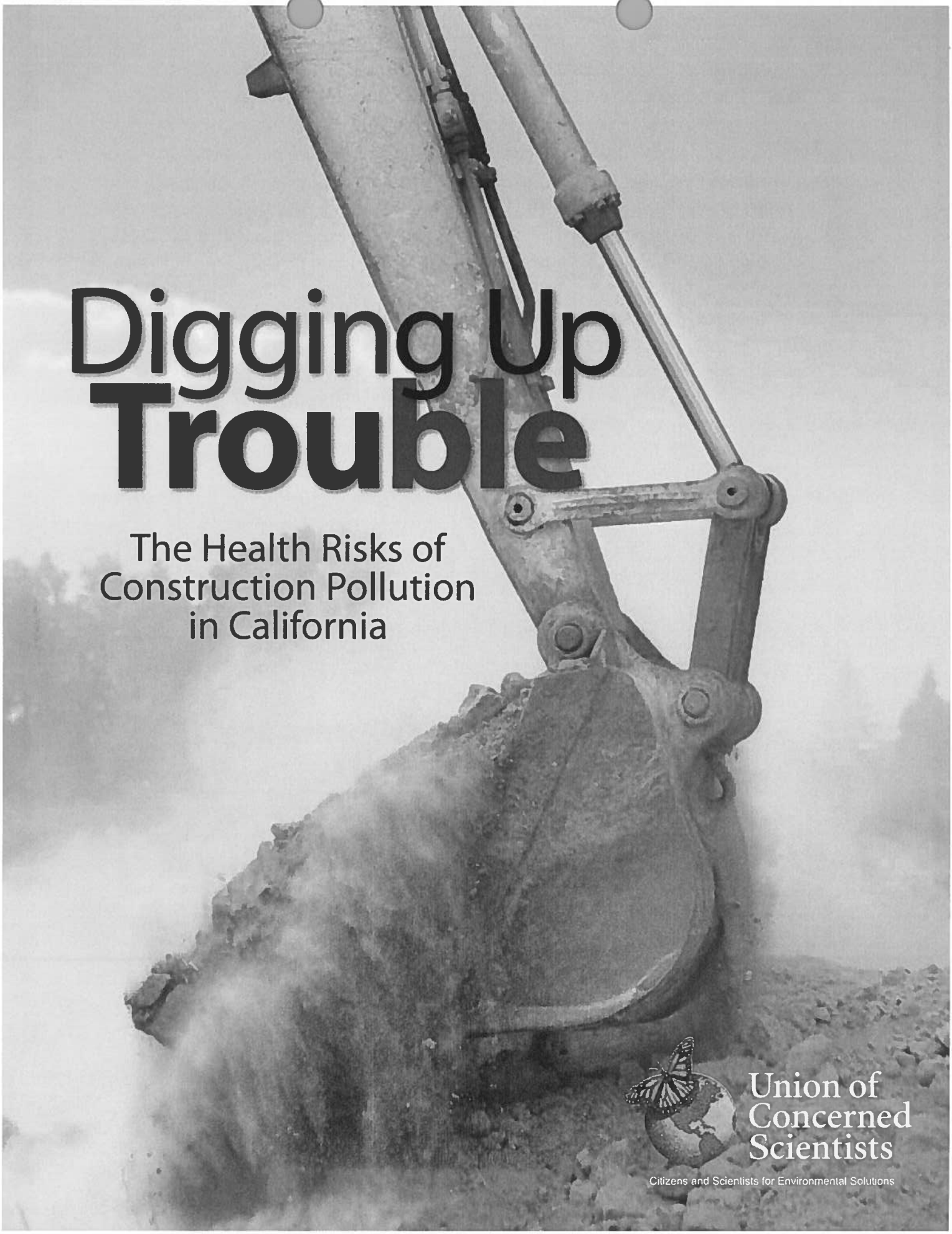

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The Health Risks of Construction Pollution in California

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Comment Letter I14

Digging Up Trouble

The Health Risks of Construction Pollution in California

DON ANAIR

Union of Concerned Scientists
November 2006

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Don Anair is a vehicles engineer in the Union of Concerned Scientists Clean Vehicles Program.

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Executive Summary

Pollution from diesel construction equipment is taking a toll on the health and economic well-being of California residents. This equipment contributes to particulate and ozone pollution that can cause severe cardiovascular and respiratory illnesses, asthma attacks, acute bronchitis, and even premature death.

This study analyzes air pollution caused by construction equipment and—for the first time—quantifies its effect on California's public health and economy, both across the state and in the five most-affected regions. In addition, we evaluate the risk of exposure to construction activity in specific cities in each of these five regions. Lagging emission standards and very old equipment have made construction equipment one of the largest sources of toxic diesel particulate matter pollution in the state, necessitating an accelerated cleanup program to protect the health of all Californians.

Using established U.S. Environmental Protection Agency (EPA) and California Air Resources Board (CARB) methods to quantify the impact of air pollution, the Union of Concerned Scientists (UCS) estimates that construction equipment emissions statewide are responsible for:

- more than 1,100 premature deaths per year
- more than 1,000 hospital admissions for cardiovascular and respiratory illness
- 2,500 cases of acute bronchitis
- tens of thousands of asthma attacks and other lower respiratory symptoms

This pollution is hurting the state's economy as well. Construction equipment is critical to the building industry (a sector of the economy worth $60 billion per year)[1] and instrumental in maintaining and building our roads and highways (on which California spent eight billion dollars last year). But the pollution from this equipment results in more than nine billion dollars in annual public health costs, including hundreds of thousands of lost work days and school absences.

Construction equipment is used extensively throughout the entire state. More than 270,000 acres of land in California were under construction permit during 2005—an area the size of Los Angeles.[2] In addition, more than 10,000 miles of state roadway were under contract for construction, repairs, or maintenance.[3]

The impact of construction pollution on public health is greatest where equipment and people mix, and 90 percent of the health and economic damage occurs in California's five most populous air basins. The South Coast air basin (which encompasses most of Los Angeles, Orange, Riverside, and San Bernardino counties) ranks first with more than 700 premature deaths and more than 650 hospitalizations for respiratory and cardiovascular illness annually. The San Francisco Bay Area and San Diego follow, with more than 150 and 89 premature deaths, respectively, every year. The San Joaquin Valley and Sacramento Valley (the two largest air basins in

1 As reported to the California Department of Finance by the California Construction Industry Research Board. Available at *http://www.dof.ca.gov/HTML/FS_DATA/LatestEconData/FS_Construction.htm*.

2 Total acres based on State Water Resources Control Board data (SWRCB 2005). The city of Los Angeles covers 300,160 acres.

3 Mileage based on ongoing contract data available from the California Department of Transportation (CALTRANS 2005).

TABLE 1 **Health Damage from Construction Pollution (by Air Basin)**

	Total Incidences					
Health Endpoint	**Statewide**	**South Coast**	**San Francisco Bay Area**	**San Diego**	**San Joaquin Valley**	**Sacramento Valley**
Premature Deaths	1,132	731	154	89	49	39
Respiratory Hospitalizations	669	383	56	50	55	30
Cardiovascular Hospitalizations	417	274	61	33	14	12
Asthma and Other Lower Respiratory Symptoms	30,118	20,941	3,406	2,127	1,284	790
Acute Bronchitis	2,494	1,729	284	177	107	66
Lost Work Days	182,940	123,439	25,713	14,014	6,241	4,617
Minor Restricted Activity Days	1,544,952	959,839	168,459	113,280	99,585	50,408
School Absences	331,040	175,339	18,472	24,689	33,282	17,492

NOTE: Values represent the mean annual incidence estimate for 2005.

California's Central Valley) round out the top five with 49 and 39 annual premature deaths, respectively.

Construction activity varies from city to city and, therefore, so does potential exposure to harmful diesel exhaust. Areas with high population density and construction activity are an obvious concern because construction equipment emissions are more likely to be occurring in close proximity to people. Nevertheless, the most densely populated cities are not the only areas with high potential for construction risk; evaluation of active construction projects finds areas outside major population centers also face risks since large-scale construction projects accompany regional population growth.

While incentive programs have begun to clean up some of this equipment, only statewide regulations can achieve the reductions in construction equipment pollution needed to truly protect public health. Cost-effective technology solutions that would help meet this regulatory goal already exist, and more will become available over the next few years. CARB should adopt a regulatory regime that will clean up existing construction equipment by retiring the oldest, most-polluting equipment and using retrofit technology where appropriate.

Chapter 1

Diesel Pollution from Construction Equipment

Highway truck and bus engine manufacturers have had to meet increasingly stringent emission regulations since the late 1980s. Construction and other off-road equipment, however, did not face new particulate matter (PM) emission standards until 1996, with some engines unregulated as late as 2003.[4] In 2004, the U.S. Environmental Protection Agency (EPA) finally forced construction equipment to meet similar standards to highway trucks and buses, requiring 90 percent reductions in nitrogen oxides (NOx) and PM for most engine sizes. These standards will phase in over a seven-year period starting in 2008, reaching full implementation in 2014 (EPA 2004).

Although these standards will significantly reduce pollutants from new engines, the full benefits will not be realized until sometime after 2030, when the long-lasting equipment currently in use today is finally retired. There are technology options available to clean up these existing machines, but neither the EPA nor the state of California currently requires them. As a result, if no additional requirements are put in place, the construction sector will continue emitting high levels of toxic and smog-forming pollution for the next two to three decades.

THE WORST OFFENDERS

The Union of Concerned Scientists (UCS) took a closer look at pollution from California's construction equipment to find out which types of equipment emit the most toxic diesel PM (or "soot") and smog-forming NOx. Most people think of trucks and buses when they think of diesel pollution, but as it turns out, the equipment repairing the road near your home or operating at a construction site near your office may be many times more polluting. Diesel construction equipment ranges from backhoes and bulldozers to paving equipment and cranes; we have identified the worst offenders.

Out of 18 categories of construction equipment identified in the 2005 California Air Resources Board (CARB) emission inventory, the five highest-polluting categories are responsible for 65 percent of PM and 60 percent of NOx emissions. In descending order, they are excavators, tractors/loaders/backhoes, crawler tractors (commonly called bulldozers), rubber-tired loaders, and skid-steer loaders (CARB 2006c).

We compared PM and NOx emissions from these types of equipment with the number of miles a new heavy-duty tractor-trailer truck (or "big rig") would have to travel to emit the same amount of pollution. The emissions of a model year 2007 big rig were estimated based on a truck traveling 55 miles per hour and operating on recently available ultra-low-sulfur diesel fuel. Hourly construction equipment emissions were calculated from equipment population estimates and CARB's 2005 emission inventory.

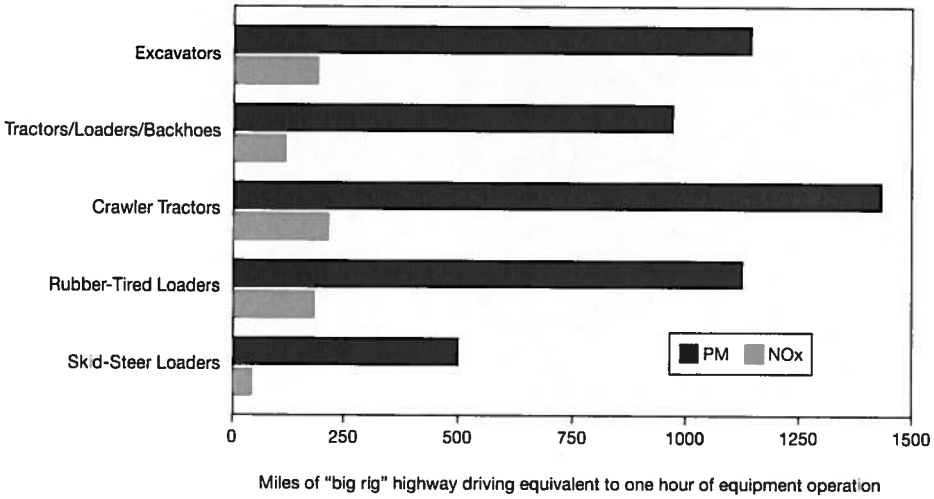
4 Tier 1 EPA nonroad engine standards did not include PM limits for engines of 50 to 175 horsepower.

TABLE 2 **Emissions by Type of Construction Equipment**

	Percent of Total PM from Construction Equipment	Percent of Total NOx from Construction Equipment	Useful Life (in years)
Excavators	17%	18%	17
Tractors/Loaders/Backhoes	16%	12%	18
Crawler Tractors (Tracked Bulldozers)	13%	13%	29
Rubber-Tired Loaders	12%	12%	21
Skid-Steer Loaders	7%	4%	13
Off-Highway Trucks	5%	9%	17
Rough-Terrain Forklifts	5%	3%	16
Graders	5%	5%	23
Off-Highway Tractors	4%	5%	31
Rollers	3%	3%	20
Trenchers	3%	2%	28
Scrapers	3%	4%	26
Cranes	3%	4%	19
Rubber-Tired Dozers	2%	2%	32
Pavers	2%	1%	26
Bore/Drill Rigs	1%	1%	10
Other Construction Equipment	0.4%	1%	16
Paving Equipment	0.3%	0.2%	24
Surfacing Equipment	0.04%	0.1%	22

NOTE: Useful life is defined as the age at which half of the equipment of a given model year has been retired.
SOURCE: Based on 2005 CARB construction emission inventory (updated as of September 2006).

FIGURE 1 **Construction Equipment Emissions Compared with a New "Big Rig"**



Excavators

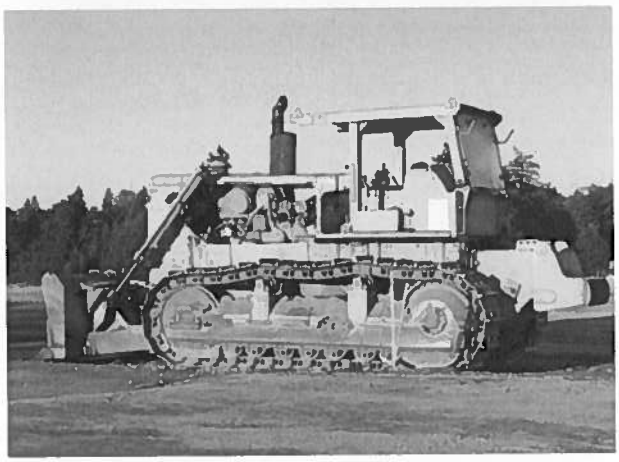
There are an estimated 19,000 excavators in California, ranging in size from about 50 to 750 horsepower. The annual PM pollution from excavators accounts for 17 percent of all PM from construction equipment. On average, an excavator operating for one hour emits as much PM as a new big rig traveling 1,100 miles, while NOx emissions are equivalent to driving a big rig about 200 miles. The useful life of this equipment is 17 years.[5]

Tractors/loaders/backhoes

These versatile pieces of equipment are commonly used on construction sites and road repair projects. More than 30,000 backhoes are operated in California every year, emitting 16 percent of all PM from construction equipment. The PM produced by the average backhoe in one hour is equivalent to driving a big rig nearly 1,000 miles, while the NOx emissions are equivalent to driving more than 100 miles. The useful life of this equipment is 18 years.

Crawler tractors (bulldozers)

These tracked vehicles are used primarily for earthmoving operations. More than 16,000 bulldozers operate in California and emit 13 percent of all PM from construction equipment. The average bulldozer operating for one hour emits the same amount of PM as a new big rig driving 1,400 miles. The NOx emissions from an hour of operation are equivalent to driving a big rig 200 miles. The useful life of a crawler tractor is an impressive 29 years.



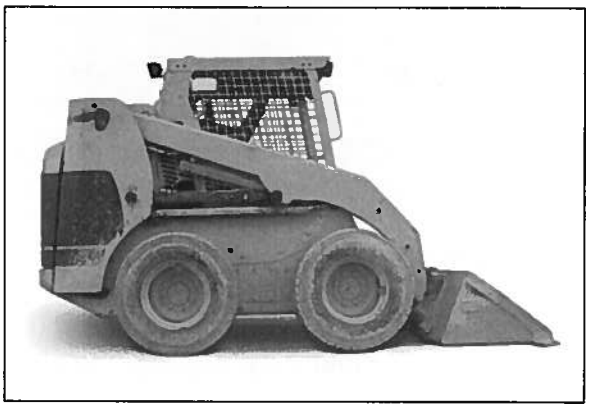
5 Useful life is defined as the age at which half of the equipment of a certain model year has been retired. The useful life, equipment populations, emissions, and other equipment specifics described in this section are based on CARB's updated off-road emission inventory model as of September 2006 (CARB 2006c).

Rubber-tired loaders

These heavy-duty vehicles, commonly used to load trucks, represent the fourth largest source of diesel emissions from construction equipment; the estimated 19,000 rubber-tired loaders in California account for 12 percent of all construction pollution. The average loader operating for one hour emits PM equivalent to driving a new big rig 1,100 miles and NOx emissions equivalent to driving 200 miles. The useful life of rubber-tired loaders is 21 years.

Skid-steer loaders

More than 29,000 of these relatively small pieces of equipment operate in California on all types of construction projects, and account for seven percent of all PM from construction equipment. Even though the average skid-steer loader delivers less than 50 horsepower (a fraction of that provided by a big rig),[6] its PM emissions from one hour of operation are equivalent to driving a new big rig 500 miles. The useful life of a skid-steer loader is 13 years.



6 A new big rig's engine can range anywhere from 300 to 600 horsepower.

Chapter 2

Health and Economic Damage from Construction Equipment

Emissions from construction equipment and other diesel vehicles are harmful to our health and well-being. The damage comes in the form of premature death, increased hospital admissions for respiratory and cardiovascular diseases, asthma attacks, and lost productivity through school absences and missed work days. Following established statistical methods, UCS has quantified the cost of diesel emissions from construction equipment in California.

The impact of several pollutants that comprise diesel exhaust must be taken into account:

- **Particulate matter (PM).** Also known as soot, these small particles (25 times smaller than the width of a human hair) are released directly from the tailpipe or formed indirectly from emissions of NOx and sulfur oxides (SOx). PM can penetrate deeply into the lungs, causing or aggravating a variety of respiratory and cardiovascular illnesses and even leading in some cases to premature death (Pope 2002, Krewski 2000, Samet 2000).
- **Smog-forming pollutants.** NOx and hydrocarbons react in the presence of sunlight to form ozone (smog), which can damage the respiratory tract, reduce lung function, exacerbate asthma, aggravate chronic lung diseases, and also cause premature death (White 1994, Koren 1995, Thurston 2001, Bell 2005). As much as 10 to 20 percent of all summertime hospital visits and admissions for respiratory illness are associated with ozone, and more than 90 percent of Californians live in areas that do not comply with federal ozone standards (Thurston 1992, 1994).
- **Air toxics.** The state of California has classified diesel exhaust and more than 40 compounds in diesel exhaust as toxic air contaminants.[7] Exposure to these chemicals can cause cancer, damage to fetuses, and other serious health and reproductive problems. CARB has estimated that diesel exhaust is responsible for 70 percent of the state's risk of cancer from airborne toxics (CARB 1998).

ESTIMATING HEALTH EFFECTS OF CONSTRUCTION POLLUTION

This analysis uses methods established by CARB and the EPA to quantify health and economic damage from diesel pollution. In March 2006, CARB released a study detailing the regional health and economic damage caused by California's goods movement system (CARB 2006a). A number of adverse health effects, or endpoints, strongly linked to diesel pollution were quantified along with an estimate of the economic costs associated with these endpoints.

7 According to the California Health and Safety Code, a toxic air contaminant is "an air pollutant which may cause or contribute to an increase in mortality or in serious illness, or which may pose a present or potential hazard to human health."

How Diesel Exhaust Damages Lungs

As PM from diesel exhaust travels through the air and is inhaled, the largest particles settle in the nose, throat, and lungs. The finest particles are able to evade the body's natural defenses (such as sneezing and coughing) and travel deep into the lungs. Once there, these particles can cause inflammation and scarring of air passageways and lung tissue, resulting in reduced oxygen flow to the rest of the body. Symptoms can range from coughing and shortness of breath to severe and fatal asthma attacks.

When inhaled, ozone—a key ingredient of smog—can also damage lungs by chemically burning delicate tissue and causing scarring. Recent evidence suggests that exposure to ozone can cause asthma in otherwise healthy children (McConnell 2002). On days with high ozone levels, health officials recommend reducing outdoor activities to lower exposure to this dangerous pollutant.

Using emission data specific to diesel construction equipment in California, we used the same methodology to quantify the damage from construction equipment pollution. Because our ability to quantify the public health impact of diesel pollution is limited, the health endpoints quantified in this analysis do not represent all of the potential damage associated with diesel pollution and are therefore conservative estimates.

Economic damage associated with construction equipment pollution is estimated by assigning each health endpoint an economic value. Economic valuations for each health endpoint are based on the cost of treating an illness, lost productivity or wages, or the value society is willing to pay to lower the risk of certain outcomes.

For further discussion of the methodology used to estimate the health and economic impact of construction pollution, please refer to the appendix.

Our analysis found that the economic and health damage caused by construction equipment pollution in California is staggering. More than 1,000 premature deaths per year can be attributed to these emissions, along with more than 1,000 hospitalizations for cardiovascular and respiratory illness, and more than 30,000 asthma attacks and other respiratory symptoms. Hundreds of thousands of lost work days and school absences equate to more than $60 million in annual economic losses. In addition, Californians collectively experience millions of days each year when air pollution restricts their activities. Overall, construction equipment pollution costs the state more than nine billion dollars every year.

TABLE 3 **Health and Economic Damage from Construction Pollution (Statewide)**

Health Endpoint	Pollutants	Total Incidences	Costs (in thousands of 2005 dollars)
Premature Deaths ($7.9 million/incidence)	PM and ozone	**1,132** (328–1930)	**8,944,256** (2,588,161–15,249,672)
Respiratory Hospitalizations ($34,000/incidence)	PM and ozone	**669** (398–933)	**22,758** (13,530–31,735)
Cardiovascular Hospitalizations ($41,000/incidence)	PM only	**417** (263–646)	**17,082** (10,795–26,491)
Asthma and Other Lower Respiratory Symptoms ($19/incidence)	PM only	**30,118** (11,686–48,110)	**572** (222–914)
Acute Bronchitis ($422/incidence)	PM only	**2,494** (-609–5,408)	**1,053** (-257–2,282)
Lost Work Days ($180/incidence)	PM only	**182,940** (155,031–210,810)	**32,929** (27,906–37,946)
Minor Restricted Activity Days ($60/incidence)	PM and ozone	**1,544,952** (988,809–2,150,641)	**92,697** (59,329–129,038)
School Absences ($88/incidence)	Ozone only	**331,040** (134,632–531,374)	**29,131** (11,848–46,761)
Total Cost			**9,140,480** (2,711,532–15,524,840)

DEFINITIONS:

Premature deaths: Premature deaths due to exposure to PM and ozone, including cardiopulmonary and lung cancer mortality.

Respiratory hospitalizations: Hospital admissions for respiratory illnesses (such as emphysema or chronic bronchitis) as a result of exposure to both PM and ozone.

Cardiovascular hospitalizations: Hospital admissions for cardiovascular illnesses (such as heart attacks or hypertension) as a result of exposure to PM.

Lower respiratory symptoms: Asthma attacks and other symptoms such as wheezing, coughing, and shortness of breath.

Acute bronchitis: Symptoms can include coughing, chest discomfort, and slight fever and can last several days.

Lost work days: Days of work missed due to symptoms resulting from exposure to PM or to take care of an individual with such symptoms.

Minor restricted activity days: Days in which high ozone and PM levels require less strenuous activities but do not result in a lost work day or school absence.

School absences: Days of school missed due to symptoms resulting from exposure to ozone.

NOTE: Mean estimates are shown in bold; ranges shown in parentheses represent the 95 percent confidence interval (i.e., there is a 95 percent chance that the actual value falls between the two values shown).

Chapter 3

Construction Pollution Impact by Region

The majority of the damage caused by construction equipment pollution occurs in areas where large numbers of people are exposed. Five of California's 15 air basins, home to more than 85 percent of the state's population, suffer more than 90 percent of the total health and economic damage from construction pollution. In each of these five air basins, which are the focus of this chapter, concerns exist in both urban and suburban areas.

Air basins are largely defined by physical features, such as mountain ranges, and meteorological conditions, such as air flow patterns, that restrict the movement of air pollution to another air basin. Air quality in a given air basin is influenced by the emission sources within it, and to a lesser degree by pollution entering from another air basin. Transport of air pollution from neighboring air basins is an ongoing area of research and, for the purposes of this analysis, construction equipment emissions are assumed to remain in the air basin in which they were generated.

WHERE PEOPLE AND CONSTRUCTION MIX

UCS also evaluated the likelihood of exposure to construction activity in specific cities within the five most-affected air basins. While construction equipment contributes to overall PM and ozone concentrations in each air basin, people who live or work near construction equipment may be at a higher risk of exposure to these dangerous pollutants.[8] Using 2000 census data and 2005 construction permit data from the California State Water Resources Control Board (SWRCB), we have identified those cities that have a higher risk of exposure to construction activity. The results show that areas where construction activity and people mix are spread throughout each region, in both urban and suburban cities and towns.

The SWRCB requires permits for construction projects that disturb more than one acre of land through clearing, grading, or excavation. We used permits from the SWRCB database for our analysis because such land disturbance generally involves the use of diesel earthmoving construction equipment. By excluding local building permits, we attempted to eliminate small projects such as single-family home construction and remodeling work that may not require the use of diesel equipment. The permits selected for this analysis were either active or issued between January 1, 2005, and December 31, 2005 (SWRCB 2005).

We then created maps using geographic information system (GIS) software to display "Construction Risk Zones" related to construction activity in each of the five studied air basins. Construction Risk Zones represent the risk of exposure to construction pollution in a given city, based on its mixture of construction activity and population density. To determine the relative risk potential for each city, we multiplied the total acreage under construction permit during 2005

8 Northeast States for Coordinated Air Use Management showed increased concentrations of diesel PM near construction sites (NESCAUM 2003). Other studies have shown an elevated risk of cancer near diesel pollution sources; these studies include a health risk assessment at a California rail yard (CARB 2005).

by population density from the 2000 census. A city's risk potential is presented in relation to other cities within the air basin, ranging from a relatively high risk to a relatively low risk.

The resulting Construction Risk Zones are based on the best information available, but it is important to note that this is not a measure of actual exposure to emissions and is only one measure of the likelihood that people and construction equipment will be in proximity to one another. Actual exposure levels depend on the amount of emissions produced by specific equipment, the types of equipment on a construction site and the length of time they operate, wind patterns and atmospheric conditions, and proximity to the emission source. These details are not available from the SWRCB permit database.

Also, because we have measured construction activity in terms of acreage, a multi-story project and a single-story project are treated equally. In addition, the construction permit data used to evaluate Construction Risk Zones does not include California Department of Transportation (Caltrans) highway projects—a major source of construction activity in the state.[9] In spite of these limitations, our Construction Risk Zone evaluation captures a majority of the largest construction sites in the state.

Please see the appendix for further discussion of the SWRCB permit data.

9 For perspective, Caltrans contracts were worth eight billion dollars in 2005 (CALTRANS 2005) while building and construction contracts were valued at $65 billion according to the California Department of Finance (CDF 2005).

SOUTH COAST

Comprising most of Los Angeles, San Bernardino, Riverside, and Orange counties, this air basin experiences the greatest degree of health and economic damage in the state from construction equipment emissions. For 2005, this includes estimates of:

- more than 700 premature deaths
- 650 hospitalizations for respiratory and cardiovascular disease
- more than 1,700 cases of acute bronchitis
- nearly 21,000 incidences of asthma attack and other lower respiratory symptoms
- 300,000 days of lost work and school absences
- close to one million days of restricted activity

This loss of life and productivity cost South Coast residents an estimated $5.9 billion.

Within the air basin, 127 cities and towns had active construction permits during 2005 accounting for more than 70,000 acres of land under construction. Areas designated as high-risk are spread throughout the region, with cities in all four counties falling in the top 10 percent of Construction Risk Zones. San Bernardino and Riverside counties each have four such cities while Los Angeles has three and Orange two. The presence of less population-dense cities such as Murrieta and Temecula in this group reflects the fact that large developments of 50 acres or more are common in these cities.

TABLE 4 **South Coast Construction Pollution Damage**

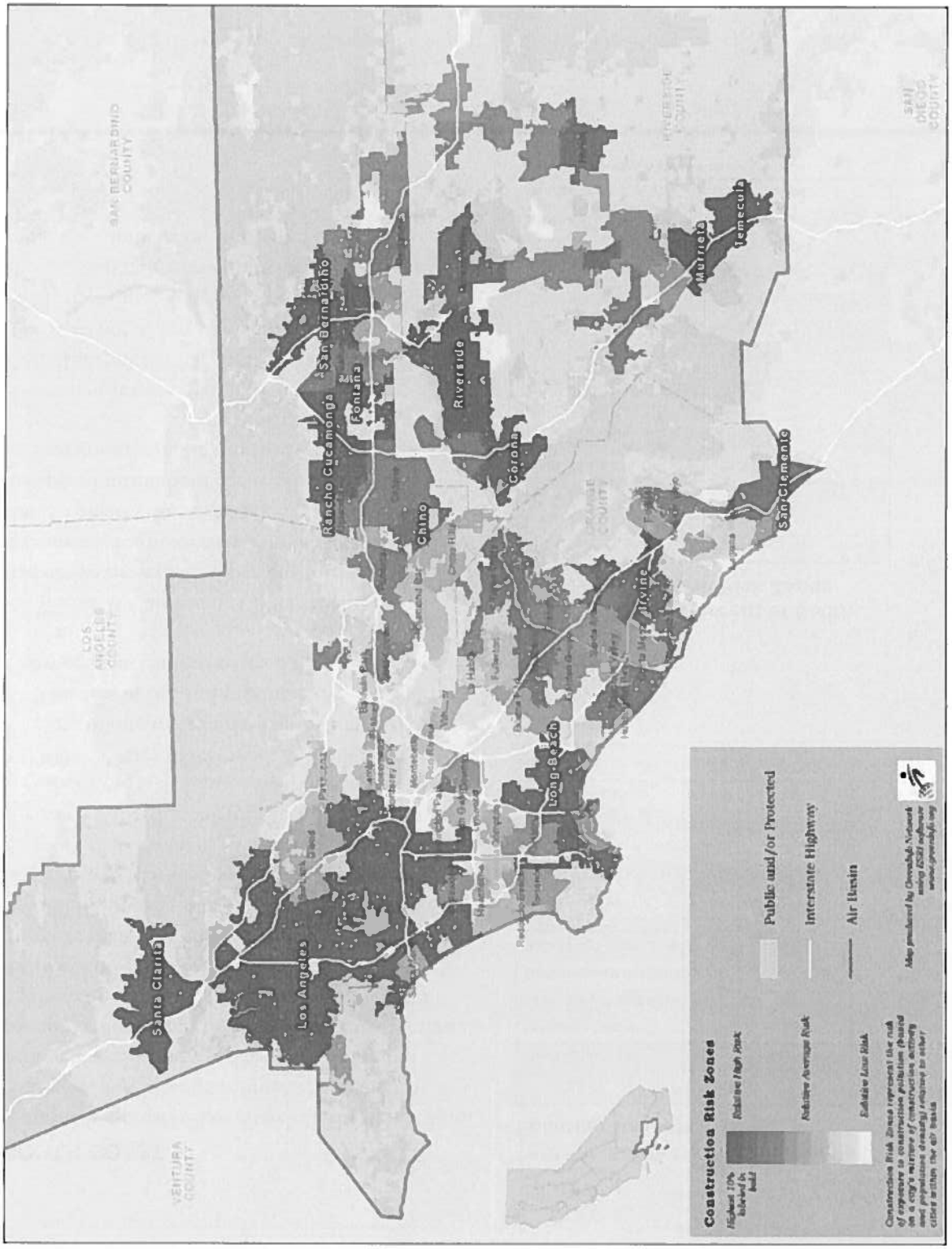
Health Endpoint	Mean Annual Incidences	Annual Costs (in thousands of 2005 dollars)
Premature Deaths	731	5,776,261
Respiratory Hospitalizations	383	13,019
Cardiovascular Hospitalizations	274	11,248
Asthma and Other Lower Respiratory Symptoms	20,941	398
Acute Bronchitis	1,729	730
Lost Work Days	123,439	22,219
Minor Restricted Activity Days	959,839	57,590
School Absences	175,339	15,430
Total Annual Cost		5,896,894

TABLE 5 **Top 10 Percent of South Coast Construction Risk Zones**

City	County
Long Beach	Los Angeles
Los Angeles	Los Angeles
Santa Clarita	Los Angeles
Irvine	Orange
San Clemente	Orange
Corona	Riverside
Murrieta	Riverside
Riverside	Riverside
Temecula	Riverside
Chino	San Bernardino
Fontana	San Bernardino
Rancho Cucamonga	San Bernardino
San Bernardino	San Bernardino

NOTE: Cities are listed in alphabetical order by county.

FIGURE 2 **Construction Pollution Risk in the South Coast Air Basin**



SAN FRANCISCO BAY AREA

This air basin comprises nine counties and is second only to the South Coast air basin in health and economic damage from construction equipment emissions. For 2005, this includes estimates of:

- more than 150 premature deaths
- 100 hospitalizations for respiratory and cardiovascular disease
- more than 280 cases of acute bronchitis
- 3,000 incidences of asthma attack and other lower respiratory symptoms
- 44,000 days of lost work and school absences
- well over 100,000 days of restricted activity

This loss of life and productivity cost Bay Area residents an estimated $1.2 billion.

Within the air basin, 80 cities and towns had active construction permits during 2005 accounting for more than 17,500 acres of land under construction. As in the South Coast, areas designated as high-risk are spread throughout the region. San Francisco and San Jose, both densely populated cities, fall in the top 10 percent of Construction Risk Zones along with less population-dense cities in Contra Costa, Alameda, and Solano counties (where large amounts of acreage are under construction).

It should be noted that the replacement of the Bay Bridge's eastern span, a multi-year, multi-billion-dollar project involving large amounts of construction equipment, is not captured in this evaluation.

TABLE 6 **San Francisco Bay Area Construction Pollution Damage**

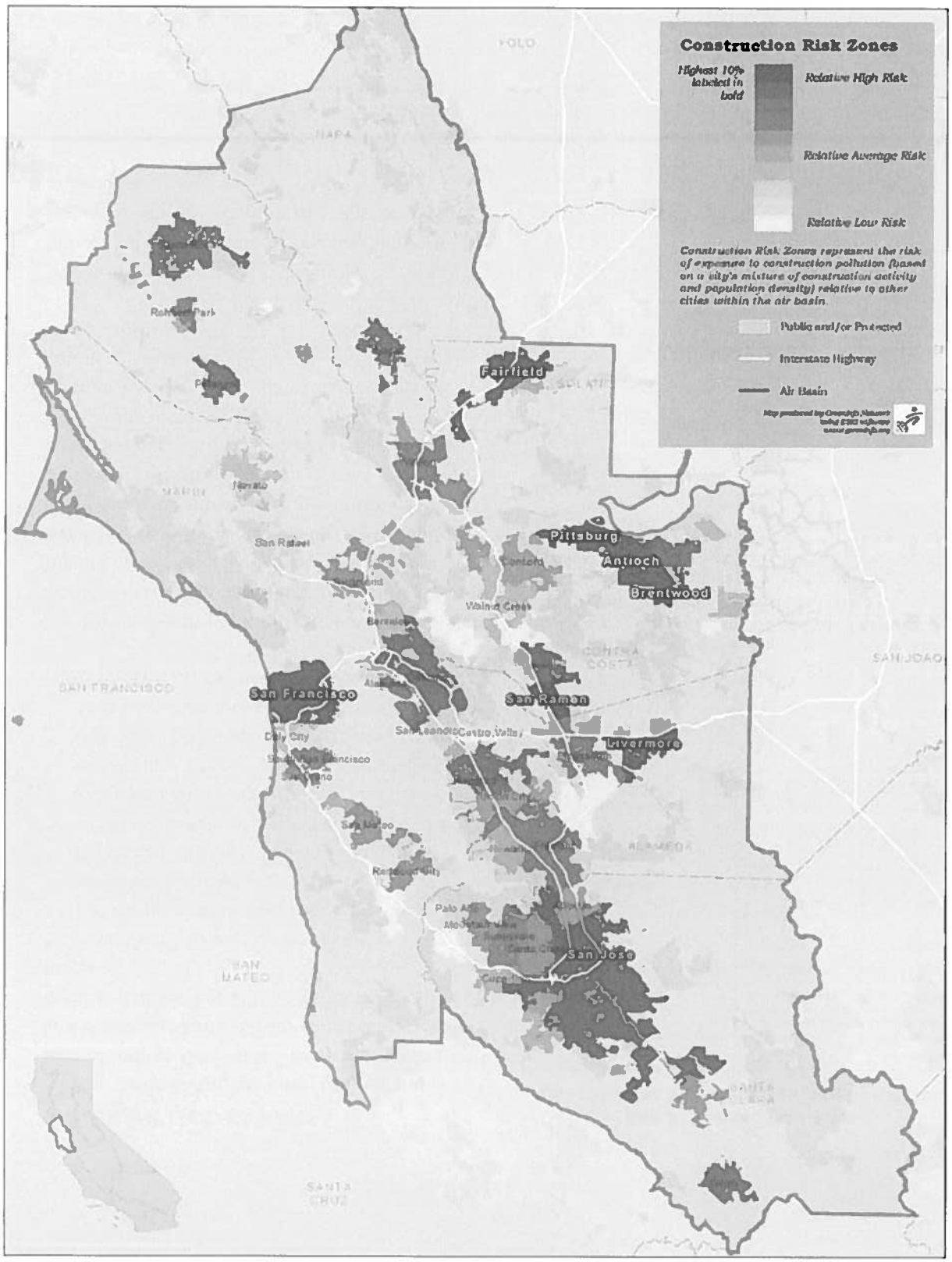
Health Endpoint	Mean Annual Incidences	Annual Costs (in thousands of 2005 dollars)
Premature Deaths	154	1,215,948
Respiratory Hospitalizations	56	1,914
Cardiovascular Hospitalizations	61	2,482
Asthma and Other Lower Respiratory Symptoms	3,406	65
Acute Bronchitis	284	120
Lost Work Days	25,713	4,628
Minor Restricted Activity Days	168,459	10,108
School Absences	18,472	1,626
Total Annual Cost		1,236,890

TABLE 7 **Top 10 Percent of San Francisco Bay Area Construction Risk Zones**

City	County
Livermore	Alameda
Antioch	Contra Costa
Brentwood	Contra Costa
Pittsburg	Contra Costa
San Ramon	Contra Costa
San Francisco	San Francisco
San Jose	Santa Clara
Fairfield	Solano

NOTE: Cities are listed in alphabetical order by county.

FIGURE 3 **Construction Pollution Risk in the San Francisco Bay Area Air Basin**



SAN DIEGO

This air basin ranks third behind the South Coast and San Francisco Bay Area for damage from construction equipment pollution. For 2005, this includes estimates of:

- nearly 90 premature deaths
- more than 80 hospitalizations for respiratory and cardiovascular disease
- more than 170 cases of acute bronchitis
- more than 2,000 incidences of asthma attack and other lower respiratory symptoms
- 38,500 days of lost work and school absences
- more than 100,000 days of restricted activity

This loss of life and productivity cost San Diego residents an estimated $718 million.

Within the air basin, 25 cities and towns had active construction permits during 2005 accounting for more than 22,500 acres of land under construction. San Diego is by far the most populated and largest city in the air basin falling in the top 10 percent of Construction Risk Zones; others include Chula Vista and Oceanside, which both have a population density similar to San Diego and more than 1,000 acres under construction permit in 2005.

TABLE 8 **San Diego Construction Pollution Damage**

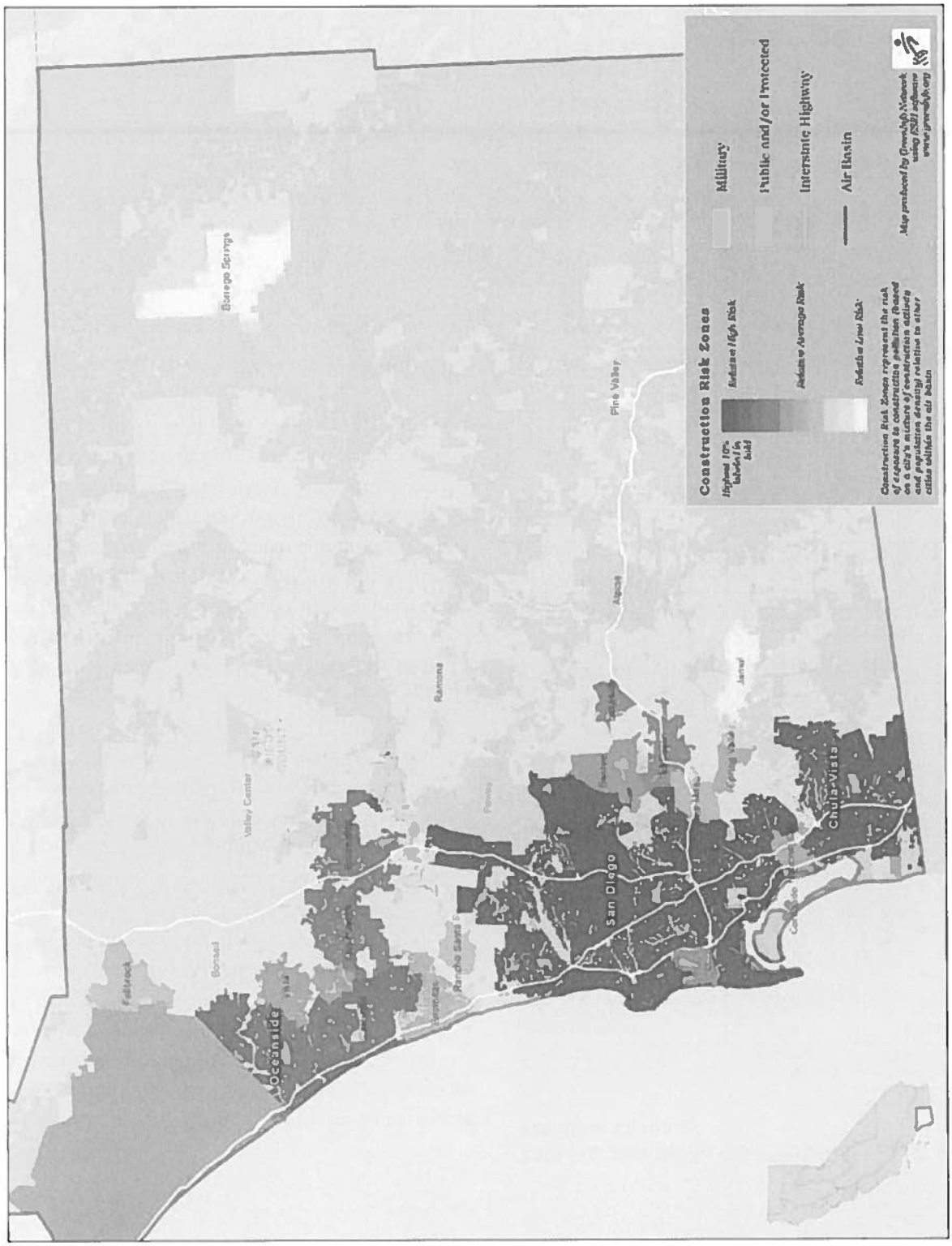
Health Endpoint	Mean Annual Incidences	Annual Costs (in thousands of 2005 dollars)
Premature Deaths	89	703,222
Respiratory Hospitalizations	50	1,703
Cardiovascular Hospitalizations	33	1,357
Asthma and Other Lower Respiratory Symptoms	2,127	40
Acute Bronchitis	177	75
Lost Work Days	14,014	2,523
Minor Restricted Activity Days	113,280	6,797
School Absences	24,689	2,173
Total Annual Cost		717,890

TABLE 9 **Top 10 Percent of San Diego Construction Risk Zones**

City	County
Chula Vista	San Diego
Oceanside	San Diego
San Diego	San Diego

NOTE: Cities are listed in alphabetical order by county.

FIGURE 4 **Construction Pollution Risk in the San Diego Air Basin**



SAN JOAQUIN VALLEY

This air basin, comprising the southern counties of California's Central Valley, ranks fourth for health and economic damage from construction equipment pollution. For 2005, this includes estimates of:

- nearly 50 premature deaths
- 70 hospitalizations for respiratory and cardiovascular disease
- more than 100 cases of acute bronchitis
- more than 1,200 incidences of asthma attack and other lower respiratory symptoms
- 39,000 days of lost work and school absences
- nearly 100,000 days of restricted activity

This loss of life and productivity cost San Joaquin Valley residents an estimated $401 million.

Within the air basin, 66 cities and towns had active construction permits during 2005 accounting for more than 32,500 acres of land under construction. The seven cities comprising the air basin's top 10 percent of Construction Risk Zones are spread throughout the valley (in six different counties) and correspond to the most populated areas.

TABLE 10 **San Joaquin Valley Construction Pollution Damage**

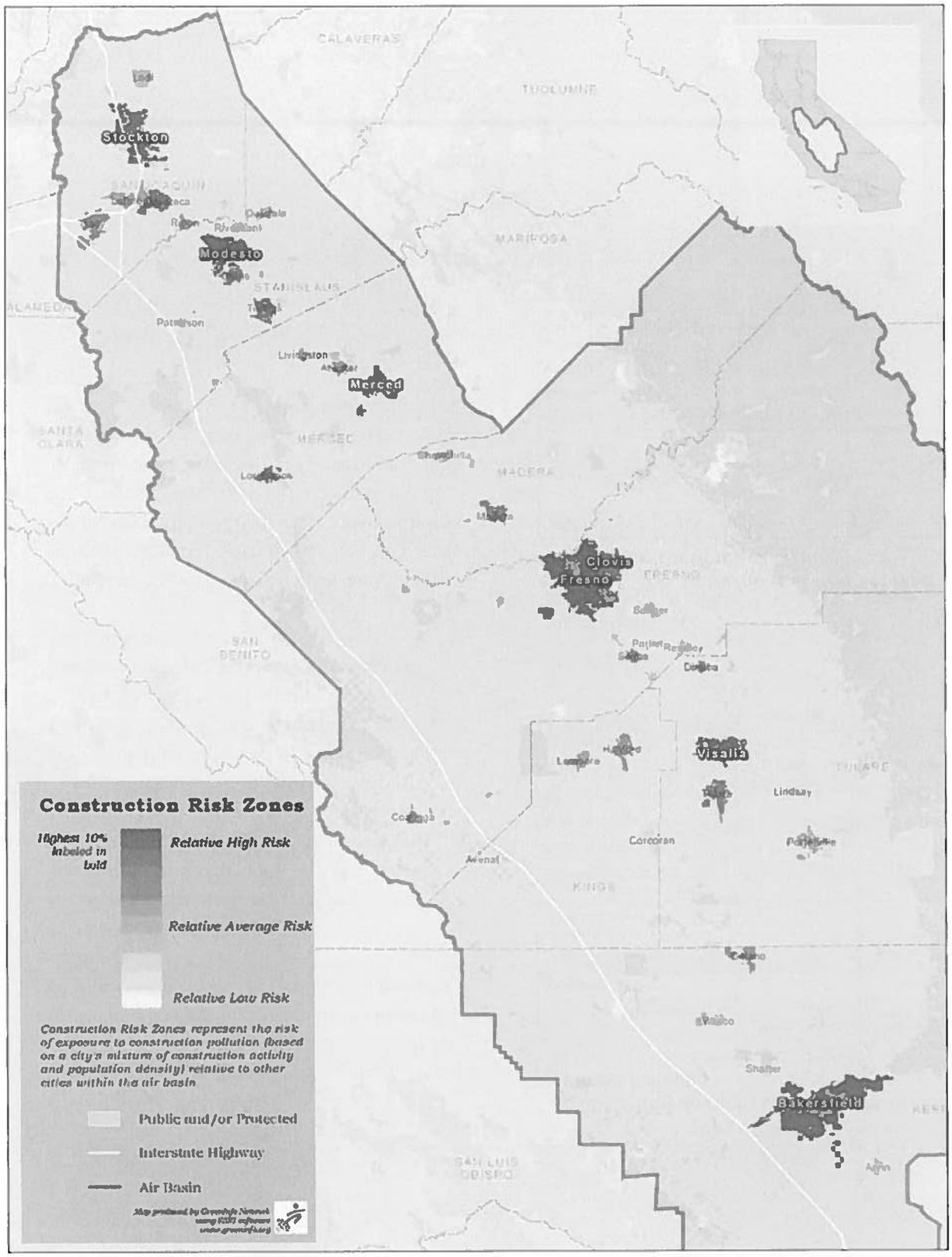
Health Endpoint	Mean Annual Incidences	Annual Costs (in thousands of 2005 dollars)
Premature Deaths	49	388,547
Respiratory Hospitalizations	55	1,858
Cardiovascular Hospitalizations	14	592
Asthma and Other Lower Respiratory Symptoms	1,284	24
Acute Bronchitis	107	45
Lost Work Days	6,241	1,123
Minor Restricted Activity Days	99,585	5,975
School Absences	33,282	2,929
Total Annual Cost		401,094

TABLE 11 **Top 10 Percent of San Joaquin Valley Construction Risk Zones**

City	County
Clovis	Fresno
Fresno	Fresno
Bakersfield	Kern
Merced	Merced
Stockton	San Joaquin
Modesto	Stanislaus
Visalia	Tulare

NOTE: Cities are listed in alphabetical order by county.

FIGURE 5 **Construction Pollution Risk in the San Joaquin Valley Air Basin**



SACRAMENTO VALLEY

This air basin, comprising the northern counties of California's Central Valley, ranks fifth for health and economic damage from construction equipment pollution. For 2005, this includes estimates of:

- nearly 40 premature deaths
- more than 40 hospitalizations for respiratory and cardiovascular disease
- more than 65 cases of acute bronchitis
- 790 incidences of asthma attack and other lower respiratory symptoms
- 22,000 days of lost work and school absences
- more than 50,000 days of restricted activity

This loss of life and productivity cost Sacramento Valley residents an estimated $314 million.

Within the air basin, 52 cities and towns had active construction permits during 2005 accounting for more than 29,000 acres of land under construction. The cities falling in the top 10 percent of Construction Risk Zones include the city of Sacramento and its suburbs Elk Grove, Roseville, and Woodland, along with Yuba City in Sutter County.

TABLE 13 **Top 10 Percent of Sacramento Valley Construction Risk Zones**

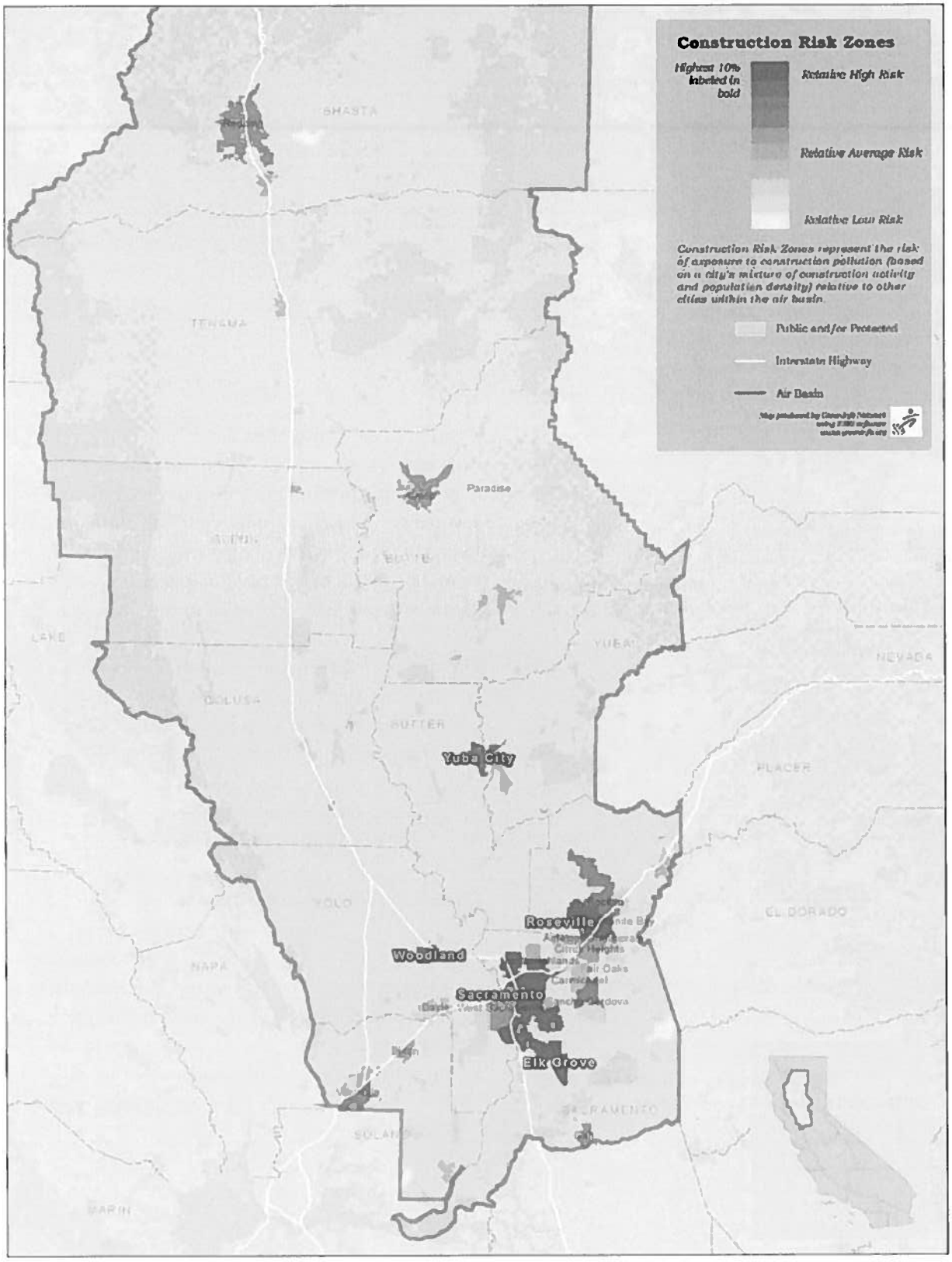
City	County
Roseville	Placer
Elk Grove	Sacramento
Sacramento	Sacramento
Yuba City	Sutter
Woodland	Yolo

NOTE: Cities are listed in alphabetical order by county.

TABLE 12 **Sacramento Valley Construction Pollution Damage**

Health Endpoint	Mean Annual Incidences	Annual Costs (in thousands of 2005 dollars)
Premature Deaths	39	306,638
Respiratory Hospitalizations	30	1,003
Cardiovascular Hospitalizations	12	493
Asthma and Other Lower Respiratory Symptoms	790	15
Acute Bronchitis	66	28
Lost Work Days	4,617	831
Minor Restricted Activity Days	50,408	3,025
School Absences	17,492	1,539
Total Annual Cost		313,571

FIGURE 6 **Construction Pollution Risk in the Sacramento Valley Air Basin**



CONCLUSIONS

Construction equipment is operating in cities and towns throughout California, releasing harmful NOx and PM emissions into the air and raising the risk of exposure to these pollutants for residents who live and work near construction sites. The likelihood of people living or working close to construction sites is highest in densely populated urban areas, but the suburbs are not free of risk from construction equipment pollution. Many projects in these areas, including new commercial and residential developments, require extensive use of construction equipment for land clearing and grading operations. Road construction and maintenance projects occurring throughout the state add additional risk.

Construction equipment pollution is therefore a health concern for all Californians.

Chapter 4

Building a Cleaner Future

Because of its long working life, high replacement cost, and lagging emission standards, diesel construction equipment will continue to pollute for decades. That means Californians will suffer from increased hospital admissions for respiratory and cardiovascular disease, asthma attacks, acute bronchitis, and even premature death—unless the state takes action to dramatically reduce construction equipment pollution.

WHAT CAN CALIFORNIA DO?

Under the federal Clean Air Act, California has the unique authority to regulate construction equipment. The state should use this authority to establish stringent new regulations that would complement its recent efforts to clean up pollution from other on-road and off-road sources of diesel pollution.[10] An effective regulatory regime for diesel construction equipment would:

- reduce diesel PM 75 percent below 2000 levels by 2010 and 85 percent below 2000 levels by 2020—which would reduce estimated annual premature deaths from construction equipment pollution by 790 (70 percent) compared with 2005
- phase out or retire the oldest, most polluting equipment
- install the best available retrofit technology on newer equipment
- require the strongest emission controls near sensitive locations such as schools, nursing homes, hospitals, and day care centers

Incentive programs have also proven effective in cleaning up construction equipment (UCS 2004). These programs should continue to fund equipment cleanup with the goal of achieving emission reductions above and beyond what regulations require.

There are a number of cost-effective ways to reduce emissions from construction and other off-road diesel equipment, allowing for flexibility in meeting reduction targets:[11]

- **Refuel.** Switching to alternative diesel fuels can achieve modest reductions in pollutants. These fuels can also facilitate the use of advanced retrofit technologies, resulting in even less pollution.
- **Repower.** The body or chassis of some equipment can last many decades, beyond the life of the original engine. Installing a new low-emission engine in an older chassis can allow the machine to run cleanly for many more years. California's Carl Moyer incentive program is currently funding some repower projects for construction equipment.[12]
- **Replace.** Replacing old equipment with a new lower-emission model ahead of schedule can result in substantial pollution reductions.

10 CARB has passed numerous regulations under its Diesel Risk Reduction Plan that set strict emission reduction targets for specific types of diesel vehicles and equipment (CARB 2005a, 2005b, 2005c, 2004b, 2003a, 2003b, 2003c, 2000).

11 Previous UCS analysis found that diesel cleanup through California's Carl Moyer incentive program achieves benefits valued at 10 times the cost of cleanup (UCS 2004).

12 Repower projects funded by the Carl Moyer incentive program must meet stringent cost-effectiveness thresholds (CARB 2000a, 2004a).

- **Retrofit.** Existing engines that can be expected to run for many more years can be retrofitted with emission control technologies that reduce PM more than 90 percent.[13]
- **Reduce idling.** Idling equipment not only pollutes, but also wastes fuel. Limiting idle time, on the other hand, saves money by reducing fuel use and wear-and-tear on the engine.

Efforts around the country and around the world are proving that the technology exists to lower construction equipment emissions. In Switzerland, for example, an aggressive regulation to curtail diesel PM emissions from construction sites has resulted in thousands of retrofits (Mayer 2004, 2005). In 2003, New York City passed an ordinance requiring that diesel equipment on all city-funded construction sites use ultra-low-sulfur fuel and be retrofitted with the best available control technology (Bradley 2006). Boston's "Big Dig" incorporated more than 200 retrofit devices on construction equipment, and Connecticut's Harbor Crossing Corridor is following suit.

In California, some air districts are funding repowers and retrofits through the Carl Moyer incentive program and, for large projects, requiring the use of cleaner construction equipment.[14] These and other groundbreaking efforts (MECA 2006) have proven the success of cleanup technology for construction equipment, but statewide action is necessary to achieve the greatest reductions and maximum health benefits.

WHAT CAN YOU DO?

By taking the following actions, individuals can help protect themselves from harmful diesel emissions and make sure that the appropriate decision makers know that Californians want diesel-powered construction equipment cleaned up:

- File a visible smoke complaint with your air district (contact information can be found at *http://www.arb.ca.gov/capcoa/roster.htm*) or CARB (call 800-952-5588 or email *vruiz@arb.ca.gov*) when you see plumes of diesel soot coming from construction equipment. Request that an inspector be sent to the site and investigate the emission source.
- Report illegal idling (commercial trucks that haul dirt or service construction sites cannot idle for more than five minutes) to CARB (visit *http://www.arb.ca.gov/enf/complaints/complaints.htm* or call 800-END-SMOG) or your local air district (contact information can be found at *http://www.arb.ca.gov/capcoa/roster.htm*). Citations for illegal idling can also be issued by local law enforcement.
- Tell your state legislative representatives (contact information can be found at *http://www.leginfo.ca.gov/yourleg.html*) and CARB (*arbboard@arb.ca.gov*) that cleaner construction equipment is important to you.
- Close your windows while diesel-powered equipment is operating near your home or office.
- Raise your concern about emissions from proposed construction in your neighborhood during the public review period, and demand that the project's environmental impact review assesses these emissions and includes a strategy for controlling them.
- Urge your city council to protect residents from construction pollution by enacting a clean-construction ordinance—especially around sensitive sites such as schools and day care centers.

13 CARB has verified retrofit technologies for use on off-road equipment. See *http://www.arb.ca.gov/diesel/verdev/verifiedtechnologies/cvt.htm*.

14 The Sacramento Metropolitan Air Quality Management District (*http://www.airquality.org/ceqa/index.shtml*) and San Luis Obispo County Air Pollution Control District (contact: Andrew Mutziger) require construction equipment pollution mitigation for some projects under the California Environmental Quality Act.

Appendix

Estimating the Health Damage and Economic Costs of Construction Pollution

Our polluted air has provided researchers a real-world laboratory for studying the impact of air pollution on people's health. Numerous epidemiological studies tracking thousands of individuals have linked PM exposure to premature death as well as cardiovascular and respiratory illnesses. Similar studies have been carried out for exposure to ozone pollution. These studies provide the basis for estimating the health benefits of reducing air pollution and are used in this study to estimate the impact of construction pollution.

The health effects quantified in this report are based on peer-reviewed epidemiological studies used by both the EPA and CARB to evaluate the benefits of reducing air pollution. These studies establish a statistically significant relationship between exposure to PM and ozone and increased incidences of specific health endpoints, which can then be quantified through a concentration-response function. The uncertainty in these estimates is quantified by presenting results as both a mean estimate of the number of incidences and a range of estimates representing the 95 percent confidence interval.[15]

Our analysis links health and economic damage to construction equipment pollution by using California-specific air quality monitoring data, county baseline health incidence rates, population estimates, and a diesel construction equipment emission inventory. PM concentrations for specific air basins were measured by CARB when identifying diesel PM as a toxic air contaminant (CARB 1998). And CARB recently evaluated concentration-response functions for specific health endpoints using diesel PM concentration estimates along with population data, baseline health incidence rates, and an inventory of diesel emission sources related to the movement of goods (CARB 2006a). As part of these efforts, air basin-specific factors were estimated (in tons of diesel pollution per incidence) for each health endpoint. UCS used these factors along with CARB's air basin-specific inventory of diesel PM, NOx, and reactive organic gases (ROG) to estimate the health effects of PM and ozone from construction equipment (CARB 2006d).

Each health endpoint covered in this report is assigned a dollar value to estimate the economic impact of diesel pollution. The EPA uses economic valuations of health endpoints to perform cost-benefit analyses of air pollution reduction measures, and our analysis reflects changes made to the EPA's hospitalization endpoints and lost work days to better reflect California-specific wage and health care data (CARB 2006a).

Premature death is the most serious health endpoint related to diesel pollution and has the greatest economic impact. Estimates of premature death resulting from exposure to fine PM are based on long-term exposure for people 30 or older, and include all causes of death (Pope 2002). Individuals with existing respiratory and cardiovascular disease and the elderly are most vulnerable, and life expectancies are shortened by months or even years (Pope 2000). Economic valuation of premature death is based on a review of studies carried

15 For a list of the epidemiological studies used, see CARB 2006a and EPA 2004.

out by the EPA and on society's "willingness-to-pay" to lower the risk of premature death (EPA 1999).

CONSTRUCTION PERMIT DATA

The California State Water Resources Control Board (SWRCB) construction permit database was chosen as the primary source for representing construction activity in California. Residential and commercial building permit data were excluded from the study due to overlapping information with the SWRCB database and the inclusion of projects that may not involve the use of diesel construction equipment.

SWRCB construction permits, which we used to calculate Construction Risk Zones, are required under the federal Clean Water Act for projects that disturb more than one acre of land. According to the SWRCB Fact Sheet for Water Quality Order 99-08-DWQ:

> *Construction activity subject to this General Permit includes clearing, grading, disturbances to the ground such as stockpiling, or excavation that results in soil disturbances of at least one acre of total land area. Construction activity that results in soil disturbances of less than one acre is subject to this General Permit if the construction activity is part of a larger common plan of development that encompasses one or more acres of soil disturbance or if there is significant water quality impairment resulting from the activity.*

Construction projects that disturb more than one acre of land generally involve the use of diesel earthmoving construction equipment. These permits, while not directly representing construction equipment activity, provide the best available indication of where large earthmoving equipment is being used.

Limitations of permit data. There are, however, some limitations to estimating construction activity from SWRCB permits.

Projects under permit may go through many different phases of construction before completion, not all of which require the use of diesel-powered construction equipment or sustained levels of construction equipment activity. Therefore, there is no guarantee that construction equipment was operated on site during a specific period of time, but permitees must pay an annual fee to the SWRCB to keep permits active. This monetary requirement should minimize the number of permitees holding active permits but not performing construction activity.

Additionally, there are some construction projects that will not appear in the SWRCB database. Projects in which storm runoff is captured in a combined sewer/storm water system do not require permits because the water treatment plant that receives the runoff is the permitted entity. Some projects in San Francisco and Sacramento, where a combined sewer system exists, may be excluded from the database as a result, but the majority of California cities do not have combined sewer/storm water systems.

Furthermore, some projects listed in the SWRCB database have incomplete location information. These details can include street address with or without number, street intersections with or without compass directions, pier number, and tract number. Mapping project location by city rather than zip code or street address allowed us to capture 90 percent of the acres under permit.

Because the size of a project is represented by the number of acres disturbed during construction, the amount of construction equipment activity may not have a linear relationship to the size

of the project. In general, large-acreage projects will likely have greater construction equipment activity than small-acreage projects. However, urban construction sites that are relatively small in area may have heavy construction equipment activity due to multi-story construction. For instance, a two-acre high-rise construction site in downtown Los Angeles may have a much higher sustained level of construction equipment activity than a two-acre single-family home construction site in the suburbs. The available data did not allow us to distinguish between single-story and multi-story construction.

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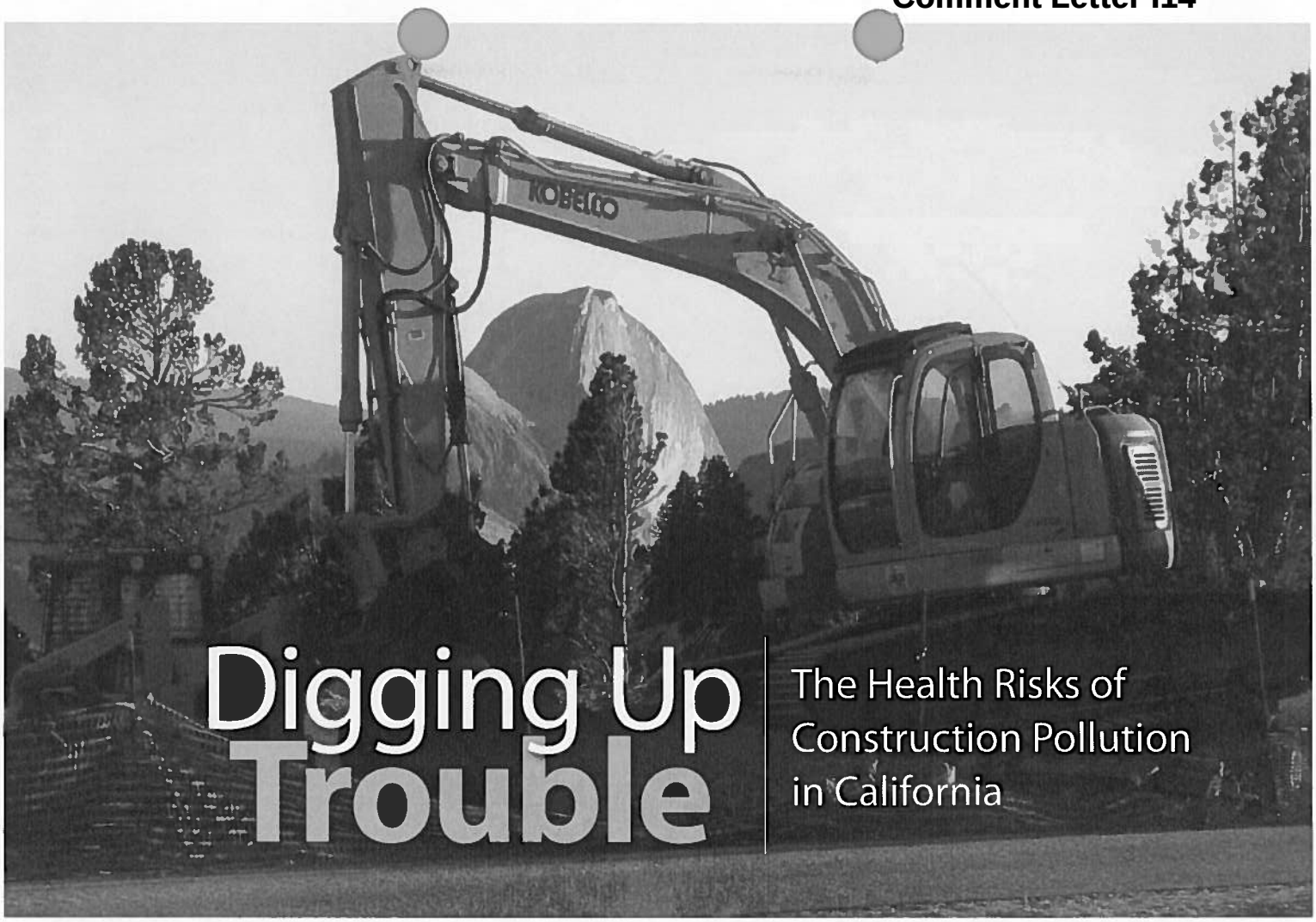
Comment Letter I14



Digging Up Trouble

The Health Risks of Construction Pollution in California

Diesel engines may conjure up images of big rigs or transit buses, but construction equipment is a leading source of diesel pollution in California. Air pollution caused by construction equipment can result in severe cardiovascular and respiratory illnesses, asthma attacks, acute bronchitis, and even premature death.

This study quantifies the effect of construction pollution on California's public health and economy, both across the state and in the five most-affected regions. The risk of exposure to construction activity is evaluated for cities in each of these regions.

Construction equipment will continue to be a significant source of pollution over the next two to three decades unless California acts now. By adopting the cost-effective technology solutions that already exist (and those that will become available over the next few years), the state can reduce this public health threat and help all Californians breathe easier.

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October 11, 2012

Via Electronic Mail and Hand Delivery

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Re: Comment re: Final Environmental Impact Report for the Mammoth Pacific I ("MP-I") Replacement Project (State Clearinghouse No: 2011022020); Clarifying General Plan Amendment 12-003(b); Condition Use Permit 12-004; Variance 12-002 & Reclamation Plan 12-001; Special Meeting Agenda Items 5 and 6.

Honorable Chair Shipley and Members of the Planning Commission, Mr. Villa:

This letter is submitted on behalf of Laborers International Union of North America, Local Union 783, and its members living in Mono County (collectively "LIUNA" or "Commenters") regarding the Final Environmental Impact for the Mammoth Pacific I (MP-1) Replacement Project (State Clearinghouse No: 2011022020), Clarifying General Plan Amendment 12-003(b), Conditional Use Permit ("CUP") 12-004, Variance 12-002 & Reclamation Plan 12-001, Special Meeting Agenda Items 5 and 6 (collectively "Project" or "Mammoth Project").

As discussed herein, after reviewing the Final Environmental Impact Report ("FEIR") for the Project together with our expert consultants, it is evident that the document fails to resolve significant deficiencies raised in prior comment letters on the Draft Environmental Impact Report ("DEIR"), Revised DEIR ("RDEIR") and Second Revised DEIR ("RDEIR2"), that lead agency Mono County ("County") failed to comply

with the California Environmental Quality Act, Public Resources Code § 21000 et seq. ("CEQA"), and with State Land Use and Planning laws, in all aspects of the Project, and the FEIR contains errors and omissions that continue to preclude accurate analysis of the Project.

As a result of these inadequacies, the FEIR fails as an informational document, fails to analyze all significant impacts of the Project, fails to identify and impose feasible mitigation measures to reduce the Project's impacts, and fails to properly analyze Project alternatives and cumulative impacts.[1] The Project and its proposed General Plan amendments also render it fatally inconsistent with the County's General Plan. As a result, the Project will result in significant environmental impacts on the Mammoth Lakes area, including its animal and plant populations, air quality, water quality, and aesthetic impacts, among other impacts. LIUNA Local 783 therefore requests that the County prepare and circulate a Supplemental Draft Environmental Impact Report ("SEIR") to address the issues raised in this and other comments, and to require implementation of feasible mitigations and alternatives required by law.

In particular, the Project will have the following adverse impacts that remain inadequately mitigated:

General Plan Inconsistency:

- The Project is inconsistent with the Mono County General Plan ("General Plan") in that it requires the County to amend the Mono County General Plan to authorize the Applicant to develop geothermal facilities within 500 feet of a watercourse within the Hot Creek Buffer Area. To remedy this inconsistency, the RDEIR2 proposed a General Plan amendment to allow geothermal development in areas that were previously prohibited in the County. The amendment is both facially inconsistent with the Plan's Conservation and Open Space Element, which requires the County to minimize impacts of geothermal energy production on water resources in the Casa Diablo area, and opens the door for new geothermal projects to develop facilities within this previously protected, sensitive habitat.

Inaccurate Project Description:

- The Project description in the FEIR is inaccurate and legally insufficient in that it:
  - Fails to describe the Project in light of the newly proposed General Plan Amendments identified for the first time in the RDEIR2.
  - The Project, as described, would violate its own proposed mitigation measures for impacts to biological resources, rendering either the Project description, or its mitigation measures, inaccurate and facially inconsistent with each other.

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[1] We reserve the right to supplement these comments at any later hearings and proceedings related to this Project. *See Galante Vineyards v. Monterey Water Dist.* (1997) 60 Cal. App. 4th 1109.

Inadequate Cumulative Impacts Analysis:

- The FEIR fails to adequately analyze cumulative impacts resulting from planned construction of the Casa Diablo IV geothermal power plant and facilities, wells, and pipelines, currently undergoing joint NEPA and CEQA review by the U.S Bureau of Land Management ("BLM") and the Great Basin Air Pollution and Control District ("GBAPCD"), including but not limited to:
    - **Hydrology**: The FEIR fails to adequately analyze cumulative impacts on the geothermal aquifer and nearby surface waterways.
    - **Seismic Activity**: Enhanced geothermal systems can trigger earthquakes as part of hydraulic fracturing. The FEIR fails entirely to analyze the cumulative impacts of Project-generated seismic activity, combined with that of the proposed Casa Grande IV facility on nearby communities and existing structures.
    - **Biological Resources**: The FEIR fails to adequately analyze cumulative impacts on fisheries dependent on Hot Creek.

Impacts on Biological Resources:

- The FEIR fails to adequately assess impacts to biological resources, including mule deer and other mammals, native plants, and fish species, including some special status species.

- The FEIR fails to disclose potentially significant impacts on species from loss of foraging from the Project's conversion of forest acreage, including in particular mule deer.

- The FEIR fails to provide a complete and valid assessment of impacts to wildlife movement corridors and habitat fragmentation.

- The FEIR fails to provide adequate information on sensitive wildlife species likely to be impacted by the Project, and fails to establish regional and ecological context for sensitive species that will be affected by the Project including, but not limited to, possible impacts on the nearby Owens tui chub.

- The FEIR fails to analyze or provide any mitigations for cumulative impacts to biological and natural resources.

- The FEIR improperly defers mitigation, and provides insufficient mitigation monitoring, of various impacts to species, including mule deer.

- The FEIR provides inadequate baseline data on migration of mule deer.

Air Quality:

- Project construction will have significant air quality impacts from excess emissions of nitrogen oxides produced during combustion (NOx) that the County has failed to properly analyze and mitigate due to reliance on inappropriately high significant thresholds borrowed from Imperial County.

- The FEIR fails to analyze diesel particulate matter ("DPM") emissions from Project construction.

- The FEIR relies on a legally improper baseline for operational emissions, given the new location of the proposed M-1 plant and the simultaneous operations of both the MP-1 and M-1 plants for up to 2 years during the M-I startup period.

Expert Comments

These comments are supported by the expert comments of expert Wildlife Ecologist Luke Macauley, M.S.

Mr. Macauley is an expert wildlife biologist and ecologist who has expertise in the areas of rare and special status plants, animal density and distribution, habitat selection, habitat restoration, interactions between wildlife and human infrastructure and activities, conservation of rare and endangered species, and on the ecology of invading species, and other species impacts relevant to this Project. His comments and curriculum vitae are attached hereto as Exhibit A and are incorporated by reference in their entirety. These expert comments are incorporated herein in full.

LIUNA Local 783 recognizes that the development of reliable renewable energy sources is critical for California's future. LIUNA supports the development of clean, renewable energy technology, including the use of geothermal power generation where feasible. All geothermal and related mineral extraction extraction projects must be properly analyzed and carefully planned to minimize impacts on the environment. Geothermal and mineral extraction projects should avoid impacts to sensitive species and habitats, and should take all feasible steps to ensure that the production of renewable energy is not done at the expense of the State's natural resources, and dependent species. Only by maintaining the highest standards in these and other ways can energy supply development be truly sustainable. Unfortunately, the Project falls short in these and other ways. As a consequence, a Subsequent or Supplemental Draft Environmental Impact Report ("SEIR") is required to analyze the Project impacts discussed above, including impacts raised by other commenters and not adequately addressed by the County, and to propose feasible mitigation measures to bring the Project in compliance with applicable laws.

Citation to FEIR Documents

The Final EIR consists of the DEIR, RDEIR, and RDEIR2, as well as all comments received on the DEIR, RDEIR, and RDEIR2, the County's Responses to

Comments, and all Appendices Exhibits thereto. These documents and their content constitute the FEIR on the proposed Project. Citations herein may refer to "DEIR" pages, "RDEIR pages", "RDEIR2" pages, or "FEIR" pages. All references are intended as citations to the Final EIR.

I. BACKGROUND

a. Mammoth Pacific I Geothermal Facility.

The existing Mammoth Pacific Unit I ("MP–I") project is a commercial geothermal development project operated by Mammoth Pacific L.P. ("MPLP") and located near Casa Diablo Hot Springs in Mono County, California. (FEIR at p. 1) The MP-I plant was the first geothermal power plant to be built at the Mammoth Pacific Complex, commencing operation in 1984 under a Condition Use Permit ("CUP") issued by Mono County. The MP-2 geothermal plant was established in 1990 under a separate Mono County CUP. (RDEIR App. L (Reclamation Plan), p. 1) The existing MP–I project consists of a binary power plant with a design capacity of about 14 megawatts ("MW"), a geothermal wellfield, production and injection fluid pipelines, and ancillary facilities that have been operating since 1984. The existing MP–I power plant site is located approximately 1,200 feet northeast of the intersection of U.S. Highway 395 and California State Route 203 on 90 acres of private (fee) land owned by Ormat Nevada, Inc. ("Ormat"), the parent company of MPLP. (FEIR at p. 1)

b. The M-I Replacement Project.

The Project proposes to replace the existing MP-I plant with a more modern M-I generation plant. The M-I replacement plant site would be located entirely on private land about 500 feet northeast of the existing MP-I power generation facilities and immediately adjacent to the existing MP-II power plant. The Project would replace the existing MP-I power generation facilities. (FEIR at p. 1) The Project was proposed by Project applicant Mammoth Pacific L.P., under the ownership of Ormat Nevada Inc., a wholly owned subsidiary of Ormat Technologies, Inc. ("MPLP"). According to the FEIR, the purpose of the Project is to replace the aging MP–I power plant with a new, more modern and efficient binary power plant while maintaining the existing geothermal wellfield, pipeline system and ancillary facilities. The proposed M–1 replacement power plant would be capable of generating, on average, approximately 18.8 MW (net) of electricity. The FEIR states that the Project would result in no net change in the rate of geothermal fluid produced and supplying the existing Casa Diablo geothermal development complex, and no substantive change to the geothermal reservoir is anticipated. (FEIR at p. 4) A pipeline will connect the replacement plant with the existing wells, and a new 12.47 KV substation / switching station will be constructed to connect the new power plant to the existing transmission line.

The Project is located approximately 2 miles west of the town of Mammoth Lakes, approximately 4 miles from the Mammoth Mountain ski resort area, and approximately 1.25 miles to the east of Mono County's office buildings. (RDEIR at p. 4-40) The project footprint will result in the grading of 5.7 acres of land, which contains 3.5

acres that is dominated by Antelope bitterbrush, an important browse species for mule deer. (RDEIR at pp. 2-1, 4-66)

During M–1 plant startup operations, the existing MP–I plant would continue to operate until the new M–1 plant becomes commercial, after which time MPLP would close and dismantle the old MP-I plant. The old MP-I plant site would be converted to an equipment storage area as part of the decommissioning process. The transition period during which both the MP–I and M–1 operations would overlap would be a period of up to two years from the date the M–1 plant begins startup operations. (FEIR at p. 4)

The M-1 plant is anticipated to operate until 2045, at which time it will be decommissioned, and both the M-I and MP-I sites, as well as the MP-2 site, will be reclaimed. Included in the reclamation will be the geothermal well sites which support the M-I, MP-I and MP-2 plants. These wells will also remain in operation until approximately 2045. (RDEIR App. L at p. 1) If the geothermal resource remains available beyond 2045, the Project's Reclamation Plan will need to be revised. (*Id.*)

The following approvals are required from Mono County for the Project:

- A Conditional Use Permit for the M-1 replacement plant (including the granting of a height exception for mechanical appurtenances) and decommissioning/reuse of the existing MP-I plant site as a storage area;
- A Variance for setback reductions from property line(s); setback reductions from streams designated by a blue line on USGS topographic maps for structures within the 5.7-acre proposed M-1 plant site; and for grading of the existing MP-I plant site for use as an equipment storage area;
- A Variance to construct an aboveground electrical transmission line;
- Clarifying General Plan Amendments;
- Grading Permit;
- Building Permits; and
- A Reclamation Plan. (RDEIR2 at p. 29)

II. STANDING

Members of LIUNA Local 783 live, work, and recreate in the immediate vicinity of the proposed Project site. These members will suffer the impacts of a poorly executed or inadequately mitigated Project, just as would the members of any nearby homeowners association, community group, or environmental group. Members of LIUNA Local 783 live and work in areas that will be affected by geothermal and mineral exploration and water source reduction, air pollution, and impacts on plant and wildlife species generated by the Project. In addition, construction workers in particular will suffer many of the most significant impacts from the Project as currently proposed, such as close proximity exposure to construction-related air pollution. Therefore, LIUNA Local 783 and its members have a direct interest in ensuring that the Project is adequately analyzed and that its environmental and public health impacts are mitigated to the fullest extent feasible.

III. LEGAL STANDARD

A. CEQA.

CEQA requires that an agency analyze the potential environmental impacts of its proposed actions in an environmental impact report ("EIR") (except in certain limited circumstances). (*See, e.g.*, Pub. Res. Code § 21100.) The EIR is the very heart of CEQA. (*Dunn-Edwards v. BAAQMD* (1992) 9 Cal.App.4th 644, 652.) "The 'foremost principle' in interpreting CEQA is that the Legislature intended the act to be read so as to afford the fullest possible protection to the environment within the reasonable scope of the statutory language." (*Communities for a Better Environment v. Calif. Resources Agency* (2002) 103 Cal. App. 4th 98, 109.)

CEQA has two primary purposes. First, CEQA is designed to inform decision makers and the public about the potential, significant environmental effects of a project. (14 Cal. Code Regs. ("CEQA Guidelines") § 15002(a)(1).) "Its purpose is to inform the public and its responsible officials of the environmental consequences of their decisions before they are made. Thus, the EIR 'protects not only the environment but also informed self-government.'" (*Citizens of Goleta Valley v. Board of Supervisors* (1990) 52 Cal. 3d 553, 564) The EIR has been described as "an environmental 'alarm bell' whose purpose it is to alert the public and its responsible officials to environmental changes before they have reached ecological points of no return." (*Berkeley Keep Jets Over the Bay v. Bd. of Port Comm'rs.* (2001) 91 Cal. App. 4th 1344, 1354 ("Berkeley Jets"); *County of Inyo v. Yorty* (1973) 32 Cal.App.3d 795, 810)

Second, CEQA requires public agencies to avoid or reduce environmental damage when "feasible" by requiring "environmentally superior" alternatives and all feasible mitigation measures. (CEQA Guidelines § 15002(a)(2) and (3); See also, *Berkeley Jets*, 91 Cal. App. 4th 1344, 1354; *Citizens of Goleta Valley v. Board of Supervisors* (1990) 52 Cal.3d 553, 564) The EIR serves to provide agencies and the public with information about the environmental impacts of a proposed project and to "identify ways that environmental damage can be avoided or significantly reduced." (Guidelines §15002(a)(2)) If the project will have a significant effect on the environment, the agency may approve the project only if it finds that it has "eliminated or substantially lessened all significant effects on the environment where feasible" and that any unavoidable significant effects on the environment are "acceptable due to overriding concerns." (Pub.Res.Code § 21081; 14 Cal.Code Regs. § 15092(b)(2)(A) & (B))

While the courts review an EIR using an "abuse of discretion" standard, "the reviewing court is not to 'uncritically rely on every study or analysis presented by a project proponent in support of its position. A 'clearly inadequate or unsupported study is entitled to no judicial deference.'" (*Berkeley Jets*, 91 Cal. App. 4th 1344, 1355 (emphasis added), quoting, *Laurel Heights Improvement Assn. v. Regents of University of California*, 47 Cal. 3d 376, 391 409, fn. 12 (1988)) As the court stated in *Berkeley Jets*, 91 Cal. App. 4th at 1355:

> A prejudicial abuse of discretion occurs "if the failure to include relevant information precludes informed decisionmaking and informed public participation,

thereby thwarting the statutory goals of the EIR process." (*San Joaquin Raptor/Wildlife Rescue Center v. County of Stanislaus* (1994) 27 Cal. App. 4th 713, 722]; *Galante Vineyards v. Monterey Peninsula Water Management Dist.* (1997) 60 Cal. App. 4th 1109, 1117; *County of Amador v. El Dorado County Water Agency* (1999) 76 Cal. App. 4th 931, 946)

B. General Plan Consistency.

State law requires each county to adopt a long-term general plan governing development in all unincorporated areas. (Gov. Code §65300; *Napa Citizens for Honest Gov't*, 91 Cal. App. 4th at 352) The general plan sits at the top of the land use planning hierarchy (*DeVita v. County of Napa* (1995) 9 Cal.4th 763, 773), and serves as a "constitution" or "charter" for all future development. (*Lesher Commc'ns v. Walnut Creek* (1990) 52 Cal.3d 531, 540) General plan consistency is "the linchpin of California's land use and development laws; it is the principle which infused the concept of planned growth with the force of law." (*deBottari v. Norco City Council* (1985) 171 Cal. App. 3d 1204, 1213)

State law mandates two levels of consistency. First, a general plan must be internally or "horizontally" consistent: its elements must "comprise an integrated, internally consistent and compatible statement of policies for the adopting agency." (Gov. Code § 65300.5; *Sierra Club v. Bd. of Supervisors* (1981) 126 Cal. App. 3d 698, 704) A general plan amendment thus may not be internally inconsistent, nor may it cause the general plan as a whole to become internally inconsistent. (*DeVita*, 9 Cal. 4th at 796, n. 12) Second, state law requires "vertical" consistency, meaning that zoning ordinances must be consistent with the general plan. (See § 65860(a)(2); *Neighborhood Action Group v. Calaveras* (1984) 156 Cal. App. 3d 1176, 1184) Consistency is found when "[t]he various land uses authorized by the ordinance are compatible with the objectives, policies, general land uses, and programs specified in the [general] plan." (*Id.* at (a)(2))

A project cannot be found consistent with a general plan if it conflicts with a general plan policy that is "fundamental, mandatory, and clear," regardless of whether it is consistent with other general plan policies. (*Endangered Habitats League v. County of Orange* (2005) 131 Cal. App. 4th 777, 782-83; *Families Unafraid to Uphold Rural El Dorado County v. Bd. of Supervisors* (1998) 62 Cal. App. 4th 1332, 1341-42) Any subordinate land use action that is not consistent with a city's current general plan is "invalid at the time it is passed." (*Lesher*, 52 Cal. 3d at 544) Findings that a zoning ordinance is consistent with its general plan must be reversed if they are based on evidence from which no reasonable person could have reached the same conclusion. (*A Local & Reg'l Monitor v. Los Angeles* (1993) 16 Cal. App. 4th 630, 648)

IV. DISCUSSION

A. THE PROJECT IS INCONSISTENT WITH THE COUNTY'S GENERAL PLAN, CREATING PER SE SIGNIFICANT IMPACTS UNDER CEQA, AND THE NEWLY PROPOSED CLARIFYING GENERAL PLAN AMENDMENT WOULD RENDER THE GENERAL PLAN INTERNALLY INCONSISTENT.

The Project is inconsistent with the Mono County General Plan ("General Plan") in that it requires the County to amend the Mono County General Plan to authorize the Applicant to develop geothermal facilities within 500 feet of a watercourse within the Hot Creek Buffer Area. To remedy this inconsistency, the RDEIR2 proposed a General Plan amendment to allow geothermal development in areas that were previously prohibited in the County. The amendment is both facially inconsistent with the Plan's Conservation and Open Space Element, which requires the County to minimize impacts of geothermal energy production on water resources in the Casa Diablo area, and opens the door for new geothermal projects to develop facilities within this previously protected, sensitive habitat.

It is well-established that the elements, data, assumptions and projections used in various parts of a general plan must be consistent with one another. (Gov. Code §65300.5; *see Concerned Citizens of Calaveras County*, 166 Cal. App. 3d at 96-97; *Sierra Club*, 126 Cal. App. 3d at 704) Additionally, general plan inconsistencies are, themselves, also potentially significant impacts under CEQA. (*See Pocket Protectors v. City of Sacramento* (2004) 124 Cal. App. 4th 903, 930, 934 (requiring project's conflicts with land use policies adopted to avoid environmental effects to be discussed in an EIR))

Here, General Plan Land Use Element, Development Standards section 15.070(B)(1)(d) expressly prohibits geothermal development within 500 feet of surface waters. It provides in relevant part:

> No geothermal development located within the Hot Creek Buffer Zone shall occur within 500 feet on either side of a surface watercourse (as indicated by a solid or broken blue line on U.S. Geological Survey 7.5- or 15-minute series topographic maps). (General Plan at LU- II-263)

Additionally, Conservation / Open Space Element, Goal 7 provides, in relevant part:

> **GOAL 7:** Minimize the visual and environmental impacts of electrical transmission lines and fluid conveyance pipelines....
> **Objective B**
> Transmission and distribution lines shall not adversely impact wildlife or fisheries.
> Policy 1: New transmission or distribution lines shall avoid open expanses of water and wetland, particularly those heavily used by birds. They shall also avoid nesting and rearing areas.
> Policy 2: Avoid the placement of transmission or distribution lines through crucial wildlife habitats, such as deer fawning and migration areas. (See Conservation/Open Space Element at V-47 to V-49)

Nevertheless, the Project proposes two variances to exempt it from critical elements of the General Plan's Land Use Element and Conservation/Open Space Element:

- A Variance for setback reductions from property line(s); setback reductions from streams designated by a blue line on USGS topographic maps for structures within the 5.7-acre proposed M-1 plant site; and for grading of the existing MP-I plant site for use as an equipment storage area;
- A Variance to construct an aboveground electrical transmission line. (RDEIR2 at p. 29)

The FEIR incorrectly concludes that the Project is consistent with the General Plan under its proposed Clarifying General Plan Amendment. The RDEIR2 proposed a General Plan Amendment to relieve the Project from the General Plan 500-foot setback requirement contained in Land Use Element Section 15.070(B)(1)(d) that will amend the Conservation/Open Space Element to authorize development of geothermal facilities within 500 feet of a watercourse within the Hot Creek Buffer Zone, as follows:

> **Conservation and Open Space Element**
> **Energy Resources, Objective D, Policy 1**
> Action 1.13: ~~No geothermal development located within the Hot Creek Buffer Zone shall occur~~ Adoption of land development regulations for geothermal development within 500 feet on either side of a surface watercourse (as indicated by a solid or broken blue line on U.S. Geological Survey 7.5- or 15-minute series topographic maps) within the Hot Creek Buffer Zone (See Mono County Land Development Regulations, Chapter 15, section 15.070(B)(1)(d).)
>
> (RDEIR2 at p. 34)

The amendment was included for the first time in the RDEIR2, in subsection 4.10 of the document, and was not included in the Project description in either the RDEIR2 or the FEIR's updated Project Location or Project Summary. (RDEIR2 at pp. 33-34; FEIR at pp. 1-4) On its face, the proposed amendment would render Section 15.070(B)(1)(d) of the General Plan facially inconsistent with Objective D, Policy 1 of the Conservation / Open Space Element, which provides in relevant pat:

> Policy 1: Geothermal exploration and development projects shall be sited, carried out and maintained by the permit holder in a manner that best protects hydrologic resources and water quality and quantity.
>
> (See Conservation/Open Space Element at V-41)

If approved, the Clarifying General Plan Amendment will render these General Plan provisions internally inconsistent with one another. The County would be exceeding its authority if it were to issue permits or variances related to the Project as described in the FEIR, based on the proposed amendment or otherwise, because the Project is inconsistent with the County's General Plan, particularly its Land Use and Conservation/ Open Space Elements. (*See Neighborhood Action Group v. County of*

Calaveras (1984) 156 Cal.App.3d 1176, 1184) In *Neighborhood Action Group*, the Court of Appeal held that "a use permit is struck from the mold of the zoning law....the zoning law must comply with the adopted general plan...[and] the adopted general plan must comply with state law." (*Id.* at 1184) The general plan delimits the authority of the permit-issuing agency; thus, where an agency issues a permit that is inconsistent with the general plan, it exceeds its legal authority and the permit is invalid. (*Id.*)

B. THE PROJECT DESCRIPTION IN THE FEIR IS INACCURATE AND IMCOMPLETE.

"An accurate, stable and finite project description is the sine qua non of an informative and legally adequate EIR." (*County of Inyo v. City of Los Angeles* (1977) 71 Cal.App.3d 185, 192; *Berkeley Jets*, 91 Cal. App. 4th 1344, 1354; *Sacramento Old City Assn. v. City Council* (1991) 229 Cal. App. 3d 1011, 1023; *Stanislaus Natural Heritage Project v. County of Stanislaus* (1996) 48 Cal. App. 4th 182, 201) "[A] curtailed or distorted project description," on the other hand, "may stultify the objectives of the reporting process. Only through an accurate view of the project may affected outsiders and public decision-makers balance the proposal's benefit against its environmental costs, consider mitigation measures, assess the advantage of terminating the proposal (i.e., the "no project" alternative) and weigh other alternatives in the balance." (*Id.;* see also, 14 CCR § 15124) As one analyst has noted:

> The adequacy of an EIR's project description is closely linked to the adequacy of the EIR's analysis of the project's environmental effects. If the description is inadequate because it fails to discuss the complete project, the environmental analysis will probably reflect the same mistake. (Kostka and Zischke, "Practice Under the California Environmental Quality Act," p. 474 (8/99 update); *see also Santiago County Water Dist. v. County of Orange* (1981) 188 Cal. App. 3d 818, 829)

A "rigorous analysis" is required to dispose of an impact as insignificant. (*Kings County Farm Bureau v. City of Hanford* (1990) 221 Cal.App.3d 692) Such a rigorous analysis is not possible is not possible if the project description is inaccurate, inconsistent, or misleading.

The Project description in the FEIR fails to comply with CEQA' s requirements because (1) the FEIR fails to describe the Project and its impacts in light of the newly proposed General Plan Amendments identified for the first time in the RDEIR2; and (2) the Project, as described, would violate its own proposed mitigation measures for impacts to biological resources, rendering either the Project description, or its mitigation measures, inaccurate and facially inconsistent with each other.

1. **The Proposed General Plan Amendment to Relieve the Project from the General Plan's 500-Foot Surface Water Setback Requirement Was Not Included in the Project Description, and Its Impacts Have Not Been Analyzed.**

The RDEIR2 proposed a General Plan Amendment to relieve the Project from the General Plan 500-foot setback requirement contained in Land Use Element Section 15.070(B)(1)(d), discussed in Section IV.A above, by amending the Conservation/Open Space Element to authorize development of geothermal facilities within 500 feet of a watercourse within the Hot Creek Buffer Zone, as follows:

> **Conservation and Open Space Element**
> **Energy Resources, Objective D, Policy 1**
> Action 1.13: ~~No geothermal development located within the Hot Creek Buffer Zone shall occur~~ Adoption of land development regulations for geothermal development within 500 feet on either side of a surface watercourse (as indicated by a solid or broken blue line on U.S. Geological Survey 7.5- or 15-minute series topographic maps) within the Hot Creek Buffer Zone (See Mono County Land Development Regulations, Chapter 15, section 15.070(B)(1)(d).)

(RDEIR2 at p. 34)

The amendment was included for the first time in the RDEIR2, in subsection 4.10 of the document, and was not included in the Project description in either the RDEIR2 or the FEIR's updated Project Location or Project Summary. (RDEIR2 at pp. 33-34; FEIR at pp. 1-4) The FEIR fails to adequately respond to this issue, raised in prior Comment Letter 12. Including a significant land use change in a subsection of the RDEIR2, and not amending the overall Project Description to both describe the Project revision and evaluate its environmental impacts, fails to satisfy CEQA's requirement to describe all aspects of the Project which may result in potentially significant environmental impacts. (14 CCR § 15124) As a result of the surface water setback reduction, the Project may result in significant surface water impacts within the Hot Creek Buffer Zone that have not been properly disclosed or analyzed in the EIR. (*See County of Inyo v. City of Los Angeles* (1981) 124 Cal. App. 3d 1, 7 (revised EIR that fails to describe or analyze surface water impacts is legally insufficient as a CEQA document))

2. **The Project Description Is Inaccurate Because It is Facially Inconsistent With Bio Protection Measure 7.**

The Project, as described in the FEIR, will install approximately 2000 feet of linear barriers in the area between the existing MP-I plant site and the replacement M-1 plant site. Specifically, the project will construct 500 feet of interconnection injection fluid pipeline and about 1,500 feet of interconnection transmission line. (FEIR, p. 4-65)

This component of the Project is directly inconsistent with Bio Protection Measure 7, which calls for no additional linear barriers to be constructed:

> "The Project shall not erect any linear barriers to movement of deer or other wildlife in the area between the existing MP-I plant site and the replacement M-1 plant site. During M-1 plant site construction, no temporary fencing or pipeline racks shall be erected in this same area during the normal periods of mule deer migration, from April 1st to May 30th or from September 15th through November 15th." (FEIR, p.4-73)

As discussed by expert Macauley, "the pipelines that would be constructed appear to be permanent, and would violate this mitigation measure. While the Applicant notes that wildlife could move both over and beneath the interconnection pipeline and transmission line conduit, it is nonetheless an additional linear barrier that clearly violates the Applicant's own proposed mitigation measures." (Exh. A at p. 8)

CEQA requires that an EIR's project description must provide "enough information to ascertain the project's environmentally significant effects, assess ways of mitigating them, and consider project alternatives." (Sierra Club v. County of Orange (2008) 163 Cal. App. 4th 523) The Mammoth Project description does exactly the opposite here. The inconsistency between the Project's described transmission lines and its required Bio Measure 7 create a presumption of a per se significant impact that was not properly disclosed or analyzed in the EIR.

The Project description must be amended, and the FEIR revised and recirculated, to correct these deficiencies.

C. THE FEIR'S CUMULATIVE IMPACTS ANALYSIS IS INADEQUATE.

The Mammoth Project is one of several existing and planned geothermal projects within the Casa Grande geothermal complex and the Great Basin Valleys Air Basin, which air basin encompasses Mono, Inyo and Alpine counties. (RDEIR at p. 4-37, 4-378) The RDEIR fails to include an adequate analysis of the Project's cumulative impacts on hydrology, seismicity, and biological resources, among other issues, as together with the existing MP-I, MP-II, PLES-I, and Basalt Canyon Pipeline facilities, and, in particular, the proposed 33 MW Casa Diablo IV Project, including its proposed wellfield expansion of up to 14 additional wells. (See Exhibit B, Casa Grande IC BLM Project webpage)

An EIR must discuss significant cumulative impacts. (CEQA Guidelines § 15130(a)) This requirement flows from CEQA section 21083, which requires a finding that a project may have a significant effect on the environment if "the possible effects of a project are individually limited but cumulatively considerable. . . . 'Cumulatively considerable' means that the incremental effects of an individual project are considerable when viewed in connection with the effects of past projects, the effects of other current projects, and the effects of probable future projects." (*See also* 14 Cal. Code Regs. § 15130(a))"Cumulative impacts" are defined as "two or more individual effects which, when considered together, are considerable or which compound or increase other environmental impacts." (*Id.* § 15355(a)) "[I]ndividual effects may be changes resulting from a single project or a number of separate projects." (*Id.*) Incremental contributions must be assessed "when viewed in connection with the effects of past projects, the

effects of other current projects, and the effects of probably foreseeable projects." (14 Cal. Code Regs. § 15065(a)(3))

"The cumulative impact from several projects is the change in the environment which results from the incremental impact of the project when added to other closely related past, present, and reasonably foreseeable probable future projects. Cumulative impacts can result from individually minor but collectively significant projects taking place over a period of time." (*Communities for a Better Environment v. Cal. Resources Agency ("CBE v. CRA")*, (2002) 103 Cal.App.4th 98, 117) A legally adequate cumulative impacts analysis views a particular project over time and in conjunction with other related past, present, and reasonably foreseeable probable future projects whose impacts might compound or interrelate with those of the project at hand. "Cumulative impacts can result from individually minor but collectively significant projects taking place over a period of time." (CEQA Guidelines § 15355(b))

As the court recently stated in *CBE v. CRA,* 103 Cal. App. 4th at 114:

> Cumulative impact analysis is necessary because the full environmental impact of a proposed project cannot be gauged in a vacuum. One of the most important environmental lessons that has been learned is that environmental damage often occurs incrementally from a variety of small sources. **These sources appear insignificant when considered individually, but assume threatening dimensions when considered collectively with other sources with which they interact.**

(Citations omitted)

In particular, the FEIR fails to adequately analyze cumulative impacts resulting from planned construction of the Casa Diablo IV geothermal power plant and facilities, wells, and pipelines, currently undergoing joint NEPA and CEQA review by the U.S Bureau of Land Management ("BLM") and the Great Basin Air Pollution and Control District ("GBAPCD"). The Casa Diablo IV Project, proposed by Mammoth Project Applicant MPLP, is to be located in the immediate vicinity of the existing MPLP geothermal projects, near the intersection of California State Route 203 and U.S. Highway 395, approximately 3 miles east of Mammoth Lakes, California, and may construct up to 14 additional geothermal wells. (Exhibit B; RDEIR p. S-17)

1. **Hydrology.**

The FEIR fails to adequately analyze cumulative impacts on the geothermal aquifer and nearby surface waterways, and the FEIR failed to adequately respond to comments on this issue.

Commenter 9C on the RDEIR stated:

> The RDEIR fails to adequately evaluate cumulative impacts that could result from the operation of the plant in conjunction with other future projects. Because cumulative impacts were not properly evaluated, they are unmitigated.

> The proposed CD-4 facility includes the drilling of up to 14 new production wells over the life of the plant (RDEIR, p. S-17). The RDEIR includes a map (Fig. 40) that shows a total of three existing production wells. Therefore, addition of CD-4 to the Casa Diablo geothermal complex will increase, by more than four times, the number of production wells in the wellfield. With the addition of the 33 MW CD-4 facility, the expansion of the well field is matched by an equally substantial increase in power generation at the Casa Diablo geothermal complex. Section S, Cumulative Effects, provides no analysis of the combined effects of MP-I, MP-II, and PLES-1 and CD-4 on the geothermal aquifer and the discharge to Hot Creek Headsprings. No analysis is provided to determine if the operation of the wells for M-1 along with the operation of the 16 proposed CD-4 wells will potentially deplete the thermal qualities of the geothermal aquifer and alter the discharge from the Hot Creek Headsprings.

(Comment Letter 9C at pp. 1-2) The FEIR fails to properly respond to these comments, and fail to provide for recirculation of the FEIR to analyze all significant impacts and to identify and impose feasible mitigation measures to reduce the Project's impacts.

2. Seismic Activity.

Enhanced geothermal systems can trigger earthquakes as part of hydraulic fracturing, as demonstrated by recent analysis of similar geothermal projects in Imperial County. (See Exhibit C, 9/11/2012 Hudson Geothermal Imperial County comments of SWAPE at pp. 5-6)

As described in the Hudson comment:

> Induced seismicity has been documented in association with number of operating geothermal fields in the United States and globally. The Geysers and the Coso geothermal fields in California have a well-known association of geothermal production and induced seismicity, producing thousands of earthquakes annually. Most are small and are not perceived by humans, but some earthquakes of up to magnitude 4 have been documented. (http://esd.lbl.gov/research/projects/induced_seismicity/egs/history.html). Communities near geothermal fields have expressed concerned about damage from single seismic events and cumulative effects. Concerns include the potential for structural damage and that small events may trigger larger events. (http://esd.lbl.gov/research/projects/induced_seismicity/egs/local_outreach.html) (Id. at p. 5)

The FEIR fails entirely to analyze the cumulative impacts of current Project-generated seismic activity, combined with that of the proposed Casa Grande IV facility on nearby communities and existing structures. This inadequacy must be addressed in a revised and recirculated EIR.

3. Biological Resources.

As discussed in Comment Letter 9C at pp. 1-2, and by wildlife expert Mr. Macauley, the FEIR fails to adequately analyze cumulative impacts on fisheries dependent on Hot Creek, as well as cumulative impacts on mule deer.

Mr. Macauley states:

> The Applicant characterizes the 5.7 acres of habitat destruction as insignificant due to the relatively small area of development in comparison to expansive public lands in the area which can meet the needs of deer in the area. However, this type of small incremental development that the Applicant describes as "a tiny fraction...of available mule deer habitat in the area," is exactly the kind of development that CEQA seeks to regulate in sections addressing cumulative impacts. The Applicant fails to meet the standard to declare insignificant cumulative impacts, especially given the conservation status of the deer in this area.
>
> The Round Valley deer population has seen "dramatic declines over the last 10 – 20 years"[2] and it is likely that any additional habitat loss, no matter how small, will contribute to cumulative impacts. The Casa Diablo herd is likely to be sensitive to any habitat loss on winter range "because deer are frequently in poor condition at the end of summer before moving onto winter range in the fall; this means that quality winter forage is critical for sustaining population numbers."[3]
>
> Additionally, the CDFG biologist on the project noted that:
>
> "The loss of *deer holding area* and migration corridor acreage is a concern not only for the G-1 Plant replacement site but for the cumulative impacts to deer from the proposed CD-4 Plant and other existing and proposed projects on Round Valley deer herd range."(emphasis added)[4]
>
> Habitat loss is widely considered the primary threat to wildlife across the country.[5] Studies on the Round Valley and Casa Diablo deer populations have also found development to be a primary threat, with recommendations of previous studies explicitly calling for keeping road and building infrastructure to a bare minimum

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[2] Ferranto SP. 2006. Conservation of mule deer in the eastern Sierra Nevada. M.S. Thesis, University of Nevada, Reno, p. 50.

[3] Ferranto SP. 2006. Conservation of mule deer in the eastern Sierra Nevada. M.S. Thesis, University of Nevada, Reno, p. 46.

[4] RDEIR Appendix C, G-1 Plant Replacement Site Visit – Summary, Mammoth Lakes, CA, March 22, 2011.

[5] Wilcove, David S., David Rothstein, Jason Dubow, Ali Phillips and Elizabeth Losos. 1998. Quantifying Threats to Imperiled species in the United States. *BioScience*. 48(8), pp. 607-615.

and avoiding locations with healthy stands of Antelope Bitterbrush as building sites.[6]

Given that development is considered a contributor to the declines in the Round Valley deer population, and given the sensitivity of the Casa Diablo herd to loss of winter habitat, any additional loss of habitat likely would result in further negative incremental impacts to deer herds.

A review of CEQA regulations clarifies that this type of negative impact is exactly what would qualify as cumulatively significant impacts.

"Cumulative impacts" refers to two or more individual effects which, when considered together, are considerable or which *compound or increase other environmental impacts*.... The cumulative impact from several projects is the change in the environment which results from the *incremental impact* of the project when added to other closely related past, present, and reasonably foreseeable probable future projects. Cumulative impacts can result from *individually minor but collectively significant* projects taking place over a period of time. (emphasis added)[7]

CEQA requires discussion of cumulative impacts in either of the following ways, which the Applicant has not performed sufficiently:

(A) A list of past, present, and probable future projects producing related or cumulative impacts, including, if necessary, those projects outside the control of the agency, or

(B) A summary of projections contained in an adopted general plan or related planning document, or in a prior environmental document which has been adopted or certified, which described or evaluated regional or areawide conditions contributing to the cumulative impact. Any such planning document shall be referenced and made available to the public at a location specified by the lead agency.[8]

While the Applicant has provided a brief assessment of current and probable future projects in relation to the current project in their response to comment, they have not discussed how past impacts may have resulted in declines of the Casa Diablo and Round Valley deer herds. While the Applicant correctly notes that CEQA directs that an EIR should not discuss impacts which do not result in part from the project evaluated in the EIR, this is not the case here. This project

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[6] Ferranto SP. 2006. Conservation of mule deer in the eastern Sierra Nevada. M.S. Thesis, University of Nevada, Reno, p 61.

[7] CEQA Section 15355.

[8] CEQA Section 15130.

will cause additional loss of deer habitat, which will contribute to the larger cumulative impacts on these deer herds.

While Cumulative Bio Measure 1 is designed to address cumulative impacts to biological resources, it is lacking in any mitigation for habitat loss due to the construction of the M-1 power plant, and as a result does not reduce the impacts to less than significant.

Mitigation can consist of avoidance or replacement of lost habitat. In this case, appropriate mitigation such as the restoration of 3.7 acres of habitat would qualify as mitigation. As the Applicant has noted the infeasibility of locating the new plant on the old plant site, an ideal site for such restoration would be on the site of the decommissioned power plant after demolition. Under the current plan, the old plant site will be converted to a *fenced* storage yard and as occasional overflow parking.[9] It is unclear whether additional fenced storage yards and overflow parking are essential for the goals of the project, and as such, restoring this area to usable habitat for deer, would do much to mitigate the impacts of habitat removal to less than significant.

While the Applicant determined that "the main use of the existing MP-I Project area by deer is as a movement corridor," this does not negate the fact that important browse, cover, and habitat for deer will be significantly impacted by the construction of the M-1 power plant.

(See Exhibit A at pp. 3-5)

4. Air Quality.

The RDEIR failed to address cumulative air quality impacts of the Project, and the FEIR failed to adequately respond to comments on this issue, or to prepare an update analysis.

In particular, the FEIR fails to consider the Project's air quality impacts in combination with the MP-I, MP-II, PLES-I, Casa Diablo geothermal complex production pipeline networks and geothermal and reinjection well fields, the Basalt Canyon Pipeline, the proposed Casa Diablo IV facility, and the Casa Diablo IV well field expansion project. The RDEIR fails to consider the combined air quality impacts of these existing facilities and projects. In particular, the cumulative impact analysis fails to consider ROG emissions from the MP-I facility, the Casa Diablo geothermal complex production pipeline networks and geothermal and reinjection well fields, and the Basalt Canyon Pipeline. This analytical deficiency renders the analysis invalid for the purpose of CEQA. The County must prepare a revised DEIR which considers the Project's air quality impacts together with past, present, and reasonably foreseeable projects.

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[9] FEIR, p. 1-1.

(see Comment Letter 9D, RDEIR at pp. 5-10) This inadequacy must be addressed in a revised and recirculated EIR.

D. THE FEIR FAILS TO ANALYZE AND MITIGATED ALL POTENTIALLY SIGNIFICANT IMPACTS OF THE PROJECT.

CEQA requires that an agency analyze the potential environmental impacts of its proposed actions in an environmental impact report ("EIR") (except in certain limited circumstances). (*See, e.g.*, Pub. Res. Code § 21100.) The EIR is the very heart of CEQA. (*Dunn-Edwards v. BAAQMD* (1992) 9 Cal.App.4th 644, 652.) "The 'foremost principle' in interpreting CEQA is that the Legislature intended the act to be read so as to afford the fullest possible protection to the environment within the reasonable scope of the statutory language." (*Communities for a Better Environment v. Calif. Resources Agency* (2002) 103 Cal. App. 4th 98, 109.)

CEQA requires public agencies to avoid or reduce environmental damage when "feasible" by requiring "environmentally superior" alternatives and all feasible mitigation measures. (CEQA Guidelines § 15002(a)(2) and (3); See also, *Berkeley Jets*, 91 Cal. App. 4th 1344, 1354; *Citizens of Goleta Valley v. Board of Supervisors* (1990) 52 Cal.3d 553, 564) The EIR serves to provide agencies and the public with information about the environmental impacts of a proposed project and to "identify ways that environmental damage can be avoided or significantly reduced." (Guidelines §15002(a)(2)) If the project will have a significant effect on the environment, the agency may approve the project only if it finds that it has "eliminated or substantially lessened all significant effects on the environment where feasible" and that any unavoidable significant effects on the environment are "acceptable due to overriding concerns." (Pub.Res.Code § 21081; 14 Cal.Code Regs. § 15092(b)(2)(A) & (B))

A prejudicial abuse of discretion occurs "if the failure to include relevant information precludes informed decisionmaking and informed public participation, thereby thwarting the statutory goals of the EIR process." (*San Joaquin Raptor/Wildlife Rescue Center v. County of Stanislaus* (1994) 27 Cal. App. 4th 713, 722]; *Galante Vineyards v. Monterey Peninsula Water Management Dist.* (1997) 60 Cal. App. 4th 1109, 1117; *County of Amador v. El Dorado County Water Agency* (1999) 76 Cal. App. 4th 931, 946)

The comments provided below are supplemental to and in accord with those provided by Mr. Macauley, LIUNA's expert consultant, which comments are attached hereto as Exhibit A.

1. The FEIR Fails to Adequately Analyze Impacts to Biological Resources.

It is the policy of the State of California to

Prevent the elimination of fish or wildlife species due to man's activities, insure that fish and wildlife populations do not drop below self-perpetuating levels, and preserve for future generations representations of all plant and animal communities.

(Pub. Res. Code § 21001(c).) An EIR may not avoid studying impacts to biological resources by proposing future study or mitigation based on future studies unless the mitigation measures and performance standards are explicit in the DEIR. (*San Joaquin Raptor Rescue Center v. County of Merced* (2007) 149 Cal.App.4th 645, 671)

As discussed below, the FEIR fails to assess impacts to wildlife, especially sensitive species and plants. Where impacts are identified, the FEIR impermissibly relies on vague, unenforceable and deferred mitigation measures, most of which lack a foundation in science and performance standards. Consequently, the FEIR must be revised to reassess impacts to biological resources and, where appropriate, propose adequate mitigation measures with definite terms and verifiable performance standards.

Deferral of mitigation measures is prohibited under CEQA:

> By adopting the condition that applicant would comply with environmental standards for sludge disposal, the County effectively removed this aspect of the project from environmental review, trusting that the Regional Water Quality Control Board and the applicant would work out some solution in the future..... Having no "relevant data" pointing to a solution of the sludge disposal problem, the County evaded its duty to engage in a comprehensive environmental review by approving the use permit subject to a condition requiring future regulatory compliance. *Sundstrom*, 202 Cal.App.3d at 309.
> [R]eliance on tentative plans for future mitigation after completion of the CEQA process significantly undermines CEQA's goals of full disclosure and informed decisionmaking; and[,] consequently, these mitigation plans have been overturned on judicial review as constituting improper deferral of environmental assessment. *Communities for a Better Environment v. City of Richmond* (2010) 184 Cal.App.4th at 92.

Similarly, an agency cannot fail to analyze potentially significant impacts, then rely on that failure to conclude that a Project has no significant impacts. An agency may not assert that there is no evidence of a significant environment impact because the agency failed to undertake an adequate environmental analysis. *(Sundstrom v. County of Mendocino* (1988) 202 Cal.App.3d 296, 311 ("The agency should not be allowed to hide behind its own failure to gather relevant data.").

a. The Project Will Result In Significant Impacts to Deer Habitat That the FEIR Fails to Properly Analyze or Mitigate.

Mr. Macauley has reviewed the FEIR and all proposed biological resources mitigations, and concludes that the FEIR's proposed mitigations are insufficient to protect sensitive Round Valley and Casa Diablo deer herds.

Mr. Macauley states:

> The location of the proposed M-1 plant site is within the general spring and fall migration path identified for members of the Round Valley and Casa Diablo deer

herds. It is also within the expansive area that may be used by winter residents of these herds. The project footprint will result in the grading of 5.7 acres of land, which contains 3.5 acres that is dominated by Antelope bitterbrush, an important browse species for mule deer.[10] Furthermore, the site is described as consisting of 1.6 acres of Jeffery Pine, 1.9 acres of Big Sagebrush Scrub, and .2 acres of Wright Buckwheat Dwarf Scrub communities on the 5.7 acre site.[11] These plant communities provide important cover and forage resources for deer.

In response to comments, the Applicant describes the habitat on the building site as degraded or absent. While *Bromus tectorum* is present on the site and is even a dominant herbaceous species in certain places, this does not make the site unsuitable for deer, especially since deer in this area feed largely on browse and not grass.[12] On the contrary, the Applicant has already described quality habitat and forage that exists on the majority of the project site:

> "Characteristics of the vegetation at and nearby the M-1 Project *meet known habitat requirements for deer* that enter the area to hold or forage as residents, or who pass through the area during normal migration. *About 3.5 acres of vegetation where bitterbrush, an important browse species, is a canopy dominant would be affected by construction of the M-1 power plant.*" (emphasis added).[13]

Indeed, this is in agreement with other research on the diet of these deer herds in the winter months, which is characterized by "> 93% shrubs, with antelope bitterbrush, sagebrush, blackbrush (*Coleogyne ramosissima*), and Gregg's ceanothus (*Ceanothus Gregii*) as the dominant shrub species. Bitterbrush is most frequent in the diet during the first few months and again in April (coinciding with spring growth). Sagebrush is most common [forage species] during mid-winter months."[14]

The Applicant has failed to recognize the significance of the habitat loss that will result from building the M-1 power plant, and mitigation should be required for this loss, especially for the habitat communities that are not mechanically or thermally disturbed. According to the Applicant's estimation, this would equal 3.7 acres.[15]

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[10] FEIR, p. 4-66.

[11] FEIR, Table 21. p. 4-64.

[12] Ferranto SP. 2006. Conservation of mule deer in the eastern Sierra Nevada. M.S. Thesis, University of Nevada, Reno, p. 50.

[13] FEIR, p. 4-66.

[14] Ferranto SP. 2006. Conservation of mule deer in the eastern Sierra Nevada. M.S. Thesis, University of Nevada, Reno, p. 50.

[15] FEIR, Table 21, p. 4-64.

(See Exhibit A at pp. 2-3)

b. The Project's Construction Schedule Will Interfere with Spring and Fall Migration of Mule Deer.

Mr. Macailey concludes that the Project's proposed Bio Mitigation measures fail to adequately address potentially significant impacts to deer migration during spring and fall. He states:

> The construction schedule overlaps with spring migration of deer, and will likely have an impact on deer during this time where deer are recovering from condition lost from winter conditions. Summary notes from a site visit with Department of Fish & Game biologist Tim Taylor note that deer migrate through the proposed project site from late April through the third week of May, depending on weather conditions.[16] Additional research on the deer in this area also found that migration began in late April and continued into May, while the fall migration occurs from September through November. [17]
>
> The spring and fall migration period overlaps with the peak periods of construction, which shows that 60 workers will be on site in May as well as September and October.[18] The peak levels of construction activity will involve on average three (3), 40–foot delivery trucks to transport material to or from the site during the construction period. In addition, four (4), 60–foot trucks per day would deliver materials to the site over an approximate 10–day period early in the construction period, which will likely have an even greater impact on pregnant does in spring migration.[19] Peak levels of construction early in this period will mean more than 7 large trucks a day may be moving to and from the site during the spring migration period. This can result in an average of 14 trips (to and from) a day in the area.

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[16] RDEIR Appendix C, G-1 Plant Replacement Site Visit – Summary, Mammoth Lakes, CA, March 22, 2011.

[17] Kucera, Thomas E. 1987. Casa Diablo Geothermal Development Project: Deer Migration Study, spring 1987.

[18] FEIR, Figure 12, p. 2-13.

[19] FEIR, Figure 12, p. 2-12.

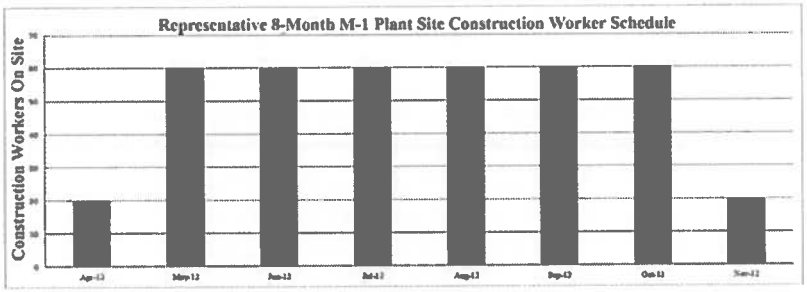

Figure 12: Representative 8-Month M-1 Plant Site Construction Worker Schedule

It is likely that construction would have significant impacts on migrating deer in the spring. While the Applicant has described the noise produced by trucks, they have not evaluated or mitigated its effect on migrating deer, particularly during the heaviest period of construction that will coincide with spring migration.

(Exhibit A at p. 7)

c. The Project as Built Violates Proposed Mitigation Measures, and Several Mitigation Measures are Insufficient to Mitigate Identified Species Impacts.

As observed by Mr. Macauley:

Bio Protection Measure 7 calls for no additional linear barriers to be constructed:

> "The Project shall not erect any linear barriers to movement of deer or other wildlife in the area between the existing MP-I plant site and the replacement M-1 plant site. During M-1 plant site construction, no temporary fencing or pipeline racks shall be erected in this same area during the normal periods of mule deer migration, from April 1st to May 30th or from September 15th through November 15th."[20]

However, the new plant construction will result in approximately 2000 feet of additional linear barriers in the area. The project will construct 500 feet of interconnection injection fluid pipeline and about 1,500 feet of interconnection transmission line.[21] While the mitigation measure calls for no construction of pipeline racks during migratory periods, the pipelines that would be constructed appear to be permanent, and would violate this mitigation measure. While the Applicant notes that wildlife could move both over and beneath the interconnection pipeline and transmission line conduit, it is nonetheless an additional linear barrier that clearly violates the Applicant's own proposed mitigation measures.

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[20] FEIR, p.4-73.

[21] FEIR, p. 4-65.

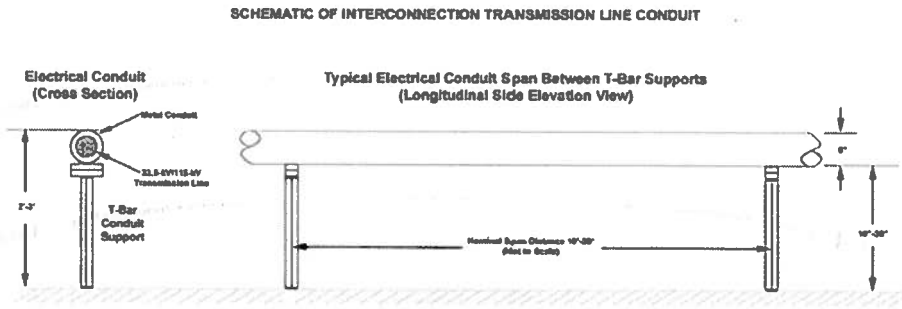

Figure 11: Schematic of Interconnection Transmission Line Conduit

Furthermore, the Applicant's conclusion that these linear facilities would not be a substantive obstacle to wildlife movement in the area is not clear. The Applicant has acknowledged that resident deer are more likely to adapt to changes in the surroundings than migratory deer.[22] As such, the assertion that an additional pipeline would not be viewed as substantive obstacles become less clear when it comes to migratory deer, which will not have opportunities to adapt to these changes.

While it is likely that deer can cross this pipeline, it adds further disturbance to migratory paths that are unlikely to be mitigated by the single crossing that has been proposed to mitigate for these impacts (additional problems with this mitigation measure will be addressed more fully below). With the addition of transmission lines, the remaining corridor passageway that is uninhibited by a pipeline will be reduced to approximately 100 feet if the proposed project is constructed.[23]

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[22] Applicant's Response to Comment 9A-12.

[23] FEIR, Figure 10, p. 2-11.

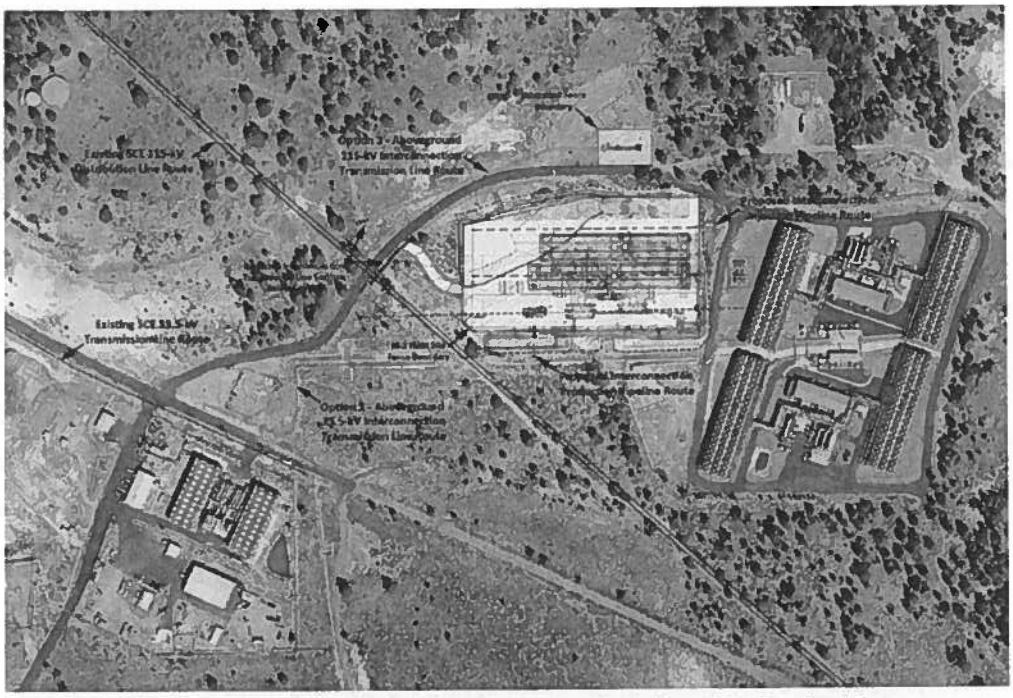

Figure 10: Interconnection Transmission Line Options, Interconnection Pipelines and New Fence Boundaries

In order to properly mitigate for the reduction of the migratory corridor, the Applicant should bury all lines to reduce potentially significant impacts to deer movement. This seems especially warranted given that general Mono County regulations require that all new utilities shall be installed underground,[24] and that the project is seeking a variance from this regulation.

The Applicant says that these transmission lines would "necessarily be located aboveground",[25] but do not provide any justification for why this is the case, when CD-4 project lines would be placed underground.

<u>Bio Protection Measure 8 Will Not Mitigate the Reduction in Movement Corridor for Migratory Deer</u>

The Applicant has proposed mitigation to reduce significant impacts to connectivity for wildlife and mule deer in Bio Protection Measure 8. However, this mitigation measure, which calls for an earthen ramp to be constructed over a pipeline, is unproven and, without further empirical support, the Applicant cannot

[24] FEIR, p. 4-5.

[25] FEIR, p. 5-8.

support the claim that it will reduce significant impacts to migratory deer to less than significant.

The Applicant acknowledges that resident deer are more likely to adapt to changes due to Project construction than migratory deer.[26] However, the Applicant's proposed mitigation for impacts to movement by deer – including movements by migratory deer – involves building a new earthen ramp over the pipeline. While this ramp is intended to serve as connectivity at least in part for migrating deer, the Applicant fails to recognize the inherent difficulty that migrating deer may have in encountering this new feature on the landscape. It is questionable that deer in the midst of migration, having never encountered this feature, will use this crossing. As such, without further empirical evidence, this mitigation measure cannot be expected to alleviate the significant impacts that will result in reduced movement connectivity for migratory mule deer.

While the Applicant has attempted to provide empirical support, the data is not provided or cited. The Applicant refers to 2011 deer studies which found that constructed crossings of this type in the Basalt Canyon area are regularly used by deer during both the residency and migratory periods. But because the data for these studies is not cited, the results are not verifiable.[27] Furthermore, close reading of the statement also suggests that while deer may be using this ramp *during both residency and migratory periods*, the vagueness of wording could mean that *only resident deer* are using the ramps *during migratory periods*. It is not clear that *any* migratory deer are using these ramps during migratory periods. If only resident deer are using these ramps, then the proposed mitigation of creating this ramp serves only to help connectivity of resident deer, and does not address significant impacts to migratory deer.

Recent and available peer-reviewed research on overpasses for connectivity has focused on road mortalities and use of overpasses, and meta-analyses have found a lack of before and after data as making "the efficacy of these techniques nearly impossible to evaluate."[28] Given the questionable efficacy of connectivity overpasses in peer-reviewed meta-analyses, the Applicant needs to provide empirical data to support the finding that an earthen ramp will mitigate for significant movement corridor impacts that the project will cause.

Description of Bio Protection Measure 8 Is Unclear

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[26] Applicant's Response to Comment 9A-12

[27] Applicant's Response to Comment 9A-13

[28] Glista, David J., Travis L. DeVault, J. Andrew DeWoody. 2009. A review of mitigation measures for reducing wildlife mortality on roadways. *Landscape and urban planning.* 91(1) p. 1-7.

While the efficacy of Bio Protection Measure 8 is doubtful, the description of the mitigation measure is vague, inaccurate, and internally inconsistent. First, the characteristics of the earthen ramp that is proposed for mitigation are not sufficiently described. While the Applicant describes the ramp it to be 30 feet wide, they do not provide any information on the slope of the ramp. Second, the Applicant describes the earthen ramp to be "tree-screened", however, there are only trees on the northern end of the proposed area for the ramp construction, and the lack of tree cover on the southern portion of the ramp will likely diminish its use. Third, the existing road on the northern portion of the proposed ramp would likely be blocked by such a ramp, and the Applicant does not address how vehicles will pass this area with a 30 foot ramp crossing the road.

The description of this proposed ramp is internally inconsistent. The Applicant notes that the "The finished crossing shall resemble the existing crossing at the SCE easement located approximately 320 feet east of the 90 degree turn."[29] However, the Applicant has described the SCE crossing as an area where the pipeline racks are *buried underground* for 50 feet.[30] In terms of mitigation for deer connectivity, burying the pipeline for a distance of 50 feet—as the pipeline is buried at the SCE easement—would certainly be superior to the creation of an earthen ramp. In fact, as suggested earlier, appropriate mitigation that would reduce connectivity impacts to less than significant would require burying all the transmission lines so as to compensate for the area that will be blocked by the construction of the M-1 power plant.

Part of Cumulative Bio Mitigation Measure 1 does not constitute mitigation for this project's impacts

Cumulative Bio Mitigation Measure 1 calls for three main actions to mitigate for cumulative impacts. The first of these calls for new projects to conduct baseline deer studies of proposed projects and monitoring deer use within and near new proposed projects.[31]

Calling for baseline deer studies without any clear and concrete performance actions does not constitute mitigation. CEQA describes five types of mitigation:

> (a) Avoiding the impact altogether by not taking a certain action or parts of an action.
> (b) Minimizing impacts by limiting the degree or magnitude of the action and its implementation.
> (c) Rectifying the impact by repairing, rehabilitating, or restoring the impacted environment.

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[29] FEIR, p. 4-73.

[30] RDEIR Appendix D, p. 25.

[31] FEIR, p. 5-12.

(d) Reducing or eliminating the impact over time by preservation and maintenance operations during the life of the action.
(e) Compensating for the impact by replacing or providing substitute resources or environments.[32]

Conducting surveys do not qualify as any of these types.

Surveys are a critically important tool for evaluating and determining mitigation measures to be taken, and this use of surveys is clearly useful. However, action items surrounding the findings of this survey data that is consistent with the definition of mitigation under CEQA is necessary. While these action items would certainly need to be site specific, and some flexibility is necessary in designing them, basic requirements or standards and resulting action items need to be described for this measure to constitute mitigation and reduce significant cumulative impacts. Some standards for action could involve standards in percentage reduction in deer use. For example, if surveys reveal that deer use of the area has ceased in connection with construction, mitigation should call for the reduction of construction activity until surveys show improvement in deer use.

Mitigation requires that some action be taken to minimize or compensate. Simply calling for studies without remedial actions does not constitute mitigation.

Bio Protection Measure 9 is Vague

Bio Protection Measure 9 calls for the designation of a movement corridor on the northeastern side of the existing Casa Diablo geothermal complex shall be maintained free from further development and mechanical disturbance.[33] The area would be designated for long-term preservation in the Reclamation Plan prepared for the County for the Casa Diablo geothermal development.

While the preservation of habitat is crucial for biological resource protection, maintaining already existing habitat and already existing corridor does qualify as mitigation in terms of preservation, however, it does not fully compensate for the loss that is occurring. This corridor to the north of the complex is currently preserved, and any development on it would have to undergo its own mitigation. It is unclear whether preserving this area alone would sufficiently mitigate for impacts caused.

Furthermore, the Applicant does not define "long-term" and does not make it clear that the land will be preserved from other development besides geothermal development.

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[32] CEQA Section 15370.

[33] FEIR, p. 4-74.

> One example of replacement and compensation that would serve to make the impacts of construction less than significant could include the restoration of degraded habitat in the area. An ideal place for such replacement of habitat and improve connectivity would be to restore the decommissioned plant site to habitat that would be usable by deer and wildlife. The use of the old site as a fenced storage yard and overflow parking lot – unusable and inaccessible to wildlife and deer – appears to be a relatively unnecessary use of this area when significant impacts are caused due to additional construction.
>
> (See Exhibit A at pp. 7-13)

The County has repeatedly failed to address these significant impacts to biological resources, despite multiple opportunities to do so, and despite substantial evidence in the form of expert comments throughout the EIR stages that have identified these impacts. The County must not be permitted to rely upon inadequate mitigation measures in light of substantial evidence that the Project will have significant, unmitigated impacts on species. The FEIR must be revised and recirculated to address these impacts.

2. The FEIR Fails to Properly Analyze the Project's Air Quality Impacts from Project Construction and Operations.

Project construction will have significant air quality impacts from excess emissions of nitrogen oxides produced during combustion ("NOx") that the County has failed to properly analyze and mitigate due to reliance on inappropriately high significant thresholds borrowed from Imperial County. (See RDEIR Comment Letter 9D). The FEIR fails to provide any analysis of toxic diesel particulate matter emissions ("DPM").

The FEIR must be revised and recirculated to fully and adequately disclose the potentially significant impacts to regional air quality and health impacts on local residents and construction workers from the Project's NOx and DPM emissions. (*See Communities for a Better Environment v. South Coast Air Quality Management Dist.* (2010) 48 Cal. 4th 310, 317 (refinery CEQA document inadequate for failure to analyze nitrogen oxide emissions, known to have significant effects on human health); *Berkeley Keep Jets Over the Bay Com. v. Bd. of Port Comrs.* (2001) 91 Cal.App.4th 1344, 1369 (EIR must include a "human health risk assessment" to address impacts from exposure to toxic air contaminants); *see also Bakersfield Citizens for Local Control v. City of Bakersfield* (2004) 124 Cal.App.4th 1184, at 1219-20 ("the health consequences that necessarily result from the identified adverse air quality impacts.... On remand, the health impacts resulting from the adverse air quality impacts must be identified and analyzed in the new EIR's.")) In particular, because construction NOX emissions estimates are so close to thresholds the FEIR should not be certified until these measures are incorporated for application to the entire project construction period.

Diesel exhaust contains nearly 40 toxic substances and may pose a serious public health risk for residents in the vicinity of the facility. Diesel exhaust has been linked to a range of serious health problems including an increase in respiratory disease, lung damage, cancer, and premature death. Fine diesel particles

are deposited deep in the lungs in the smallest airways and can result in increased respiratory symptoms and disease; decreased lung function, particularly in children and individuals with asthma; alterations in lung tissue and respiratory tract defense mechanisms; and premature death. Exposure to diesel exhaust increases the risk of lung cancer. It also causes non-cancer effects including chronic bronchitis, inflammation of lung tissue, thickening of the alveolar walls, immunological allergic reactions, and airway constriction. As early as 1988, the National Institute for Occupational Safety and Health identified diesel exhaust as a potential occupational carcinogen. In 1998, the California Air Resources Board ("CARB") formally identified the particulate fraction of diesel exhaust as a toxic air contaminant and concluded that exposure to diesel exhaust particulate matter causes cancer and acute respiratory effects. The U.S. EPA followed suit in 2002 and concluded that "long-term (i.e., chronic) inhalation exposure is likely to pose lung cancer hazard to humans, as well as damage the lung in other ways depending on exposure. Short term (i.e., acute) exposures can cause irritation and inflammatory symptoms of a transient nature... The assessment also indicates that evidence for exacerbation of existing allergies and asthma symptoms is emerging."Diesel exhaust is estimated to contribute to more than 75% of the added cancer risk from air toxics in the United States.

The FEIR must be revised and recirculated to address these significant impacts, and to prepare a legally adequate Health Risk Assessment for exposure to sensitive receptors in close proximity to Project construction.

3. The FEIR Relies on a Legally Improper Baseline for Operational Emissions.

Every CEQA document must start from a "baseline" assumption. The CEQA "baseline" is the set of environmental conditions against which to compare a project's anticipated impacts. *Communities for a Better Environment v. So Coast Air Qual. Mgmnt. Dist.* (2010) 48 Cal. 4th 310, 321. Section 15125(a) of the CEQA Guidelines (14 C.C.R., § 15125(a)) states in pertinent part that a lead agency's environmental review under CEQA:

> "...must include a description of the physical environmental conditions in the vicinity of the project, as they exist at the time [environmental analysis] is commenced, from both a local and regional perspective. This environmental setting will normally constitute the baseline physical conditions by which a Lead Agency determines whether an impact is significant."

(See, *Save Our Peninsula Committee v. County of Monterey* (2001) 87 Cal.App.4th 99, 124-125 ("*Save Our Peninsula*.") As the court of appeal has explained, "the impacts of the project must be measured against the 'real conditions on the ground,'" and not against hypothetical permitted levels. (*Save Our Peninsula*,87 Cal.App.4th 99, 121-123.) As the court has explained, using such a skewed baseline "mislead(s) the public" and "draws a red herring across the path of public input." (*San Joaquin Raptor Rescue Center v. County of Merced* (2007) 149 Cal.App.4th 645, 656; *Woodward Park Homeowners v. City of Fresno* (2007) 150 Cal.App.4th 683, 708-711.)

By relying on the existing MP-I emissions as a baseline, the FEIR fails to utilize the proper baseline for its operation air emissions, given the new location of the proposed M-1 plant, and the planned simultaneous operations of both the MP-1 and M-1 plants for up to 2 years during the M-I startup period. (See RDEIR at pp. 4-36 to 4-48; Comment Letter 9-D.

This inaccurate baseline renders the FEIR legally deficient as a matter of law.

E. THE COUNTY SHOULD PREPARE AND RECIRCULATE A SUPPLEMENTAL FEIR.

Recirculation of an EIR prior to certification, as here, is addressed in CEQA § 21092.1, and CEQA Guidelines §15088.5. "When significant new information is added to an environmental impact report after notice has been given pursuant to Section 21092 ... ***but prior to certification***, the public agency shall give notice again pursuant to Section 21092, and consult again pursuant to Sections 21104 and 21153 before certifying the environmental impact report." PRC § 21092.1.

"Significant new information" includes:

> (1) A new significant environmental impact would result from the project or from a new mitigation measure proposed to be implemented.
>
> (2) A substantial increase in the severity of an environmental impact would result...
>
> (3) A feasible project alternative or mitigation measure considerably different from others previously analyzed would clearly lessen the significant environmental impacts of the project...
>
> (4) The draft EIR was so fundamentally and basically inadequate and conclusory in nature that meaningful public review and comment were precluded.
>
> 14 CCR §15088.5; *Mountain Lion Coal. v. Fish and Game Comm'n* (1989) 214 Cal.App.3d 1043.

In *Mountain Lion,* the court held that when a detailed project analysis is not prepared until the FEIR, then the document must be recirculated for public comment.

> If we were to allow the deficient analysis in the draft EID[34] to be bolstered by a document that was never circulated for public comment ... we would be subverting the important public purposes of CEQA. Only at the stage when the draft EID is circulated can the public and outside agencies have the opportunity to analyze a proposal and submit comment. No such right exists upon issuance of a final EID unless the project is substantially modified or new information becomes available. (See Cal. Code Regs., tit. 14, § 15162.) To evaluate the draft EID in conjunction with the final EID in this case would only countenance the practice of releasing a report for public consumption that hedges on important

[34] EID is essentially the same as an EIR since the Dept. of Fish and Game had a certified environmental program.

> environmental issues while deferring a more detailed analysis to the final EID that is insulated from public review.

Mountain Lion, 214 Cal.App.3d at 1052.

In *Laurel Heights Impr. Assn. v. Reg. of Univ. of Cal.* (1993) 6 Cal. 4th 1112 ("*Laurel Heights II*, the Supreme Court explained that Section 21092 favors EIR recirculation prior to certification. The Court stated:

> ***Section 21092.1 was intended to encourage meaningful public comment.*** (See State Bar Rep., supra, at p. 28.) Therefore, new information that demonstrates that an EIR commented upon by the public was so fundamentally and basically inadequate or conclusory in nature that public comment was in effect meaningless triggers recirculation under section 21092.1. (See, *Mountain Lion Coalition v. Fish & Game Com., supra*, 214 Cal.App.3d 1043.)

Laurel Heights II, 6 Cal.4th at 1130 (emph. added).

Here, the FEIR has failed to properly analyze cumulative impacts of the Project in conjunction with both existing and reasonably forseeable future projects in the Casa Grande geothermal basin, has failed entirely to analyze cumulative seismic impacts the Projects, and fails to adequately analyze or mitigate impacts to biological resources.

The FEIR must be revised to address these many impacts. Unless the FEIR is revised to address these deficiencies and unless that FEIR is recirculated for further public review, the public and decision makers will be deprived of an opportunity for full input and informed decision making.

V. CONCLUSION

LIUNA Local Union No. 783 believes the Project FEIR is wholly inadequate and requires significant revision, recirculation and review. Moreover, LIUNA believes that the Project as proposed would result in too many unmitigated adverse impacts on the environment to be justified. California is in need of renewable energy. However, that energy cannot be obtained at the expense of other resources of the State. The Mammoth Project will result in significant that have not been adequately considered, creating the potential for great harm to humans and the natural environment. All of these considerations weigh against approval of the project as proposed.

Thank you for your attention to these comments. Please include this letter and all attachments hereto in the record of proceedings for this project.

Sincerely,

Richard T. Drury
Christina M. Caro
Lozeau Drury LLP
Attorneys for Laborers' International Union of North America (LIUNA), Local Union No. 783

EXHIBIT A

October 10, 2012

Ms. Christina Caro
Lozeau | Drury LLP
410 12th Street, Suite 250
Oakland, CA 94607

Subject: Comments on the Final Environmental Impact Report for the Mammoth Pacific I Replacement Project

Dear Ms. Caro:

This letter contains my comments on the Final Environmental Impact Report ("FEIR") prepared for Mammoth Pacific Limited Partnership's ("Applicant") proposed Mammoth Pacific I Replacement Project. The project involves replacing the aging Mammoth Pacific Unit I (MP–I) power plant with a new, more modern and efficient binary power plant (M–1), while maintaining the existing geothermal wellfield, pipeline system and ancillary facilities. The proposed location is on private land approximately 500 feet northeast of the existing MP I facility. Hereafter, I refer to the project at the proposed location as the "Project."

I am an environmental scientist with five years of academic and professional experience in wildlife ecology, rangeland management, and natural resource management. To date, I have served as a biological resources expert for six renewable energy projects, including a geothermal project. My experience in this regard includes preparing testimony for the California Energy Commission and assisting clients with evaluations of biological resource issues. I have five years of experience with the U.S. Department of Justice, where I worked in the Antitrust Division, the Office of Public Affairs, and the U.S. Attorney's Office, from which I have gained experience with regulatory compliance and legal proceedings. My educational background includes a B.A. in Liberal Arts from the University of Notre Dame, and an M.S. in Range Management from the University of California, Berkeley. I am currently a Ph.D. candidate in Environmental Science, Policy, and Management at the University of California, Berkeley.

The comments contained herein are based on a review of the environmental documents prepared for the Projects, a review of scientific literature pertaining to biological resources known to occur in Mono County, consultations with additional biological resource experts, and the knowledge and experience I have acquired during more than ten years of working in the field of law and natural resources management.

Citation to FEIR Documents

The Final EIR consists of the DEIR, RDEIR, and RDEIR2, as well as all comments received on the DEIR, RDEIR, and RDEIR2, the County's Responses to Comments, and all Appendices Exhibits thereto. These documents and their content constitute the FEIR on the proposed Project. Citations herein may refer to "DEIR" pages, "RDEIR pages", "RDEIR2" pages, or "FEIR" pages. All references are intended as citations to the Final EIR.

Significant Impacts to Deer Habitat

The location of the proposed M-1 plant site is within the general spring and fall migration path identified for members of the Round Valley and Casa Diablo deer herds. It is also within the expansive area that may be used by winter residents of these herds. The project footprint will result in the grading of 5.7 acres of land, which contains 3.5 acres that is dominated by Antelope bitterbrush, an important browse species for mule deer.[1] Furthermore, the site is described as consisting of 1.6 acres of Jeffery Pine, 1.9 acres of Big Sagebrush Scrub, and .2 acres of Wright Buckwheat Dwarf Scrub communities on the 5.7 acre site.[2] These plant communities provide important cover and forage resources for deer.

In response to comments, the Applicant describes the habitat on the building site as degraded or absent. While *Bromus tectorum* is present on the site and is even a dominant herbaceous species in certain places, this does not make the site unsuitable for deer, especially since deer in this area feed largely on browse and not grass.[3] On the contrary, the Applicant has already described quality habitat and forage that exists on the majority of the project site:

> "Characteristics of the vegetation at and nearby the M-1 Project *meet known habitat requirements for deer* that enter the area to hold or forage as residents, or who pass through the area during normal migration. *About 3.5 acres of vegetation where bitterbrush, an important browse species, is a canopy dominant would be affected by construction of the M-1 power plant.*" (emphasis added).[4]

Indeed, this is in agreement with other research on the diet of these deer herds in the winter months, which is characterized by "> 93% shrubs, with antelope bitterbrush, sagebrush, blackbrush (*Coleogyne ramosissima*), and Gregg's ceanothus (*Ceanothus Gregii*) as the dominant shrub species. Bitterbrush is most frequent in

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[1] FEIR, p. 4-66.
[2] FEIR, Table 21. p. 4-64.
[3] Ferranto SP. 2006. Conservation of mule deer in the eastern Sierra Nevada. M.S. Thesis, University of Nevada, Reno, p. 50.
[4] FEIR, p. 4-66.

the diet during the first few months and again in April (coinciding with spring growth). Sagebrush is most common [forage species] during mid-winter months."[5]

The Applicant has failed to recognize the significance of the habitat loss that will result from building the M-1 power plant, and mitigation should be required for this loss, especially for the habitat communities that are not mechanically or thermally disturbed. According to the Applicant's estimation, this would equal 3.7 acres.[6]

Significant Cumulative Impacts to Deer Habitat

The Applicant characterizes the 5.7 acres of habitat destruction as insignificant due to the relatively small area of development in comparison to expansive public lands in the area which can meet the needs of deer in the area. However, this type of small incremental development that the Applicant describes as "a tiny fraction...of available mule deer habitat in the area," is exactly the kind of development that CEQA seeks to regulate in sections addressing cumulative impacts. The Applicant fails to meet the standard to declare insignificant cumulative impacts, especially given the conservation status of the deer in this area.

The Round Valley deer population has seen "dramatic declines over the last 10 – 20 years"[7] and it is likely that any additional habitat loss, no matter how small, will contribute to cumulative impacts. The Casa Diablo herd is likely to be sensitive to any habitat loss on winter range "because deer are frequently in poor condition at the end of summer before moving onto winter range in the fall; this means that quality winter forage is critical for sustaining population numbers."[8]

Additionally, the CDFG biologist on the project noted that:

> "The loss of *deer holding area* and migration corridor acreage is a concern not only for the G-1 Plant replacement site but for the cumulative impacts to deer from the proposed CD-4 Plant and other existing and proposed projects on Round Valley deer herd range."(emphasis added)[9]

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[5] Ferranto SP. 2006. Conservation of mule deer in the eastern Sierra Nevada. M.S. Thesis, University of Nevada, Reno, p. 50.
[6] FEIR, Table 21, p. 4-64.
[7] Ferranto SP. 2006. Conservation of mule deer in the eastern Sierra Nevada. M.S. Thesis, University of Nevada, Reno, p. 50.
[8] Ferranto SP. 2006. Conservation of mule deer in the eastern Sierra Nevada. M.S. Thesis, University of Nevada, Reno, p. 46.
[9] RDEIR Appendix C, G-1 Plant Replacement Site Visit – Summary, Mammoth Lakes, CA, March 22, 2011.

Habitat loss is widely considered the primary threat to wildlife across the country.[10] Studies on the Round Valley and Casa Diablo deer populations have also found development to be a primary threat, with recommendations of previous studies explicitly calling for keeping road and building infrastructure to a bare minimum and avoiding locations with healthy stands of Antelope Bitterbrush as building sites.[11]

Given that development is considered a contributor to the declines in the Round Valley deer population, and given the sensitivity of the Casa Diablo herd to loss of winter habitat, any additional loss of habitat likely would result in further negative incremental impacts to deer herds.

A review of CEQA regulations clarifies that this type of negative impact is exactly what would qualify as cumulatively significant impacts.

> "Cumulative impacts" refers to two or more individual effects which, when considered together, are considerable or which *compound or increase other environmental impacts....* The cumulative impact from several projects is the change in the environment which results from the *incremental impact* of the project when added to other closely related past, present, and reasonably foreseeable probable future projects. Cumulative impacts can result from *individually minor but collectively significant* projects taking place over a period of time. (emphasis added)[12]

CEQA requires discussion of cumulative impacts in either of the following ways, which the Applicant has not performed sufficiently:

> (A) A list of past, present, and probable future projects producing related or cumulative impacts, including, if necessary, those projects outside the control of the agency, or
>
> (B) A summary of projections contained in an adopted general plan or related planning document, or in a prior environmental document which has been adopted or certified, which described or evaluated regional or areawide conditions contributing to the cumulative impact. Any such planning document shall be referenced and made available to the public at a location specified by the lead agency.[13]

While the Applicant has provided a brief assessment of current and probable future projects in relation to the current project in their response to comment, they have not discussed how past impacts may have resulted in declines of the Casa Diablo and Round Valley deer herds. While the Applicant correctly notes that CEQA directs that an EIR should not discuss impacts which do not result in part from the project evaluated in the EIR, this is not the case here. This project will cause

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[10] Wilcove, David S., David Rothstein, Jason Dubow, Ali Phillips and Elizabeth Losos. 1998. Quantifying Threats to Imperiled species in the United States. *BioScience*. 48(8), pp. 607-615.
[11] Ferranto SP. 2006. Conservation of mule deer in the eastern Sierra Nevada. M.S. Thesis, University of Nevada, Reno, p 61.
[12] CEQA Section 15355.
[13] CEQA Section 15130.

additional loss of deer habitat, which will contribute to the larger cumulative impacts on these deer herds.

While Cumulative Bio Measure 1 is designed to address cumulative impacts to biological resources, it is lacking in any mitigation for habitat loss due to the construction of the M-1 power plant, and as a result does not reduce the impacts to less than significant.

Mitigation can consist of avoidance or replacement of lost habitat. In this case, appropriate mitigation such as the restoration of 3.7 acres of habitat would qualify as mitigation. As the Applicant has noted the infeasibility of locating the new plant on the old plant site, an ideal site for such restoration would be on the site of the decommissioned power plant after demolition. Under the current plan, the old plant site will be converted to a *fenced* storage yard and as occasional overflow parking.[14] It is unclear whether additional fenced storage yards and overflow parking are essential for the goals of the project, and as such, restoring this area to usable habitat for deer, would do much to mitigate the impacts of habitat removal to less than significant.

While the Applicant determined that "the main use of the existing MP-I Project area by deer is as a movement corridor," this does not negate the fact that important browse, cover, and habitat for deer will be significantly impacted by the construction of the M-1 power plant.

The Applicant Fails to Recognize Significant Differences Between Spring and Fall Migration Resulting in Inadequate Baseline Data To Evaluate Impacts to Migrating Deer

The Applicant has not conducted deer surveys in the spring. In response to comments raised about incomplete understanding of deer due to a lack of spring surveys, the respondent replies that there is "only one movement corridor, and therefore no possibility of seasonal variation in migratory routes."[15] They add that there is "no basis for suspecting spring migrants would respond differently than fall migrants to environmental constants." The Applicant notes that "it is reasonable to conclude that neither the location nor the magnitude of seasonal movements vary significantly within the 5.7 acre project area and adjacent movement corridor."

The Applicant is misinformed. It is unclear what is meant by "only one movement corridor," as there are 2-3 gaps between the current buildings at the site and additional movement paths around the outside of these buildings. There is clearly the possibility of deer to prefer certain routes over others, and given the limited survey data, the Applicant is unable to determine what those may be.

[14] FEIR, p. 1-1.
[15] Applicant's Response to Comment 9A-03.

Furthermore, while the Applicant may describe spring and fall seasons as "environmental constants," the different stages of vegetative growth between seasons and the different life cycle stage of deer are two notable differences that the Applicant fails to realize. In the fall, female deer are often with young fawns, while in spring they are often pregnant.

Kucera (1987) describes this pattern in further detail:

> *"The spring migration begins in April, when deer leave their winter ranges and move to intermediate altitudes. They congregate in "staging areas" for as long as six weeks, feeding on spring vegetation and regaining condition lost over the winter, until they move to summer ranges. Here, mainly west of the Sierra Crest, fawns are produced and reared. The fall migration back to the winter range typically is more rapid than that of the spring, and usually is patterned by fall storms. Deer arrive on the winter range during September, October and November, breed in December and January, and begin the annual cycle again.*[16]

Furthermore, summary notes from a site visit with Department of Fish & Game biologist Tim Taylor notes that the proposed plant site is part of the Round Valley Deer Herd holding area prior to migration, where deer regain condition that is lost over the winter. Spring holding areas are of particular importance because does -- heavy with unborn fawns - need to be well fed along the way to their summer ranges in order to have successful reproduction.[17]

It is clear that significant seasonal differences exist between spring and fall migration patterns. While fall migration tends to be more rapid and brought on by fall storms, it is highly likely that there will be different movement patterns associated with spring migration, which will result in a more prolonged period in which the deer are moving through and using the area for much needed nutrition, especially for does to support pregnancy. The impacts to deer by the project, and the amount of use in the area are likely to be far greater in the spring than what can be estimated from fall survey counts.

It is critical to have this knowledge to properly evaluate the impacts that the project will have on migratory corridors and habitat for deer. Without this data, the Applicant cannot conclude that mitigation will be adequate to reduce impacts to less than significant levels.

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[16] Kucera, Thomas E. 1987. Casa Diablo Geothermal Development Project: Deer Migration Study, spring 1987.

[17] Rogers, RD. Protecting and Managing Deer Winter Range at Antelope Valley Wildlife Area. Outdoor California magazine, September – October 1999.

Construction Schedule Will Interfere with Spring and Fall Migration

The construction schedule overlaps with spring migration of deer, and will likely have an impact on deer during this time where deer are recovering from condition lost from winter conditions. Summary notes from a site visit with Department of Fish & Game biologist Tim Taylor note that deer migrate through the proposed project site from late April through the third week of May, depending on weather conditions.[18] Additional research on the deer in this area also found that migration began in late April and continued into May, while the fall migration occurs from September through November. [19]

The spring and fall migration period overlaps with the peak periods of construction, which shows that 60 workers will be on site in May as well as September and October.[20] The peak levels of construction activity will involve on average three (3), 40–foot delivery trucks to transport material to or from the site during the construction period. In addition, four (4), 60–foot trucks per day would deliver materials to the site over an approximate 10–day period early in the construction period, which will likely have an even greater impact on pregnant does in spring migration.[21] Peak levels of construction early in this period will mean more than 7 large trucks a day may be moving to and from the site during the spring migration period. This can result in an average of 14 trips (to and from) a day in the area.

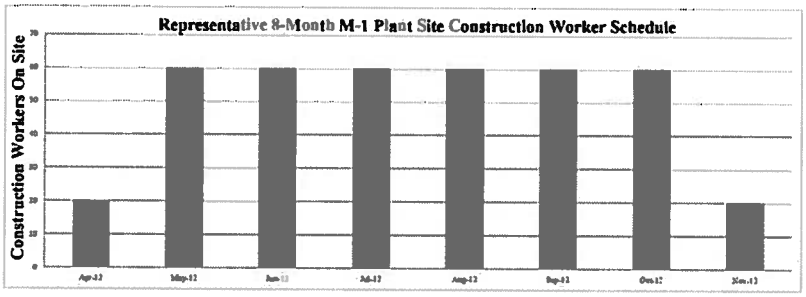

Figure 12: Representative 8-Month M-1 Plant Site Construction Worker Schedule

It is likely that construction would have significant impacts on migrating deer in the spring. While the Applicant has described the noise produced by trucks, they have not evaluated or mitigated its effect on migrating deer, particularly during the heaviest period of construction that will coincide with spring migration.

Project Violates Proposed Mitigation Measure

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[18] RDEIR Appendix C, G-1 Plant Replacement Site Visit – Summary, Mammoth Lakes, CA, March 22, 2011.
[19] Kucera, Thomas E. 1987. Casa Diablo Geothermal Development Project: Deer Migration Study, spring 1987.
[20] FEIR, Figure 12, p. 2-13.
[21] FEIR, Figure 12, p. 2-12.

Bio Protection Measure 7 calls for no additional linear barriers to be constructed:

> "The Project shall not erect any linear barriers to movement of deer or other wildlife in the area between the existing MP-I plant site and the replacement M-1 plant site. During M-1 plant site construction, no temporary fencing or pipeline racks shall be erected in this same area during the normal periods of mule deer migration, from April 1st to May 30th or from September 15th through November 15th."[22]

However, the new plant construction will result in approximately 2000 feet of additional linear barriers in the area. The project will construct 500 feet of interconnection injection fluid pipeline and about 1,500 feet of interconnection transmission line.[23] While the mitigation measure calls for no construction of pipeline racks during migratory periods, the pipelines that would be constructed appear to be permanent, and would violate this mitigation measure. While the Applicant notes that wildlife could move both over and beneath the interconnection pipeline and transmission line conduit, it is nonetheless an additional linear barrier that clearly violates the Applicant's own proposed mitigation measures.

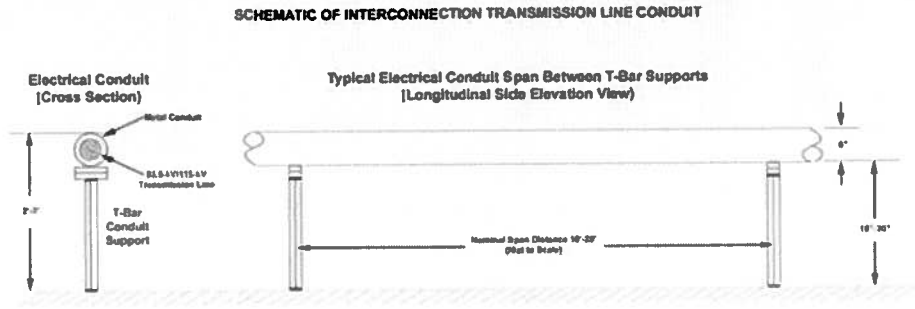

Figure 11: Schematic of Interconnection Transmission Line Conduit

Furthermore, the Applicant's conclusion that these linear facilities would not be a substantive obstacle to wildlife movement in the area is not clear. The Applicant has acknowledged that resident deer are more likely to adapt to changes in the surroundings than migratory deer.[24] As such, the assertion that an additional pipeline would not be viewed as substantive obstacles become less clear when it comes to migratory deer, which will not have opportunities to adapt to these changes.

While it is likely that deer can cross this pipeline, it adds further disturbance to migratory paths that are unlikely to be mitigated by the single crossing that has been proposed to mitigate for these impacts (additional problems with this mitigation measure will be addressed more fully below). With the addition of

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[22] FEIR, p.4-73.
[23] FEIR, p. 4-65.
[24] Applicant's Response to Comment 9A-12.

transmission lines, the remaining corridor passageway that is uninhibited by a pipeline will be reduced to approximately 100 feet if the proposed project is constructed.[25]

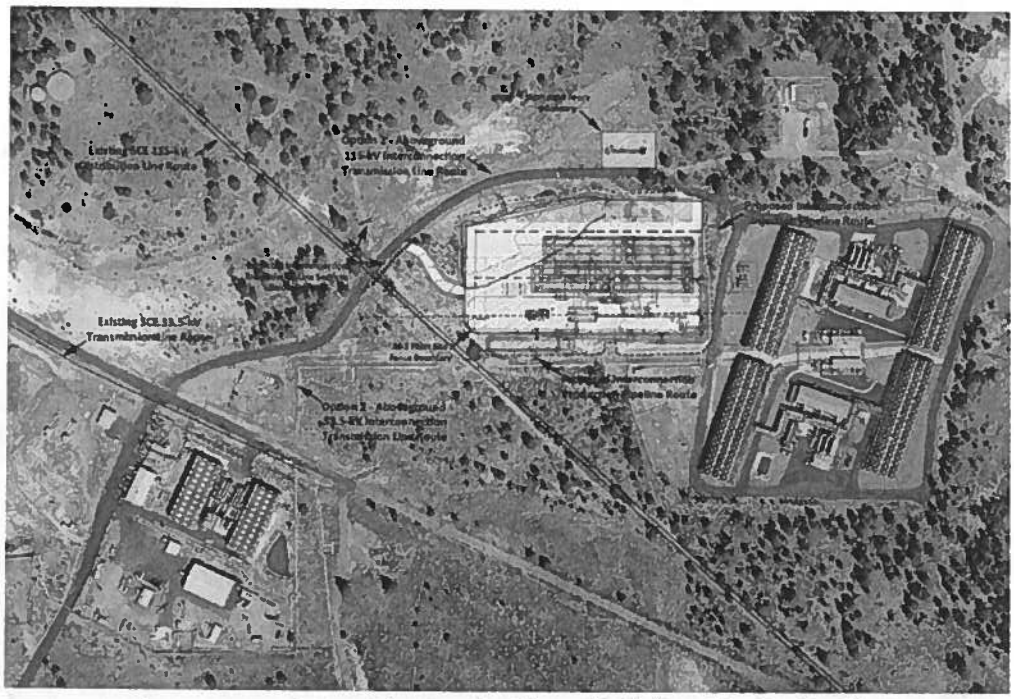

Figure 10: Interconnection Transmission Line Options, Interconnection Pipelines and New Fence Boundaries

In order to properly mitigate for the reduction of the migratory corridor, the Applicant should bury all lines to reduce potentially significant impacts to deer movement. This seems especially warranted given that general Mono County regulations require that all new utilities shall be installed underground,[26] and that the project is seeking a variance from this regulation.

The Applicant says that these transmission lines would "necessarily be located aboveground",[27] but do not provide any justification for why this is the case, when CD-4 project lines would be placed underground.

Bio Protection Measure 8 Will Not Mitigate the Reduction in Movement Corridor for Migratory Deer

The Applicant has proposed mitigation to reduce significant impacts to connectivity for wildlife and mule deer in Bio Protection Measure 8. However, this mitigation measure, which calls for an earthen ramp to be constructed over a pipeline, is

[25] FEIR, Figure 10, p. 2-11.
[26] FEIR, p. 4-5.
[27] FEIR, p. 5-8.

unproven and, without further empirical support, the Applicant cannot support the claim that it will reduce significant impacts to migratory deer to less than significant.

The Applicant acknowledges that resident deer are more likely to adapt to changes due to Project construction than migratory deer.[28] However, the Applicant's proposed mitigation for impacts to movement by deer – including movements by migratory deer – involves building a new earthen ramp over the pipeline. While this ramp is intended to serve as connectivity at least in part for migrating deer, the Applicant fails to recognize the inherent difficulty that migrating deer may have in encountering this new feature on the landscape. It is questionable that deer in the midst of migration, having never encountered this feature, will use this crossing. As such, without further empirical evidence, this mitigation measure cannot be expected to alleviate the significant impacts that will result in reduced movement connectivity for migratory mule deer.

While the Applicant has attempted to provide empirical support, the data is not provided or cited. The Applicant refers to 2011 deer studies which found that constructed crossings of this type in the Basalt Canyon area are regularly used by deer during both the residency and migratory periods. But because the data for these studies is not cited, the results are not verifiable.[29] Furthermore, close reading of the statement also suggests that while deer may be using this ramp *during both residency and migratory periods*, the vagueness of wording could mean that *only resident deer* are using the ramps *during migratory periods*. It is not clear that *any* migratory deer are using these ramps during migratory periods. If only resident deer are using these ramps, then the proposed mitigation of creating this ramp serves only to help connectivity of resident deer, and does not address significant impacts to migratory deer.

Recent and available peer-reviewed research on overpasses for connectivity has focused on road mortalities and use of overpasses, and meta-analyses have found a lack of before and after data as making "the efficacy of these techniques nearly impossible to evaluate."[30] Given the questionable efficacy of connectivity overpasses in peer-reviewed meta-analyses, the Applicant needs to provide empirical data to support the finding that an earthen ramp will mitigate for significant movement corridor impacts that the project will cause.

<u>Description of Bio Protection Measure 8 Is Unclear</u>

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[28] Applicant's Response to Comment 9A-12
[29] Applicant's Response to Comment 9A-13
[30] Glista, David J., Travis L. DeVault, J. Andrew DeWoody. 2009. A review of mitigation measures for reducing wildlife mortality on roadways. *Landscape and urban planning.* 91(1) p. 1-7.

While the efficacy of Bio Protection Measure 8 is doubtful, the description of the mitigation measure is vague, inaccurate, and internally inconsistent. First, the characteristics of the earthen ramp that is proposed for mitigation are not sufficiently described. While the Applicant describes the ramp it to be 30 feet wide, they do not provide any information on the slope of the ramp. Second, the Applicant describes the earthen ramp to be "tree-screened", however, there are only trees on the northern end of the proposed area for the ramp construction, and the lack of tree cover on the southern portion of the ramp will likely diminish its use. Third, the existing road on the northern portion of the proposed ramp would likely be blocked by such a ramp, and the Applicant does not address how vehicles will pass this area with a 30 foot ramp crossing the road.

The description of this proposed ramp is internally inconsistent. The Applicant notes that the "The finished crossing shall resemble the existing crossing at the SCE easement located approximately 320 feet east of the 90 degree turn."[31] However, the Applicant has described the SCE crossing as an area where the pipeline racks are *buried underground* for 50 feet.[32] In terms of mitigation for deer connectivity, burying the pipeline for a distance of 50 feet—as the pipeline is buried at the SCE easement—would certainly be superior to the creation of an earthen ramp. In fact, as suggested earlier, appropriate mitigation that would reduce connectivity impacts to less than significant would require burying all the transmission lines so as to compensate for the area that will be blocked by the construction of the M-1 power plant.

Part of Cumulative Bio Mitigation Measure 1 does not constitute mitigation for this project's impacts

Cumulative Bio Mitigation Measure 1 calls for three main actions to mitigate for cumulative impacts. The first of these calls for new projects to conduct baseline deer studies of proposed projects and monitoring deer use within and near new proposed projects.[33]

Calling for baseline deer studies without any clear and concrete performance actions does not constitute mitigation. CEQA describes five types of mitigation:

> (a) Avoiding the impact altogether by not taking a certain action or parts of an action.
> (b) Minimizing impacts by limiting the degree or magnitude of the action and its implementation.
> (c) Rectifying the impact by repairing, rehabilitating, or restoring the impacted environment.

[31] FEIR, p. 4-73.
[32] RDEIR Appendix D, p. 25.
[33] FEIR, p. 5-12.

> (d) Reducing or eliminating the impact over time by preservation and maintenance operations during the life of the action.
> (e) Compensating for the impact by replacing or providing substitute resources or environments.[34]

Conducting surveys do not qualify as any of these types.

Surveys are a critically important tool for evaluating and determining mitigation measures to be taken, and this use of surveys is clearly useful. However, action items surrounding the findings of this survey data that is consistent with the definition of mitigation under CEQA is necessary. While these action items would certainly need to be site specific, and some flexibility is necessary in designing them, basic requirements or standards and resulting action items need to be described for this measure to constitute mitigation and reduce significant cumulative impacts. Some standards for action could involve standards in percentage reduction in deer use. For example, if surveys reveal that deer use of the area has ceased in connection with construction, mitigation should call for the reduction of construction activity until surveys show improvement in deer use.

Mitigation requires that some action be taken to minimize or compensate. Simply calling for studies without remedial actions does not constitute mitigation.

Bio Protection Measure 9 is Vague

Bio Protection Measure 9 calls for the designation of a movement corridor on the northeastern side of the existing Casa Diablo geothermal complex shall be maintained free from further development and mechanical disturbance.[35] The area would be designated for long-term preservation in the Reclamation Plan prepared for the County for the Casa Diablo geothermal development.

While the preservation of habitat is crucial for biological resource protection, maintaining already existing habitat and already existing corridor does qualify as mitigation in terms of preservation, however, it does not fully compensate for the loss that is occurring. This corridor to the north of the complex is currently preserved, and any development on it would have to undergo its own mitigation. It is unclear whether preserving this area alone would sufficiently mitigate for impacts caused.

Furthermore, the Applicant does not define "long-term" and does not make it clear that the land will be preserved from other development besides geothermal development.

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[34] CEQA Section 15370.
[35] FEIR, p. 4-74.

One example of replacement and compensation that would serve to make the impacts of construction less than significant could include the restoration of degraded habitat in the area. An ideal place for such replacement of habitat and improve connectivity would be to restore the decommissioned plant site to habitat that would be usable by deer and wildlife. The use of the old site as a fenced storage yard and overflow parking lot – unusable and inaccessible to wildlife and deer – appears to be a relatively unnecessary use of this area when significant impacts are caused due to additional construction.

Sincerely,

Luke Macaulay, M.S.

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EDUCATION

UNIVERSITY OF CALIFORNIA, BERKELEY — **Berkeley, California**
Environmental Science, Policy, and Management — **2008-Present**

Ph.D. Student – Fall 2010 - Present: Dr. Reginald Barrett.
Topic: ***Wildlife Management Intensity for Hunting: Economic and Environmental Effects in Oak Woodlands***

- Interview landowners, wildlife management consultants, Cooperative Extension staff, and state fish & game officials to gather economic and environmental data about ranch operations with hunting in Texas and California
- Present research to landowner groups and academic seminars
- Utilize GIS mapping software to assess environmental impacts of management activities

Masters of Science: Range Management - Spring 2010

- GPA: 4.0
- Environmental Economics
- Graduate Wildlife Biology Seminar
- Management of Rangeland Ecosystems
- Grazing Management Plans for Cowell and Macedo Ranches (CA State Parks)
- Ecological Data Analysis – Statistics

UNIVERSITY OF NOTRE DAME — **South Bend, Indiana**
College of Arts and Letters — **1998-2002**

Bachelor of Arts: Program of Liberal Studies, a Great Books Program
Second Major: Spanish; ***Study Abroad in Toledo, Spain***

- GPA: 3.6; Cum Laude; Recipient of Father Wilson Scholarship
- Summer Service Fellowship in El Salvador

EXPERIENCE

UNIVERSITY OF CALIFORNIA, BERKELEY — **Berkeley, California**
Environmental Science, Policy, and Management — **April 2008 – Present**

Researcher – East Bay Regional Parks – Spring 2008- Present

- Perform bird surveys, vegetation transects and invertebrate sampling in grasslands of East Bay Regional Parks
- Analyze data to determine how factors (particularly grazing) are affecting native species presence and diversity
- Draft portions of annual report to inform park management on composition of grassland and effects of grazing

UC Berkeley Center for Forestry – Fall 2010:

- Evaluated and provided future recommendations of Cooperative Extension Integrated Hardwood Management Program in California

Visiting Scholar – Spain: ***Consejo Superior de Investigaciones Cientificas*** **– Fall 2009**

- Conducted field work on research projects in Spanish oak savannas involving tree growth and productivity
- Interviewed Spanish researchers and visited research sites in Andalucia region of Spain

Graduate Student Instructor – American Wildlife: Conservation and Identification – Fall 2008

- Prepared and revised lectures and exams, teaching ~50 students about 180 wildlife species and their conservation
- Due to unexpected absence of professor, doubled anticipated GSI responsibilities to keep course on schedule

INDEPENDENT ENVIRONMENTAL CONSULTING — **May 2009 – Present**

Renewable Energy Environmental Impact Review

- Evaluate environmental impacts for solar mega-projects in Mojave Desert on BLM land and geothermal power plant at "The Geysers" of Sonoma County; research and evaluate claims of impacts to special status plant and wildlife species; evaluate survey techniques; assess wildlife corridor needs
- Attend hearings and submit data requests and testimony to California Energy Commission to ensure thorough consideration of environmental impacts

POINT REYES NATIONAL SEASHORE — **Point Reyes National Seashore, California**
University of California, Berkeley, and National Park Service — **December 2007 – March 2008**

Graduate Research Fieldwork

- Investigated the mechanisms driving the population dynamics of wild free-ranging tule elk

- Utilized radio telemetry to conduct relocations of radio-collared tule elk; conduct field necropsies of tule elk; collect elk fecal samples to examine diet, stress levels, and disease prevalence

HILL & KNOWLTON — **San Francisco, California**
Global Public Relations and Public Affairs Consultancy — **May 2007 – December 2007**

Senior Account Executive

- Consulted for diverse group of clients including Hewlett-Packard, Qualcomm, University of California (UC) Medical Centers, Natural Selection Foods, and the Kauffman Foundation
- Developed crisis communications strategy and proactive messaging for food safety emergencies
- Managed news announcements from conception to execution including: identified target audience and publication; performed competitive and industry research; conducted outreach; and developed written materials
- Wrote and posted updates and fliers online about union negotiations for 19,500 employees in UC Medical Centers
- Developed, promoted, and managed www.ucnurses.com and www.ucpatientcaretechs.com
- Managed $300,000 public relations budget for one client

UNITED STATES DEPARTMENT OF JUSTICE — **San Francisco, California**
U.S. Attorney's Office – Northern District of California — **September 2004 – April 2007**

Spokesman -- Public Affairs Officer

- Drafted public statements, op-eds, letters to editors, award nominations and press releases (over three per week)
- Advised and strategized with top management in creating and disseminating message to the media
- Issues included: Steroids and perjury investigations into athletes (Balco), California leopard shark poaching and a $1.5 million partnership for rehabilitation, stock options backdating, Enron and Reliant energy market fraud
- Prepared management for interviews with reporters: created briefing memos, talking points, Q&As, and fact sheets
- Organized and moderated press conferences: determined message, briefed speakers, and led preparatory meetings
- Fielded approximately 15-25 media inquiries daily; explained office work & initiatives in on-the-record interviews
- Conducted on-camera media interviews; attended Justice Department training for on-camera interviews
- Crisis response team: responsible for coordinating media response across multiple government agencies
- Initiated and implemented student intern program: interviewed, trained, and managed interns
- Involved in front page coverage in the *Wall Street Journal*, *New York Times*, *San Francisco Chronicle* and others
- Featured in San Francisco Examiner profile

UNITED STATES DEPARTMENT OF JUSTICE — **Washington, DC**
Office of Public Affairs and Antitrust Division — **August 2002 – September 2004**

Press Assistant – Antitrust Division, 2003-2004: Created media briefs; provided public affairs support for *U.S. v. Oracle* antitrust trial; assisted with organization of press conferences for Attorney General John Ashcroft

Paralegal Specialist, 2002-2003: Drafted detailed investigative reports for antitrust investigations; appointed lead paralegal for three multi-billion dollar transactions in the defense, turbine, and waste industries

PHILMONT BACKPACKING RANCH — **Cimarron, New Mexico**
Boy Scouts of America — **Summers of 1999 and 2001**

Program Counselor: Taught Boy Scouts about Native American and pioneering traditions of the Southwest
2001 – Pioneering: Certified muzzleloader rifle instructor; taught blacksmithing; lived in primitive cabin conditions;
1999 – Native American Tradition: Arrowhead-making, teepees, sweat lodges, Native American cultural traditions

PUBLICATIONS, ACHIEVEMENTS, ORGANIZATIONS, INTERESTS

- National Science Foundation Graduate Research Fellowship Program – Honorable Mention 2010
- Invertebrate Analysis in *East Bay Regional Parks Annual Monitoring Report*. UC Berkeley. 2009.
- Outstanding Graduate Student Instructor Award - Fall 2008
- 2008 Range Management Scholarship Award
- Wildlife Society: Webmaster of San Francisco Bay Area Chapter 2009-2011
- Eagle Scout
- Biking, hunting, archery, surfing, hiking, fishing, backpacking, skiing, archaeology
- Fluent in Spanish: comprehension, speaking, reading, and writing

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Review

A review of mitigation measures for reducing wildlife mortality on roadways

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ABSTRACT

A growing literature in the field of road ecology suggests that vehicle/wildlife collisions are important to biologists and transportation officials alike. Roads can affect the quality and quantity of available wildlife habitat, most notably through fragmentation. Likewise, vehicular traffic on roads can be direct sources of wildlife mortality and in some instances, can be catastrophic to populations. Thus, connectivity of habitat and permeability of road systems are important factors to consider when developing road mortality mitigation systems. There are a variety of approaches that can be used to reduce the effects of roads and road mortality on wildlife populations. Here, we briefly review wildlife-crossing structures, summarize previous wildlife road mortality mitigation studies, describe common mitigation measures, and discuss factors that influence the overall effectiveness of mitigation strategies. Because there are very few road mortality studies "before" and "after" the installation of wildlife-crossing structures, their efficiency is nearly impossible to evaluate. However, simple and relatively inexpensive measures reviewed herein can almost certainly reduce the number of collisions between wildlife and automobiles.

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1. Introduction

Although roads provide some ecological benefits, such as maintenance of grassland plants in intense agricultural areas (Forman, 2000), they also can act as both physical and biological barriers to many wildlife species (Forman and Alexander, 1998; Jackson, 2000). Roads can affect the quality and quantity of available wildlife habitat, most notably through fragmentation. Likewise, vehicular traffic on roads can be direct sources of wildlife mortality, and in some instances, can be catastrophic to animal populations (Langton, 1989a). Many other ecological effects of roads on species, soils, and water have been identified, with effects varying in distance outward from meters to kilometers (Ellenberg et al., 1991; Forman, 1995). "Road-effect zones" impact an estimated 15–20% of the land mass in the United States (Forman and Alexander, 1998).

Collisions with automobiles are a major source of direct mortality in some animal populations (Romin and Bissonette, 1996; Trombulak and Frissell, 2000; Gibbs and Shriver, 2002; Glista et al., 2008). Lalo (1987) estimated vertebrate mortality on roads in the United States at 1 million individuals per day. A variety of mitigation approaches are used to reduce the effects of roads and road mortality on wildlife populations. In general, these approaches fall into one of two categories: the modification of motorist behavior and/or the modification of animal behavior. Modification of motorist behavior often involves speed limits, lights, and signs, whereas modification of animal

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behavior often involves habitat alterations and/or installation of wildlife-crossing structures (Romin and Bissonette, 1996; Forman et al., 2003). Wildlife-crossing structures range from exclusion fences and culverts to overpass/underpass systems (Romin and Bissonette, 1996). Many structures are designed to reduce large animal–vehicle collisions (Forman et al., 2003). Such structures should be designed to allow safe passage for animals, promote habitat connectivity, be accessible, and encourage natural movements.

Unfortunately, the frequency at which road mortality mitigation measures are implemented does not correlate with their perceived effectiveness; the most promising measures often are the least used. For example, Romin and Bissonette (1996) reported that many U.S. states used wildlife-crossing signs and public awareness programs to reduce automobile collisions with large animals, although most state natural resource agencies admitted that the effectiveness of such measures was largely unknown to them. Conversely, relatively few U.S. states used fences, overpasses, and underpasses to reduce collisions, even though most agencies that used them reported that these structures were effective. Undoubtedly, economic factors often dictate the choice of road mortality mitigation measures that are implemented. Moreover, evaluations of mitigation success often are based on opinion rather than research (Forman et al., 2003). Poor road mortality mitigation designs do little to minimize road effects on wildlife and are generally a waste of time and money. Furthermore, poorly designed structures can interrupt natural processes that can lead to various ecological problems such as overgrazing, increased erosion, or population declines (Forman et al., 2003).

A growing literature in the field of road ecology suggests that vehicle/wildlife collisions can be major sources of vertebrate mortality and thus potentially limit wildlife populations (Aresco, 2005). For example, one recent study documented nearly 10,000 mortality events over 17 months at a single site (Glista et al., 2008). Mitigation measures that potentially reduce such collisions have been developed, and transportation officials should be aware of methods to reduce wildlife mortality on roadways. In this review, we summarize previous wildlife road mortality mitigation monitoring studies, describe some of the most common mitigation measures employed, and discuss factors that lead to the overall effectiveness of road mortality mitigation measures (Table 1).

2. Types of crossing structures

Pipe culverts are relatively small structures (0.3–2 m diameter) made of concrete, smooth steel, or corrugated metal designed to carry water under roads. Europe has led the way in implementing smaller pipe-style culverts, also referred to as "amphibian tunnels" (Forman et al., 2003; Fig. 1). Box culverts, generally larger than pipe culverts, also are used to allow water to pass under roads. Unlike pipe culverts, they usually remain dry except in periods of heavy runoff. Culverts may be used by a variety of wildlife species to cross roads (Yanes et al., 1995; Rodriguez et al., 1996; Clevenger and Waltho, 2000). Kaye et al. (2005) reported that spotted turtles (*Clemmys guttata*, a state threatened species) used a box culvert under a highway improvement project to move between two habitats in MA, United States. The use of a system consisting of a retaining well, box culverts, and pipe culverts reduced wildlife road mortality by 93.5% in the Paynes Prairie State Preserve, FL, United States (Dodd et al., 2004). Clevenger et al. (2001) monitored 36 culverts along the Trans-Canada highway and found a total of 618 crossings by a minimum of 9 species, with an average of 2.8 species at each culvert. In Australia, Taylor and Goldingay (2004) recorded 17 different vertebrate species

Fig. 1. Amphibian tunnel for mitigating road mortality (Federal Highway Administration, 2002).

using purpose-built fauna culverts in combination with exclusion fencing under the Pacific Highway. Of all wildlife-crossing structures, culverts may be one of the most economical. Furthermore, with some modification (e.g., the addition of drift fences, habitat modification at entrances, incorporation of dry ledges in culverts frequently inundated with water), preexisting culverts often may be used as crossings. A drawback to some culverts is that their size may not promote use by larger animals. Also, care must be taken to ensure that culverts remain open for animals to use.

Wildlife underpasses, also known as wildlife bridges, are large underpasses that provide a relatively unconfined passage for wildlife (Jackson and Griffin, 2000). Where roads cross over water or other roads, underpasses can provide a passageway for many wildlife species, especially those that use riparian corridors. In situations where underpasses hold excessive amounts of water, ledges can be incorporated into their designs to allow animal passage. Veenbaas and Brandjes (1999) reported that mammals used all (100%) existing highway underpasses along waterways, and 75% of underpasses were used by amphibians. Underpasses with the largest diameters were used most frequently by mammals; this relationship did not hold for amphibians. Passages with extended banks were used by more species overall. Some advantages to underpasses are that they can utilize natural terrain features to promote animal crossings and can accommodate a greater variety of species. Unfortunately, underpasses can be expensive due to construction costs, such as in instances where they must span large riparian areas.

Overpasses for wildlife are primarily designed for larger animals such as large carnivores and ungulates. They can range in width from 30 to 50 m to over 200 m on each end (Jackson and Griffin, 2000; Forman et al., 2003). Overpasses are sometimes referred to as "green bridges", a term used to describe wildlife overpasses with relatively large strips of natural vegetation crossing over roads (Bekker et al., 1995). "Landscape connectors" are especially wide overpasses that maintain the connectivity of horizontal ecological flows across the landscape (Forman et al., 1997). Wildlife overpasses accommodate a larger variety of species than do underpasses (Jackson and Griffin, 2000).

Van Wieren and Worm (2001) reported that a wildlife overpass in the central Netherlands was used frequently by large mammals, specifically red deer (*Cervus elaphus*) and wild boar (*Sus scrofa*). They also noted that animal crossings had increased almost threefold since previous monitoring in 1989 and suggested that the increase was due to habituation of red deer to the structure. Keller (1999) also noted that ungulates, most notably roe deer

Table 1
Wildlife passage monitoring studies (modified from Forman et al., 2003).

Study	Mitigation measure(s)	Location	Target species (or group)	Monitoring duration	Species encountered
AMBS Consulting (1997)[a]	Underpasses	New South Wales, Australia	Unspecified	9 months in 1997	Unspecified
Aresco (2005)	Drift fence and culverts	FL, USA	Reptiles and amphibians	April 2000–November 2003	Reptiles and amphibians
Ballon (1985)[a]	Unspecified	Upper Rhine, France	Unspecified	9 months in 1985	Ungulates
Cain et al. (2003)	Bridges and culverts	TX, USA	Bobcats	August 1997–May 1999	Bobcats
Clevenger (1998)[a]	Underpasses and overpasses	Alberta, Canada	Unspecified	January 1998–December 1998	Large mammals
Clevenger and Waltho (1999)	Dry drainage culverts	Alberta, Canada	Small- and medium-sized mammals	74 days in late winter/early spring	Weasels
Clevenger and Waltho (2000)[a]	Underpasses and culverts	Alberta, Canada	Large mammals	January 1995–March 1996, November 1996–June 1998	Elk
Clevenger and Waltho (2005)	Underpasses and overpasses	Alberta, Canada	Large mammals	November 1997–August 2000	Deer
Dodd et al. (2004)	Culverts	FL, USA	Unspecified	March 2001–March 2002	Southern leopard frogs
Donaldson (2005)	Underpasses	VA, USA	Large mammals	June 2004–May 2005	White-tailed deer
Fitzgibbon (2001)	Culverts	Vancouver, Canada	Amphibians and small mammals	2000	Weasels
Foresman (2001)	Culverts	MT, USA	Small mammals	January 2001-August 2001	Unspecified
Foster and Humphrey (1995)[a]	Underpasses	FL, USA	Florida panthers	2 months, 16 days in 1995	Medium- to large-sized mammals
Hunt et al. (1987)[a]	Tunnels	New South Wales, Australia	Unspecified	2 months in 1987	Small- to medium-sized mammals
Jackson (1996)	Amphibian tunnels	MA, USA	Spotted salamanders	Spring 1998	Spotted salamanders
Jackson and Tyning (1989)[a]	Drift fences and tunnels	MA, USA	Spotted salamanders	1988	Spotted salamanders
Jones (2000)	Reflectors, ramps, and pipes	Tasmania	Eastern quolls, Tasmanian devils	October 1990–April 1993	Unspecified
Kaye et al. (2005)	Culverts	MA, USA	Spotted turtles	April 2004–July 2004	Unspecified
Keller (1999)	Overpasses	Switzerland, Germany, France, and Netherlands	Unspecified	Unspecified	Roe deer
Land and Lotz (1996)[a]	Underpasses	FL, USA	Florida panthers	Unspecified	Raccoons, white-tailed deer
Langton (2002)	Amphibian tunnels	England	Amphibians	Unspecified	Common toad
LaPoint et al. (2003)	Various under-road passages	NY, USA	Unspecified	March 2002–April 2002	Raccoons
Lesbarreres et al. (2004)	Amphibian tunnels	France	Common toad, water frogs, agile frogs	February 2001–May 2001	Water frogs, common toads
Pfister et al. (1997)[a]	Overpasses	Switzerland, Germany, France, Netherlands	Unspecified	2 years	Mammals
Puky and Vogel (2003)	Various types of passages	Hungary	Amphibians	Unspecified	Unspecified
Reed et al. (1975)[a]	Underpasses	WY, USA	Deer	2 years	Ungulates
Rodriguez et al. (1996)[a]	Culverts, underpasses, and overpasses	Montes de Toledo, Spain	None	September 1991–July 1992	Small mammals
Roof and Wooding (1996)[a]	Underpasses	FL, USA	Black bears	December 1994–December 1995	Rabbits
Rosell et al. (1997)[a]	Underpasses	Catalonia, Spain	Unspecified	11 months in 1997	Unspecified
Taylor and Goldingay (2004)	Culverts	New South Wales, Australia	Unspecified	Spring/summer 2000	Bandicoots
Van Wieren and Worm (2001)	Overpasses	Netherlands	Mammals	1989, 1994, 1995	Red deer
Veenbaas and Brandjes (1999)[a]	Various types of passages	Netherlands	Unspecified	Unspecified	Mice, voles
Woods (1990)[a]	Underpasses	Alberta, Canada	Unspecified	3 years	Ungulates
Yanes et al. (1995)[a]	Culverts	Central Spain	None	Four seasonal periods over 1 year	Small mammals

[a] Cited in Forman et al. (2003).

(*Capreolus capreolus*), were the most frequent users of wildlife overpasses in Switzerland, Germany, France, and the Netherlands. At two overpass structures in Banff National Park, Canada, along the Trans-Canada Highway, Clevenger and Waltho (2005) reported that elk (*Cervus elaphus*) and deer (*Odocoileus* spp.) were large mammals that most frequently used the structures. Some advantages of overpasses are that they are less confining, quieter, maintain ambient conditions of rainfall, temperature, and light, and can serve as both passageways for wildlife and intermediate habitats for smaller animals (e.g., small mammals, reptiles, and amphibians) (Jackson and Griffin, 2000). One of the drawbacks of overpasses is that they often are the most expensive option due to their large size and construction costs.

3. Factors influencing the effectiveness of crossing structures

Several factors affect the ability of a crossing structure to facilitate wildlife movements. Location of crossing structures is very important and may be the most important factor predicting effectiveness (Podloucky, 1989; Foster and Humphrey, 1995; Yanes et al., 1995; Land and Lotz, 1996; Rodriguez et al., 1996; Clevenger and Waltho, 2000). Location is especially vital for smaller, less mobile species such as reptiles and amphibians (Jackson and Griffin, 2000). Rodriguez et al. (1996) suggested that crossing structures should be placed in areas of suitable habitat and that passages implemented near continual disturbance (e.g., excessive human presence) were less frequently used by several wildlife species (e.g., carnivores and ungulates).

The dimensions of structures are also important in designing passageways for vertebrates (Ulbrich, 1984; Ballon, 1985 [as cited in Yanes et al., 1995]). The size and shape of a particular structure may be the determining factor for crossing success (Reed et al., 1975; Ballon, 1985; Cain et al., 2003; Clevenger and Waltho, 2005). In Europe, hourglass-shaped overpasses are used regularly by wild boar, but not by red deer that become unnerved or frightened by the constriction at the center (Vassant et al., 1993 [as cited in Forman et al., 2003]). For some species, the relative openness in a passage may be more important than overall size (Foster and Humphrey, 1995; Clevenger and Waltho, 2005). Structures along the Trans-Canada Highway with high openness ratios (short in length, high and wide) were used most often by grizzly bears (*Ursus arctos horribilis*), wolves (*Canis lupus*), elk, and deer, whereas more constrictive structures were used more often by black bears (*Ursus americanus*) and cougars (*Felis concolor*) (Clevenger and Waltho, 2005). Tunnels that allow animals to see the other end were positively correlated with use by some species (Rosell et al., 1997 [as cited in Jackson and Griffin, 2000]). Conversely, some studies (Rodriguez et al., 1996; Clevenger and Waltho, 1999) have suggested that smaller passages may be better for some small mammals. There is some evidence that predators use crossing structures to increase prey capture (Hunt et al., 1987; Foster and Humphrey, 1995), which can limit the use of crossing structures by prey species. Culverts and underpasses that are exposed, restricted, or narrow may reduce the effectiveness of escape mechanisms of prey species (Reed et al., 1975; Yanes et al., 1995; Clevenger et al., 2001).

Approaches to structures also can affect their use by animals (Veenbaas and Brandjes, 1999; Clevenger and Waltho, 2000). The availability of cover (or lack thereof) at the approach to a crossing structure can determine whether a particular species will use it. Natural vegetation can enhance the "attractiveness" of crossing structures to animals and allow a continuity of habitat. Cover may influence the use of crossings by small to mid-sized mammals (Hunt et al., 1987; Rodriguez et al., 1996; Clevenger and Waltho, 1999), but deter other species like deer and other ungulates if it restricts their vision (Pedevillano and Wright, 1987; Clevenger and Waltho, 2000).

The use of fencing and/or barrier walls in conjunction with passages can help prevent animal access to roads and facilitate movement of animals towards crossing structures (Ratcliffe, 1983; Feldhamer et al., 1986; Jackson and Tyning, 1989; Jackson, 1996; AMBS Consulting, 1997; Bissonette and Hammer, 2000; Jackson and Griffin, 2000; Dodd et al., 2004). A barrier wall in conjunction with a culvert system was effective in reducing wildlife road mortality 93.5% in the Paynes Prairie State Preserve, Florida (Dodd et al., 2004). For many larger species, fencing is necessary because of their inherent avoidance of passages. Many ungulates avoid underpasses unless there is no other way to cross a road (Ward, 1982) and mountain lions traveling along streams are known to leave the stream and cross over highways rather than use under-road culverts (Beier, 1995). Fencing in the absence of crossing structures, however, can be detrimental, because it can act as a barrier to natural movements and contribute to habitat fragmentation (Jaeger and Fahrig, 2004). Fencing should extend far enough to either side of a crossing structure to promote guidance to the structure. The length of fencing often is dictated by the target species and the surrounding terrain. Because there is no universal design that works well for all roads, we recommend that transportation officials work with wildlife biologists to customize fencing regimes.

Moisture, temperature, light, substrate, and noise (disturbance) all can influence whether animals will use wildlife passages (Langton, 1989b; Mansergh and Scotts, 1989; Beier, 1995; Yanes et al., 1995; Jackson, 1996). Amphibians generally require moist conditions during migration, thus designing passages to allow rain to moisten the passage may be important (Jackson, 1996). Langton (1989b) reported that temperature differences between the interior and exterior of culverts may dissuade use by some amphibian species. The ability of air to flow freely through a passage (e.g., by using grate tops rather than solid tops) may help negate temperature differences and allow freer use by a wider range of species. Moreover, open tops will allow more ambient light to enter crossing structures. Jackson and Tyning (1989) noted that increased natural light in tunnels accelerated the rate at which spotted salamanders (*Ambystoma maculatum*) would cross. Conversely, artificial light often may deter animals from using a crossing structure (Reed, 1981; Jackson, 2000).

The inclusion of a natural substrate within a crossing structure can provide continuity of habitat and may encourage animals to pass (Yanes et al., 1995; Jackson, 2000). In controlled experiments between bare concrete tunnels, soil-lined tunnels, and open grass, Lesbarreres et al. (2004) found that water frogs (*Rana esculenta*) and common toads (*Bufo bufo*) preferred the tunnels to the grass, whereas agile frogs (*Rana dalmatina*) preferred grass. Use and crossing success were both higher in the soil-lined tunnel. Mougey (1996) suggested that frogs are deterred from bare concrete due to its alkalinity. Juvenile western toads (*Bufo boreas*) and red-legged frogs (*Rana aurora*) showed greater movement in culverts with substrate as opposed to culverts without (Bernard, 2000 [as cited in Fitzgibbon, 2001]).

Noise levels (e.g., traffic) can influence animal use of crossing structures (Clevenger and Waltho, 2000, 2005; Jackson, 2000). In Banff National Park, Canada, carnivore and ungulate movements through passages near the town of Banff were significantly affected by human activity and noise (Clevenger and Waltho, 2000). As such, planners should consider the use of noise-reducing materials during construction of crossing structures.

4. Nonstructural methods

Financial considerations are often a major concern when considering the implementation of wildlife road mortality mitigation measures. Cost can be extremely variable depending on the method chosen, availability of materials, and scale of the project. Usually, however, nonstructural methods are less expensive than structural methods. Bank et al. (2002) reported on a variety of nonstructural methods of road mortality mitigation currently being researched in Europe. These include: (1) olfactory repellents whereby scented foam is sprayed on vegetation and structures along the road, (2) ultrasound, (3) road lighting (which may have negative consequences for nesting birds), (4) population control (e.g., hunting), and (5) habitat modification, used primarily to keep animals away from roads or increase driver and animal visibility. Development of less expensive alternatives to expensive structures (e.g., overpasses) would allow wider use and promote permeability of road corridors (Forman et al., 2003). Biological consequences of nonstructural methods are not well understood, and more research is needed to ascertain their effectiveness.

Although it is impossible to predict exactly where and when animals will appear on roads, motorists who are aware of the potential for animal crossings can sometimes help mitigate wildlife road mortality. The use of signs and/or speed bumps to reduce speed and enhancing speed limit enforcement may help reduce road mortality of wildlife in areas of known animal crossings. High-speed traffic is often considered one of the main causes of wildlife–vehicle collisions (Pojar et al., 1975; Case, 1978). Wildlife-crossing signs also can be installed in areas of intense animal activity to help make drivers more aware of wildlife presence, although their effectiveness is questionable (Pojar et al., 1975; Aberg, 1981 [as cited in Groot Briunderink and Hazebroek, 1996]). Even stuffed mule deer (*Odocoileus hemionus*) placed in road rights-of-way failed to evoke a reaction from many drivers (D.F. Reed, personal communication [as cited in Groot Briunderink and Hazebroek, 1996]), suggesting that traffic control is one of the most difficult options in wildlife road mortality mitigation.

5. Mitigation for birds

Although most wildlife road mortality mitigation measures focus on mammals, reptiles, and amphibians, roads also can affect birds through fragmentation, isolation, and direct mortality. Although most birds possess the ability to fly over roads rather than walk or run across them, they also have some unique problems. Birds often define territories by the use of songs, and if those songs cannot be heard over (or are distorted by) vehicular traffic noise, males may find it difficult to attract and keep mates (Ferris, 1979; Reijnen et al., 1995). Traffic noise could potentially force males to conduct wider searches for females and bring them closer to roads. Many migrating species rely on starlight navigation (Emlen, 1975), thus light pollution from a variety of sources, including highway lighting, may cause birds to become disoriented, resulting in collisions with automobiles (Ogden and Evans, 1996). Non- or low-flying birds (e.g., quail, turkeys, owls), birds that forage at ground level, and scavengers are even more susceptible to road mortality because of their habits (Stoner, 1925). Therefore, birds present several road mortality mitigation challenges compared to other vertebrates. Jacobson (2005) addressed several of these problems and suggested possible solutions, including the reduction of noise and light pollution.

6. Conclusions

Everyone (transportation officials, wildlife biologists, the general populace) can agree that collisions between vehicles and wildlife are undesirable. Unfortunately, the reduction of such collisions is difficult and nuanced because of many factors, including economics, human attitudes, and wildlife biology. The inherent problem when designing effective wildlife-crossing structures concerns the need to accommodate high priority species while maintaining an economic and structurally sound building plan. When possible, target sites for road mortality mitigation should be identified *a priori* in consultation with transportation planners and wildlife biologists, but more often are identified *a posteriori*. Either way, mitigation approaches usually are targeted for a particular species or group of organisms. Although many studies have reported on the use of various structures for reducing road mortality, relatively few have measured the success of such structures. As such, more research is needed concerning the effectiveness of various road mortality mitigation programs. Although specific recommendations are best made in consultations among planners, engineers, and local biologists, we provide below some general recommendations regarding wildlife collision reduction:

(1) Preconstruction planning is generally more economical than retrofitting existing roads and potentially could be considered during environmental impact assessments.
(2) Connectivity of habitat and permeability of road systems are important factors.
(3) Financial considerations may dictate nonstructural approaches to collision reduction, but structural methods are probably more effective (and more expensive).
(4) Finally, the efficiency of road mortality mitigation approaches should be determined via a post-implementation monitoring program.

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CASA DIABLO GEOTHERMAL DEVELOPMENT PROJECT:

DEER MIGRATION STUDY, SPRING 1987

Thomas E. Kucera

INTRODUCTION

A proposal has been made to develop a geothermal electric generating plant in the southwest portion of Long Valley in Mono County, California. The development, known as the Casa Diablo Geothermal Project, has raised concerns with respect to potential deleterious impacts on migratory mule deer (*Odocoileus hemionus*) which use the project area and vicinity. The Biotic Assessment of the project prepared in January 1987 was considered by the management agencies involved to be deficient in data on migratory mule deer in the area. The present investigator was subsequently contracted to gather data to allow an assessment of the importance of the area to migratory deer through an annual cycle, i.e., spring, summer and fall. No wintering activity is to be expected. This report concerns only the period of spring migration.

This part of the Eastern Sierra Nevada is known for its visual and biological resources, and the quality of the natural environment. Among the most important components of this natural environment, symbolically, esthetically and economically, are the impressive numbers of mule deer. Only in the last three years has intensive ecological research on these animals been conducted. It is now known that more than half of the 6000 deer which winter near Bishop migrate to the north and pass near the town of Mammoth Lakes to get to their summer ranges (Kucera, unpubl.). The annual life cycle of deer in the Eastern Sierra Nevada may be divided into four periods: winter, spring migration and staging, summer, and fall migration. These seasonal movements are a response to the seasonal availability of habitat, and as parts of

a component system, all are important in maintaining deer populations.

Most deer in this part of the Eastern Sierra winter at lower elevations some 20 airline miles to the southeast and east of the proposed geothermal area (Figure 1). Several "herds" as defined by the California Department of Fish and Game (DFG) are of concern in the present situation. These are the Buttermilk and Sherwin Grade herds, which winter in Round Valley, at the base of the eastern escarpment of the Sierra Nevada just west of Bishop, and the Casa Diablo herd, which winters between the Benton Range and the White Mountains, from the Casa Diablo Peak area north past the town of Benton (DFG 1984, 1985a, 1985b).

The spring migration begins in April, when deer leave their winter ranges and move to intermediate altitudes. They congregate in "staging areas" for as long as six weeks, feeding on spring vegetation and regaining condition lost over the winter, until they move to summer ranges. Here, mainly west of the Sierra Crest, fawns are produced and reared. The fall migration back to the winter range typically is more rapid than that of the spring, and usually is patterned by fall storms. Deer arrive on the winter range during September, October and November, breed in December and January, and begin the annual cycle again.

The objective of the present work is to describe and quantify the amount, timing and specific locations of mule deer use of the Casa Diablo Geothermal Project Area ("Study Area") during the Spring 1987 deer migration. This information is designed to meet the information needs of public resource management and planning agencies with respect to baseline

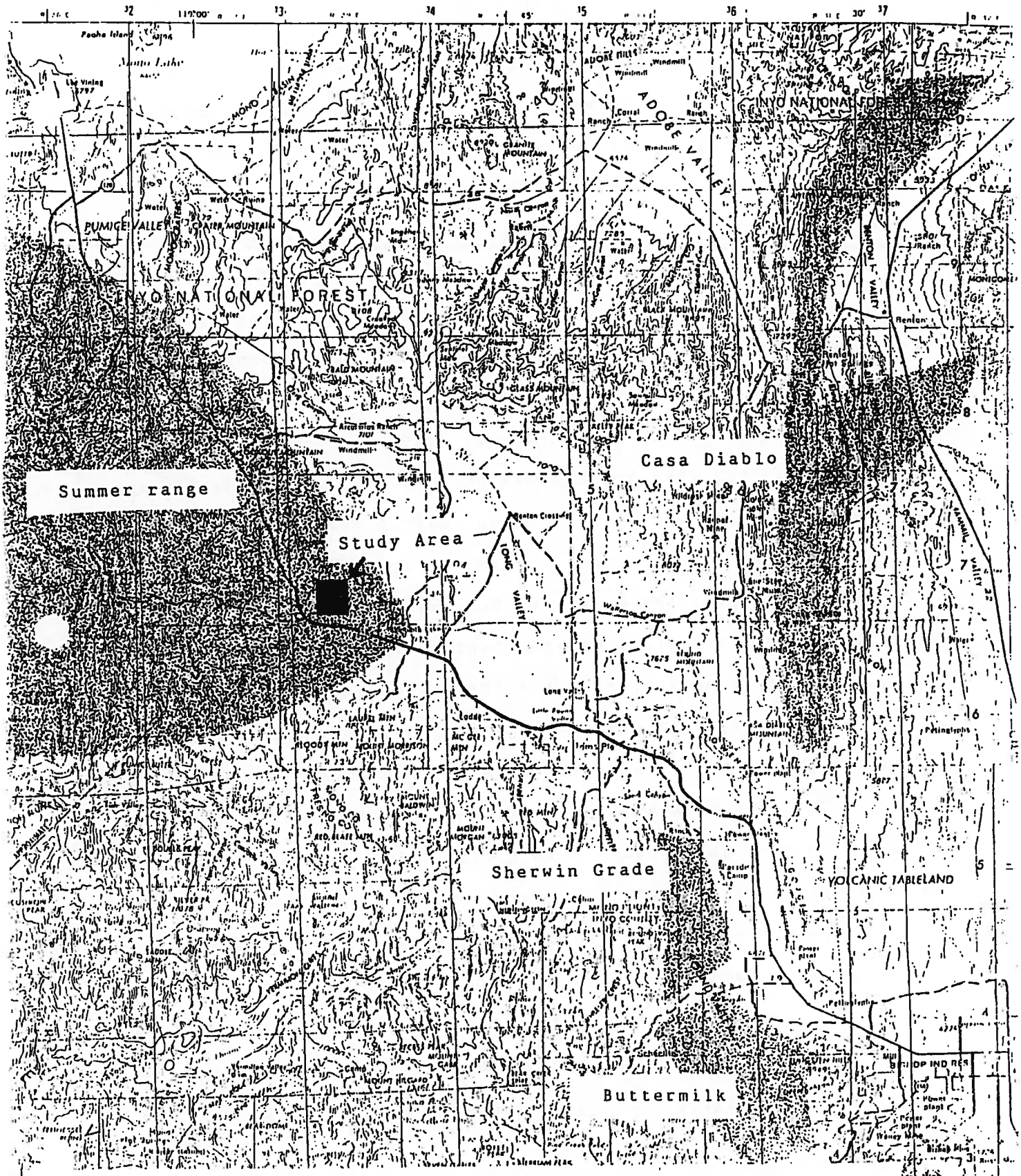

Figure 1. Regional map indicating locations of Buttermilk, Sherwin Grade and Casa Diablo Winter ranges, and approximate summer ranges of deer using the Long Valley area on migration.

conditions in the Study Area, and to assist in assessing impacts to deer of a geothermal development and designing measures to reduce those impacts.

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This investigation was conducted under a contract from Environmental Management Associates, Brea CA. Some of the data presented here are from a larger investigation of Eastern Sierra deer supported by the Bishop Resource Area of the Bureau of Land Management, the California Department of Fish and Game, Inyo and Mono Counties, the University of California, Berkeley, and several private funding organizations. Most of the fieldwork was conducted by Timothy Taylor.

The data in this report are to be used solely for the purposes of planning and analyzing potential environmental impacts of the proposed Casa Diablo Geothermal Project, and are not for publication, citation, or other use without the permission of the author.

STUDY AREA

The Casa Diablo Geothermal Study Area is located in portions of Sections 29 and 32 of T. 3 S, R. 28 E, Mono County, CA (Figure 2). It is immediately north of Highway 395, approximately 3 miles east of the town of Mammoth Lakes. The land is a mixture of both public and private ownership.

METHODS

A track survey route was laid out on the dirt roads which pass through the Study Area (Figure 2). This route was divided and marked into 20 sections each 0.1 miles long except Section 1, which was 0.2 miles long. In adition, the dirt road leading from

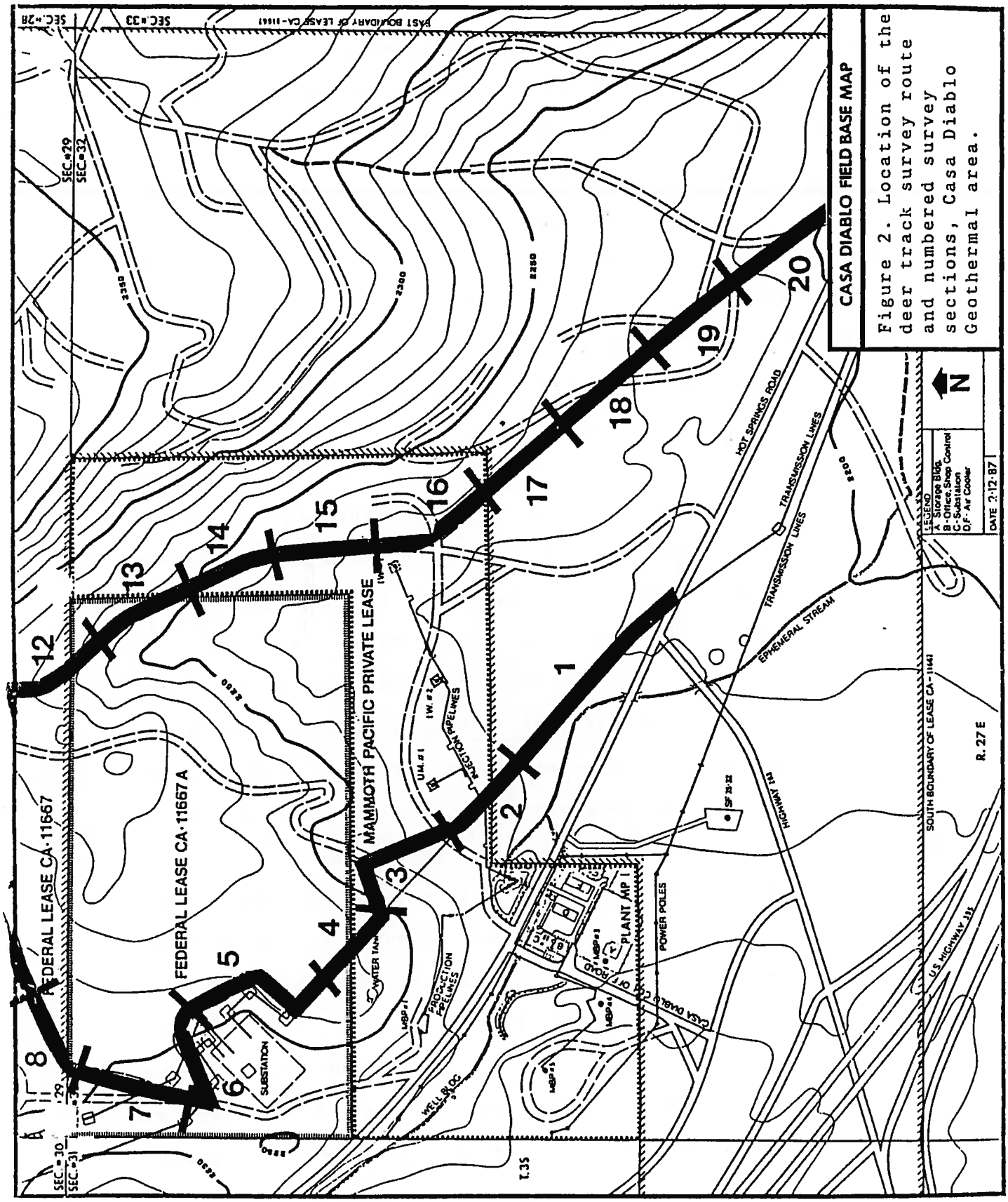


Figure 2. Location of the deer track survey route and numbered survey sections, Casa Diablo Geothermal area.

Hot Springs Road to well SF 35-32 was included in the surveys.

Beginning on 21 April 1987, the entire route was cleared of tracks and a tracking substrate prepared by dragging it with a "sled" of automobile tires pulled by a vehicle. This was done in late afternoon, and the following morning, the route was walked or driven and all deer tracks observed on the road were counted, both by survey section and by direction of travel. Data recorded were the number of individual deer making the observed tracks and their direction of travel. Because the route was dragged each evening before a survey to obliterate all tracks, the tracks counted on the surveys were made by animals within approximately the previous 12-18 hours. Recording tracks by survey section was designed to give a quantitative picture of the local pattern of deer movement in the Study Area. Recording tracks by direction of movement was designed to allow separation of back-and-forth or very localized movements from migrational movements.

RESULTS

1. Timing of deer activity

Figure 3 shows the total number of tracks made by individual deer throughout the period of study, presented without regard to direction of movement. A pattern of a gradual increase in the number of tracks throughout the period is apparent, with the greatest number of tracks counted, 20, on 13 June.

Figure 4 shows the breakdown of tracks counted on the surveys by direction of movement. Movements to the north and west are generally in the direction of the spring migration; those to the south and east west are opposite. Thus, subtracting the south and east-moving tracks from the north and west-moving ones,

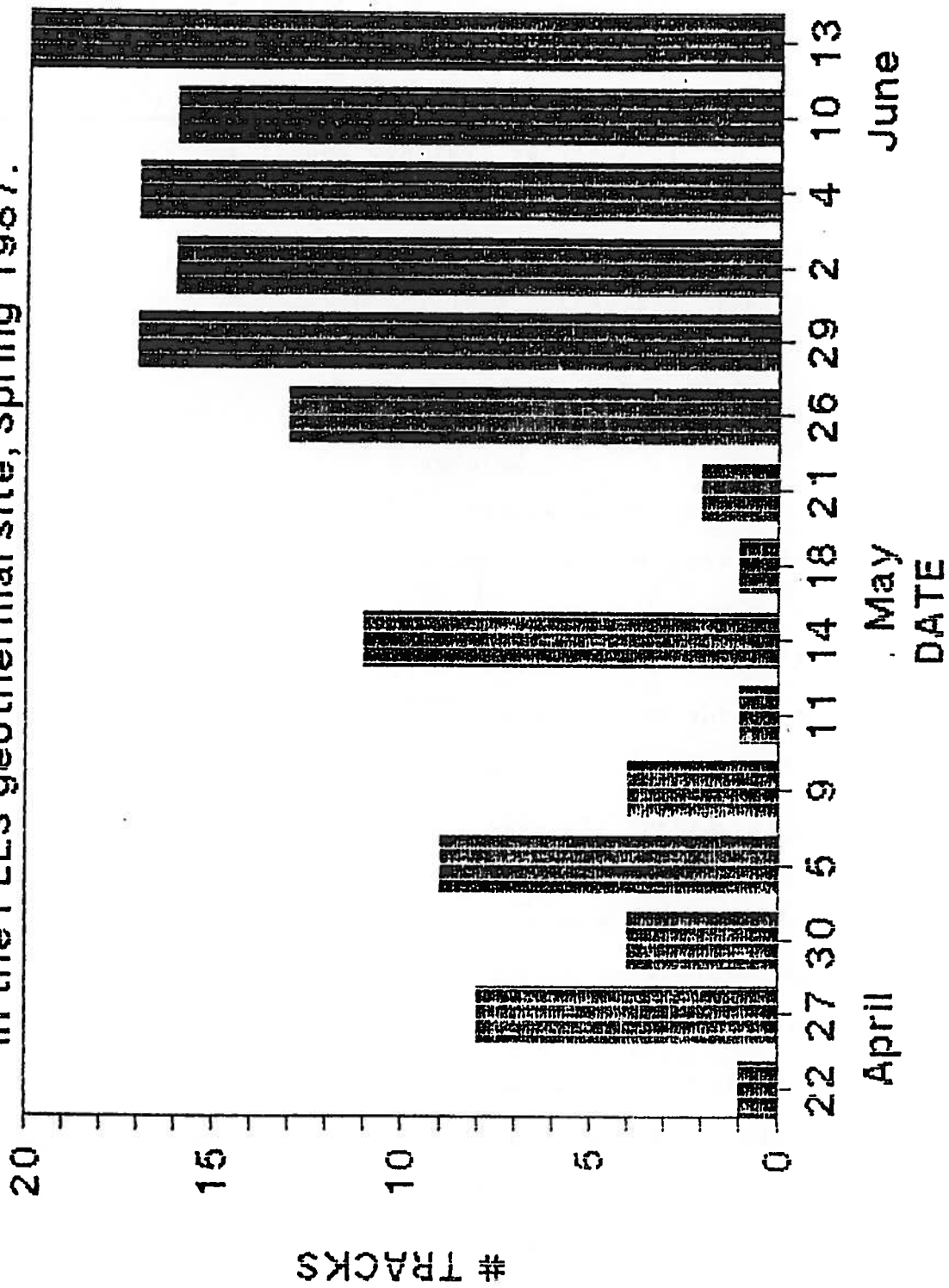


Figure 3. Total deer tracks counted on surveys in the PLES geothermal site, Spring 1987.

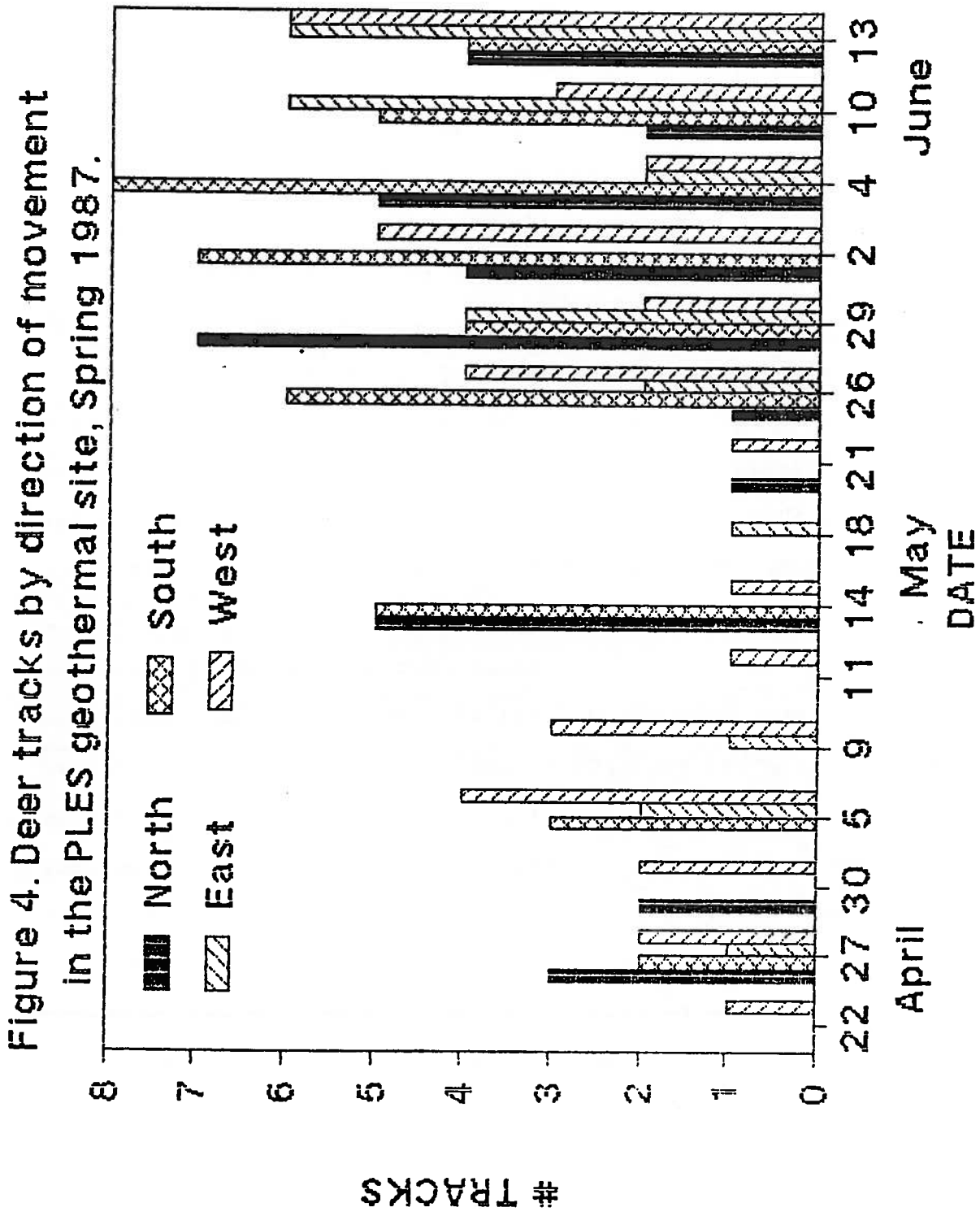


Figure 4. Deer tracks by direction of movement in the PLES geothermal site, Spring 1987.

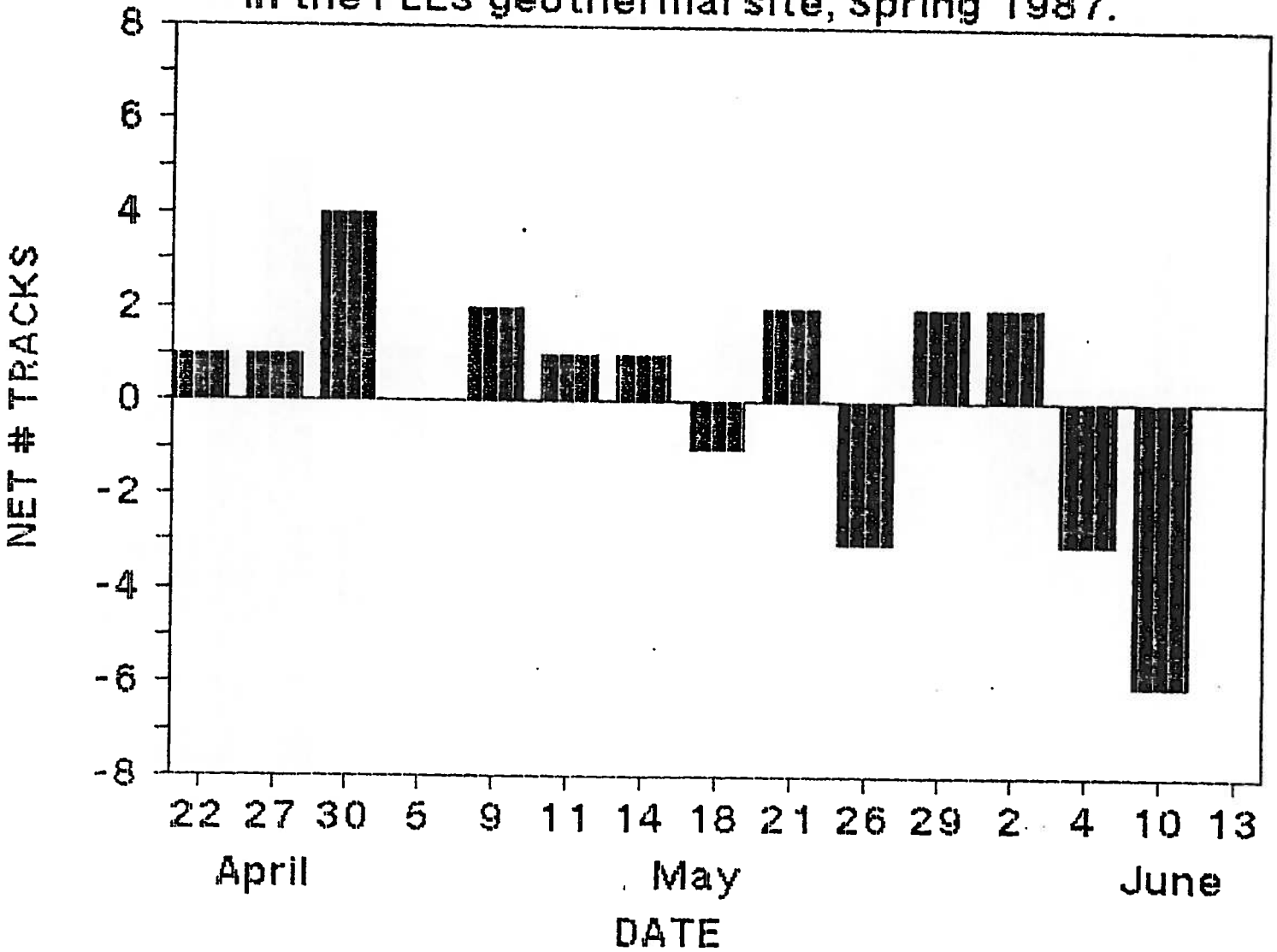
respectively, yields a crude estimate of the net number of deer moving through between the the dragging of the route and the survey. This is shown in Figure 5, in which the number of tracks heading south was subtracted from those heading north, and the number of tracks heading east was subtracted from those heading west, on each survey. Negative numbers may be interpreted as indicating predominantly localized, nondirectional movements. As indicated in Figure 5, most migrational movements in the Study Area occurred throughout late April and May. Beginning in late May, the negative net track numbers indicate fewer directional or migrational movements and more local movements, likely from deer on what will be their summer range.

2. Locations of deer movements

Figure 6 presents the total number of deer tracks by survey section counted during the spring of 1987. The large number of tracks indicated for Section 1 is somewhat misleading because that section is twice as long as the others. With this in mind, the distribution of tracks in the survey sections appears rather uniform. The net tracks by survey section are presented in Figure 7. No consistent pattern of movements is indicated. It is apparent that directional movements occurred in Sections 8, 10-12 and 18-20, which correspond to the most northerly and northwesterly, and southwesterly portions, respectively, of the Study Area.

Additionally, on the road to well SF 35-32, single sets of west-moving tracks were observed on 10, 18, 21 and 26 May. Throughout the survey period, only two deer were observed; on 4 June, 2 adult females were seen near Sections 10 and 11. No

Figure 5. Net numbers of tracks by direction of movement in the PLES geothermal site, Spring 1987.



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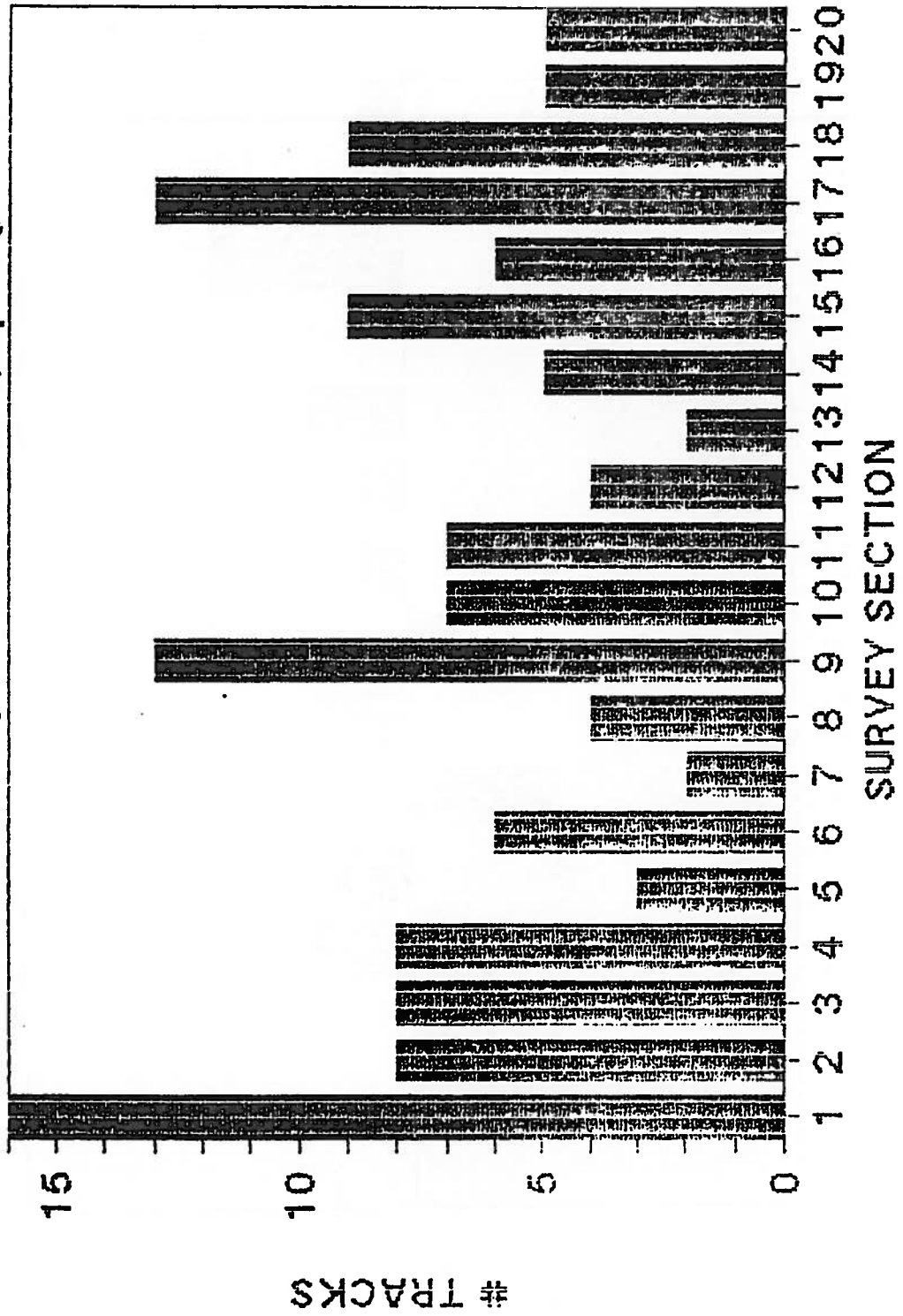

Figure 6. Total numbers of tracks counted by survey section in the PLES geothermal site, Spring 1987.

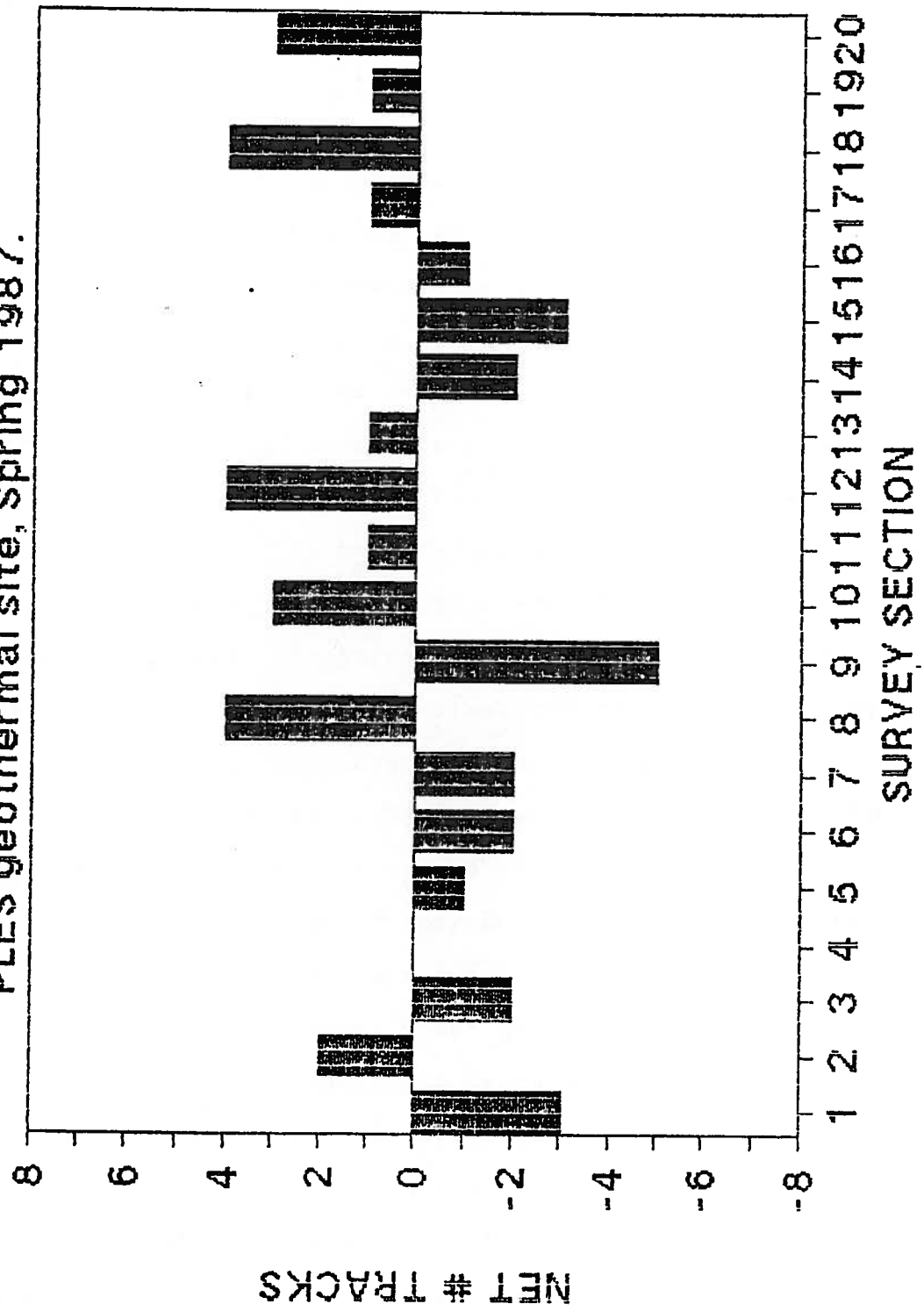

Figure 7. Net numbers of tracks by survey section, PLES geothermal site, Spring 1987.

specific areas of deer movement or well-defined concentration areas were apparent from covering the area on foot.

DISCUSSION

Results of the spring 1987 track surveys indicate a generally somewhat dispersed pattern of deer activity in and movement through the Study Area. No well-defined migration trails were observed, and the track counts indicate deer activity in all sections. One could make the rather weak case that Figure 7 shows a preference for the less developed portions of the area, i.e., Sections 8, 10-13, and 17-20, but the data are hardly compelling.

Nevertheless, deer movement through the area was apparent, and the number of animals involved can be at least roughly estimated. On the assumption that the period of spring migration was 15 April to 2 June, the 12 surveys covered approximately 25% of the 48 days in this period. The net number of tracks during this period was 13 (Figure 5). Assuming this to be a reasonable approximation of the number of deer actually moving through between the time the road was dragged and when tracks were counted the next morning, a total of 52 (13/0.25) deer moved through the Study Area during the survey period. This does not take into account those deer that may have moved through during the day. Making the assumption that 75% of deer would migrate at night (between dragging and counting) and 25% would migrate during the day, a grand total of 69 (45/0.75) deer moving through during the spring period can be estimated, given the stated assumptions.

This estimate of 69 deer is meant only as an approximation of the number of deer using the Study Area on spring migration.

Potential sources of error, e.g., multiple counts of the same animal, or tracks missed because of poor tracking medium, are impossible to quantify. However, the precise number is not important; what matters is the estimate of magnitude. There certainly are not hundreds or thousands of animals using the area, as is the case in other local areas, but likely there are dozens. This movement does not appear to be concentrated in any localized portion of the Study Area, but is dispersed throughout it, which may not be surprising given its relatively small area and lack of extreme topography. It is likely that deer from three designated "herds" are involved: the Buttermilk, Sherwin Grade, and the Casa Diablo herds. Radioed or otherwise marked deer from all three herds have been observed in the vicinity of the Study Area.

Recent radio-telemetry information indicates that, in general, most of the Buttermilk and Sherwin Grade deer which migrate north do so along the base of the mountains west of Highway 395. Likewise, most Casa Diablo deer move along the base of the Glass Mountains northwest of the Study Area. A portion of each herd, however, does move near or right through the Study Area. The specific areas used as migration corridors are probably dictated as such by both local topography and tradition.

Impacts of geothermal development on these migrating deer are difficult to predict precisely, but in a general sense are a function both of the location, amount and kinds of changes associated with the development, and of the availability of potential alternate travel routes. It seems to be the case that deer activity is rather dispersed throughout the area. The

locations of the proposed project facilities (Fig. 8), including a number of proposed wells, pipelines, and a transmission line and access road, as well as the power plant site, in general are adjacent to the existing geothermal plant and facilities. Assuming a "worst case" scenario, one in which deer completely avoid the proposed facilities and associated human disturbance, it is difficult to see how making several dozen deer move several hundred yards around the facilities would constitute a great hardship. Given the existing terrain, such an avoidance would likely have a trivial impact on migrating deer. Of course, certain facilities, e.g., fences, pipelines, etc., could be designed to minimize any impacts to deer and to facilitate their passage.

From the standpoint of deer migration, the locations of the proposed facilities (Figure 8) are preferable to those of the alternate site (Figure 9). This latter alternative would move the power plant to the northeast, across Hot Springs Road, and effectively increase the area impacted by the project. In general, the more concentrated an area of disturbance, the less will be its deleterious impacts.

Thus, at present, alternate routes for spring migration exist, giving deer an opportunity to avoid the project area if developed. However, there are proposals for additional developments in the region. Although it is impossible to discuss thoroughly the impacts of a project without reference to the context in which the project occurs, a regional summary and analysis taking such additional projects into account are not within the scope of the present work. No doubt the consequences

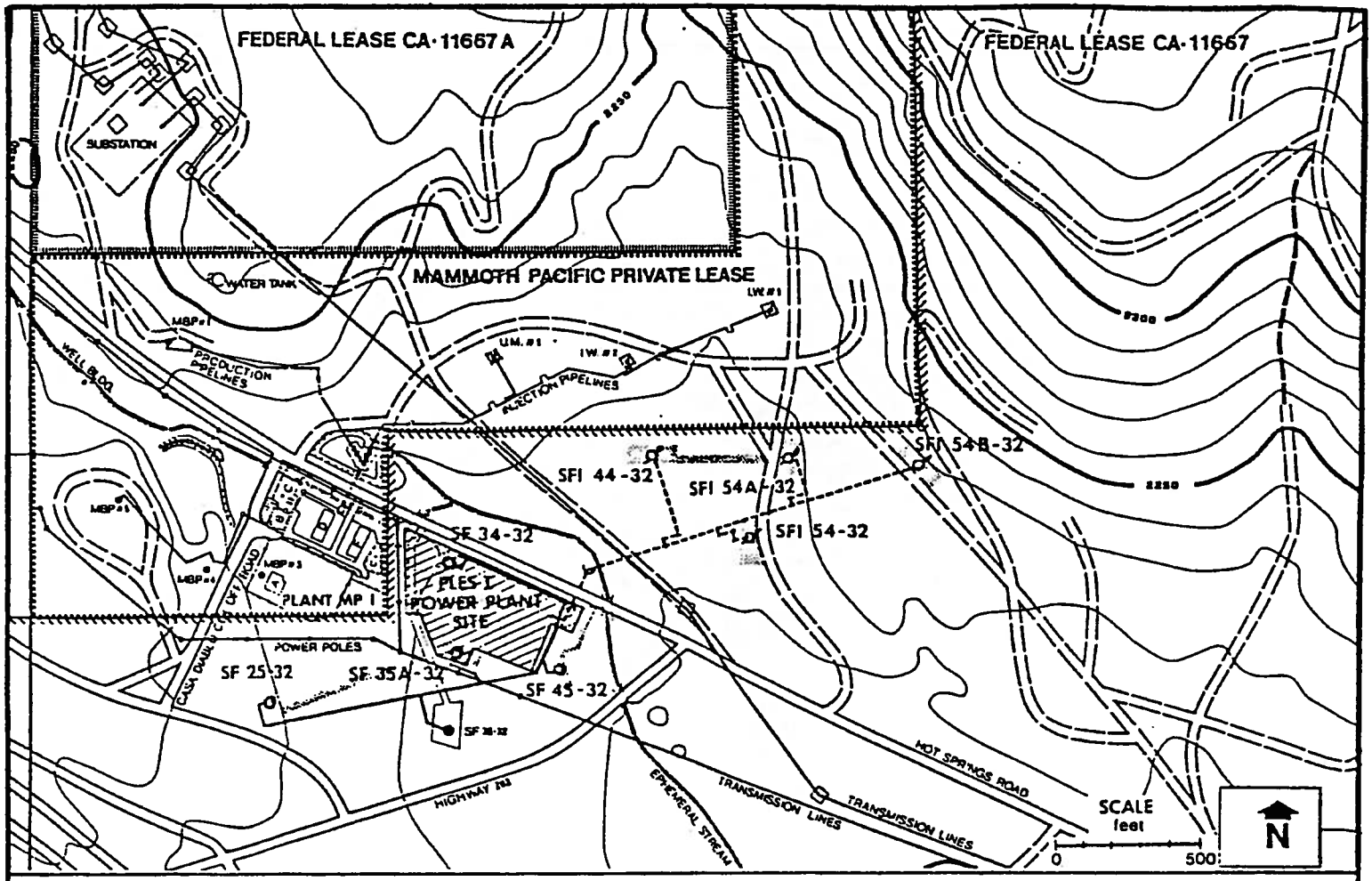

Figure 8. Proposed facilities locations, Casa Diablo Geothermal area.

- Proposed Production Well
- Existing Production Well (SF 35-32)
- Proposed Injection Well
- New Access Road and Well Sites
- Production Pipeline
- Injection Pipeline
- New Electric Transmission Line

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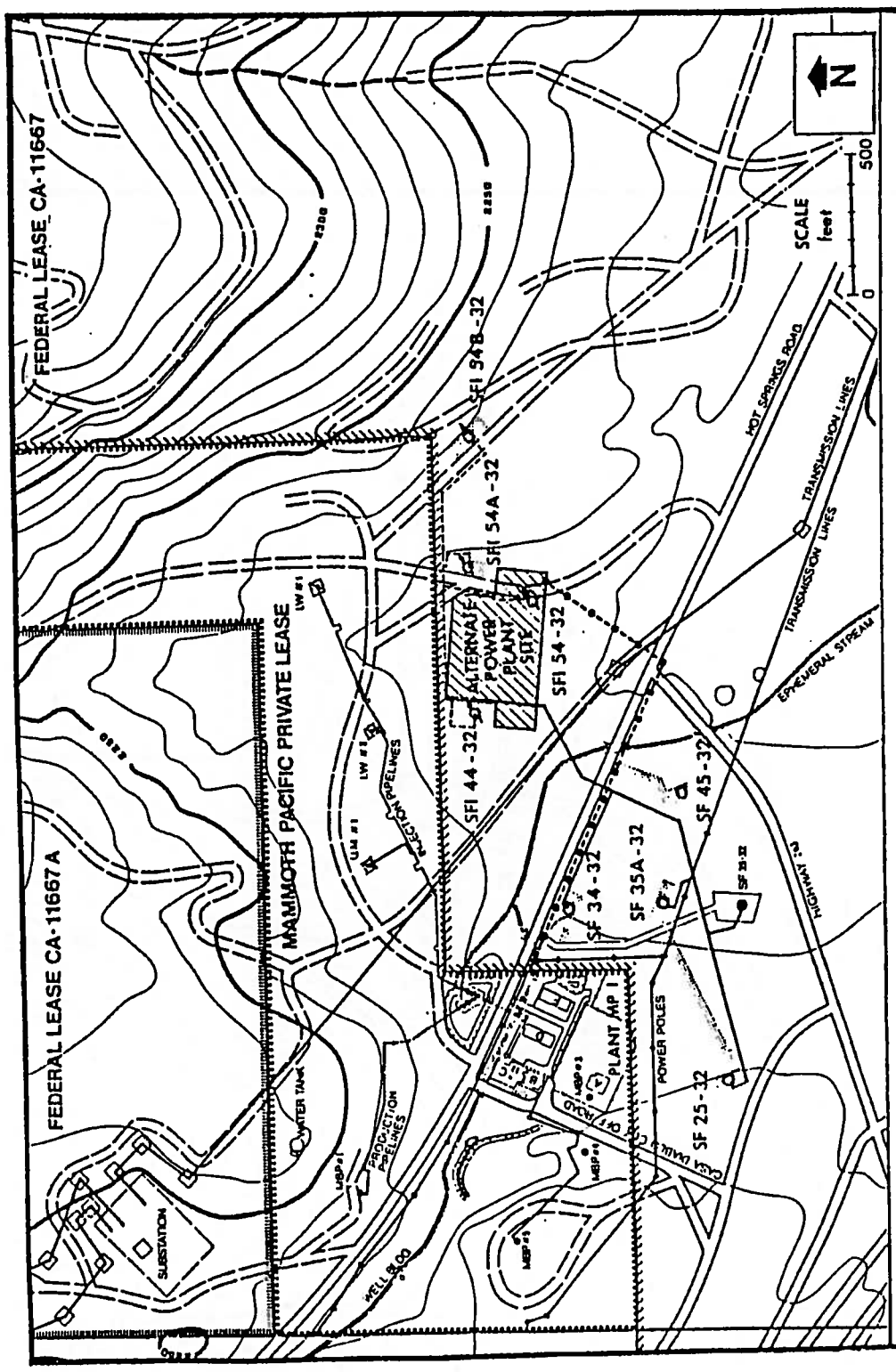

Figure 9. Alternate facilities locations, Casa Diablo Geothermal area.

of some of these proposed projects, because of their nature, size, and/or geographic location, are potentially much greater than those to be anticipated from Casa Diablo. Others may be more benign. A comprehensive study of the cumulative impact of potential development, however desirable from a resource management perspective, is not possible within the time constraints of this project.

The present investigation and discussion indicate that the Casa Diablo Geothermal Project, considered by itself, will likely not have a significant impact upon the spring migration. In the worst and unlikely case that deer avoid the project entirely, there are at present alternate routes available to allow migrating deer to reach their summer ranges. Thus, the Casa Diablo Geothermal Project by itself will likely have minimal negative impact.

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Quantifying Threats to Imperiled Species in the United States

Assessing the relative importance of habitat destruction, alien species, pollution, overexploitation, and disease

David S. Wilcove, David Rothstein, Jason Dubow, Ali Phillips, and Elizabeth Losos

Biologists are nearly unanimous in their belief that humanity is in the process of extirpating a significant portion of the earth's species. The ways in which we are doing so reflect the magnitude and scale of human enterprise. Everything from highway construction to cattle ranching to leaky bait buckets has been implicated in the demise or endangerment of particular species. According to Wilson (1992), most of these activities fall into four major categories, which he terms "the mindless horsemen of the environmental apocalypse": overexploitation, habitat destruction, the introduction of non-native (alien) species, and the spread of diseases carried by alien species. To these categories may be added a fifth, pollution, although it can also be considered a form of habitat destruction.

Surprisingly, there have been relatively few analyses of the extent to which each of these factors—much less the more specific deeds encompassed by them—is responsible for endangering species. In general, scientists agree that habitat destruction is currently the primary lethal agent (Ehrlich 1988, Wilson 1992), followed by the spread of alien species (Wilson 1992). However, apart from several notable exceptions—including studies of North American fishes by Williams et al. (1989), endangered plants and animals in the United States by Flather et al. (1994, 1998), aquatic organisms by Richter et al. (1997), and imperiled birds by Collar et al. (1994)—few quantitative studies of threats to species have been conducted. More such studies are needed to provide conservationists, land stewards, and decision makers with a better understanding of the relationships between specific human activities and the loss of biodiversity.

Habitat loss is the single greatest threat to biodiversity, followed by the spread of alien species

In this article, we quantify the extent to which various human activities are imperiling plant and animal species in the United States. Our analysis has two parts: a coarse-scale examination of the numbers and types of US species imperiled by the major categories of threats, and a fine-scale analysis of the types of habitat destruction affecting US plants and animals protected under the federal Endangered Species Act (ESA). We also speculate on how these threats have changed over time and are likely to change in the future. We conclude with a brief discussion of the implications of our findings for the long-term protection of imperiled species in the United States.

An overview of the threats

To obtain an overview of the threats to biodiversity in the United States, we tabulated the number of species threatened by five categories of threats: habitat destruction, the spread of alien species, overharvest, pollution (including siltation), and disease (caused by either alien or native pathogens). We restricted this coarse-scale analysis to imperiled plants and animals occurring within the 50 states and falling into any of four categories: all full species of mammals, birds, reptiles, amphibians, and fish with status ranks of "possibly extinct," "critically imperiled," or "imperiled," as determined by The Nature Conservancy (TNC) in association with the Network of Natural Heritage Programs and Conservation Data Centers (Master 1991); all full species of freshwater mussels, butterflies and skippers, tiger beetles, and dragonflies and damselflies with status ranks of possibly extinct, critically imperiled, or imperiled, as determined by TNC; all full species of vascular plants with status ranks of possibly extinct or

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Table 1. Taxonomic breakdown of species used in the coarse-scale analysis. Included are species classified as imperiled by The Nature Conservancy and all species, subspecies, and populations that, as of January 1996, are listed as endangered or threatened under the Endangered Species Act or have been formally proposed for listing.

	Number of imperiled species	Number of imperiled species with threats data	Percentage of imperiled species with threats data
Vertebrates	541	494	91
Mammals	88	85	97
Birds	101	98	97
Reptiles	40	38	95
Amphibians	69	60	87
Fishes	243	213	88
Invertebrates	471	331	70
Dragonflies and damselflies	33	18	54
Freshwater mussels	150	102	68
Crayfish	110	67	61
Tiger beetles	8	6	75
Butterflies and skippers	46	33	72
Other invertebrates	124	104	84
Plants	1478	1055	71
Total	2490	1880	75

critically imperiled, as determined by TNC; and all species, subspecies, or vertebrate populations listed by the US Fish and Wildlife Service (USFWS) or the National Marine Fisheries Service as threatened or endangered or officially proposed for listing under the ESA as of 1 January 1996. (The ESA permits the listing of species and subspecies of plants and animals as well as "distinct population segments" of vertebrates.) A total of 2490 imperiled species, subspecies, and populations fit these criteria.

Information on the threats to each of these species, subspecies, and populations was obtained from a number of sources, including the *Federal Register* (i.e., the listing notices published for all species designated as threatened or endangered under the ESA), a survey of biologists conducted by Richter et al. (1997) for aquatic species, the Natural Heritage Central Databases managed by TNC, and interviews with specialists in particular species groups and geographical regions. We included only known threats and excluded potential or hypothetical ones. We did not attempt to distinguish between ongoing and historical threats, partly because such information is usually lacking and partly because the distinction itself is problematic in the case of habitat destruction. Nor did we try to distinguish between major and minor threats to each species because such information was not consistently available. In a few cases, it was impossible to assign a particular human activity to one of the major threat categories; we excluded these activities from our coarse-scale analysis.

We were able to obtain information on threats for 1880 (75%) of the 2490 imperiled species, subspecies, and populations that met our criteria for inclusion in this study (Table 1). (For 52 of the species, we could not identify any anthropogenic threats.) We used the resulting database to determine the relative significance of the major threats categories and to investigate differences between species groups in their vulnerability to particular threats. We compared the distribution of threats among plants and animals, among vertebrate and invertebrate animals, and within vertebrate classes. We also compared the distribution of threats among terrestrial and aquatic species, Hawaiian and mainland vascular plants, and Hawaiian and mainland birds. For all comparisons, statistical significance was assessed using the chi-squared contingency test (two-tailed).

We emphasize at the outset that there are some important limitations to the data we used. The attribution of a specific threat to a species is usually based on the judgment of an expert source, such as a USFWS employee who prepares a listing notice or a state Fish and Game employee who monitors endangered species in a given region. Their evaluation of the threats facing that species may not be based on experimental evidence or even on quantitative data. Indeed, such data often do not exist. With respect to species listed under the ESA, Easter-Pilcher (1996) has shown that many listing notices lack important biological information,

Table 2. Percentages of species in different groups that are imperiled by habitat degradation and loss, alien species, pollution, overexploitation, and disease. Categories are nonexclusive and therefore do not sum to 100.

Cause	All species (n = 1880)	Vertebrates (n = 494)	Invertebrates (n = 331)	Plants (n = 1055)	Mammals (n = 85)	Birds (n = 98)	Reptiles (n = 38)	Amphibians (n = 60)	Fishes (n = 213)	Freshwater mussels (n = 102)	Crayfish (n = 67)	Tiger beetles (n = 6)	Butterflies and skippers (n = 33)	Other invertebrates (n = 104)
Habitat degradation/loss	85	92	87	81	89	90	97	87	94	97	52	100	97	94
Alien species	49	47	27	57	27	69	37	27	53	17	4	0	36	52
Pollution	24	46	45	7	19	22	53	45	66	90	28	0	24	19
Overexploitation	17	27	23	10	45	33	66	17	13	15	0	33	30	46
Disease	3	11	0	1	8	37	8	5	1	0	0	0	0	0

including data on past and possible future impacts of habitat destruction, pesticides, and alien species. Depending on the species in question, the absence of information may reflect a lack of data, an oversight, or a determination by USFWS that a particular threat is not harming the species. The extent to which such limitations on the data influence our results is unknown.

Ranking the threats

Table 2 presents a summary of the percentages of species that are imperiled by habitat loss, alien species, pollution, overexploitation, and disease. Not surprisingly, habitat destruction and degradation emerged as the most pervasive threat to biodiversity, contributing to the endangerment of 85% of the species we analyzed (Figure 1). Indeed, habitat loss is the top-ranked threat (in terms of the number of species it affects) for all species groups. Competition with or predation by alien species is the second-ranked threat in the overall analysis, affecting 49% of imperiled species.

Alien species affect a higher proportion of imperiled plants (57%) than animals (39%); this difference is statistically significant (chi square = 60.23, d.f. = 1, $P<<0.001$). However, certain groups of animals (most notably birds and fish) appear to be as broadly affected as plants by alien species. There is also an unsurprising biogeographic component to the alien species problem: Higher proportions of Hawaiian birds and plants than continental birds and plants are threatened by alien species (Table 3, Figure 2). Similarly, a much higher proportion of Hawaiian birds is threatened by disease than is the case for continental birds. By contrast, nearly the same proportion of Hawaiian plants and continental plants are affected by disease (Table 3, Figure 3).

For all aquatic animal groups (amphibians, fish, dragonflies and damselflies, freshwater mussels, and crayfish), pollution is second only to habitat loss as a cause of endangerment. Our finding that a large number of aquatic species are threatened by pollution may reflect the fact that our definition of pollution includes siltation, which is one of the leading threats to aquatic biodiversity in North America (Richter et al. 1997).

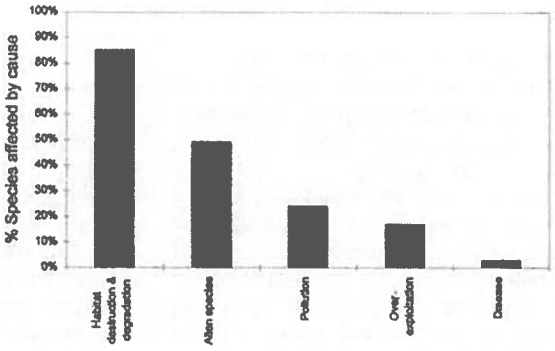

Figure 1. The major threats to biodiversity. Data refer to species classified as imperiled by The Nature Conservancy and to all endangered, threatened, and proposed species, subspecies, and populations protected under the Endangered Species Act. See also Table 2.

A closer look at habitat destruction

Given the primacy of habitat destruction as a threat to biodiversity, we examined its causes in greater detail. For this fine-scale analysis, we focused exclusively on US species, subspecies, and populations that have been added to the federal endangered species list or have been formally proposed for such listing by USFWS as of 1 January 1996. We focused on listed species because more information is usually available for them than for imperiled but unlisted species. We also included species that are federally listed or proposed for listing from Puerto Rico, the US Virgin Islands, and the Pacific Trust Territories. A total of 1207 species, subspecies, and populations was included in this phase of the analysis (Figure 4). (USFWS has listed as endangered all Hawaiian snails of the genus *Achatinella*. Approximately 41 species in that genus have been described to date, of which at least 18 are thought still to survive. However, USFWS did not treat these species individually in its formal listing notice in the *Federal Register*. For the purposes of this part of our analysis, we have therefore counted the entire genus as one "species.")

Categorizing habitat destruction. For the fine-scale analysis, we divided habitat destruction and degradation into 11 major categories (see box page 611). As in the coarse-scale analysis, we did not distinguish between current and historical threats or between major and minor threats. In many instances, the apparent threat to a species was actually spawned by another threat. Wherever possible, we attributed threats to their ultimate cause, based on the information in the *Federal Register*. For example, logging operations near a stream can lead to siltation, which is harmful to certain rare fishes and mussels. Thus, logging rather than siltation would have been scored as the threat to those fishes and mussels. For all comparisons of the prevalence of specific threats in different species groups, statistical significance was assessed using the chi-squared contingency test (two-tailed).

Again, we note some caveats with

Table 3. Percentages of imperiled birds and plants in Hawaii and in the continental United States that are threatened by habitat degradation and loss, alien species, pollution, overexploitation, and disease. Categories are nonexclusive and therefore do not sum to 100.

Cause	Continental US birds (n = 56)	Hawaiian birds (n = 42)	Continental US plants (n = 641)	Hawaiian plants (n = 414)
Habitat degradation/loss	88	93	90	66
Alien species	48	98	30	99
Pollution	38	2	12	0
Overexploitation	39	24	13	6
Disease	4	81	1	0

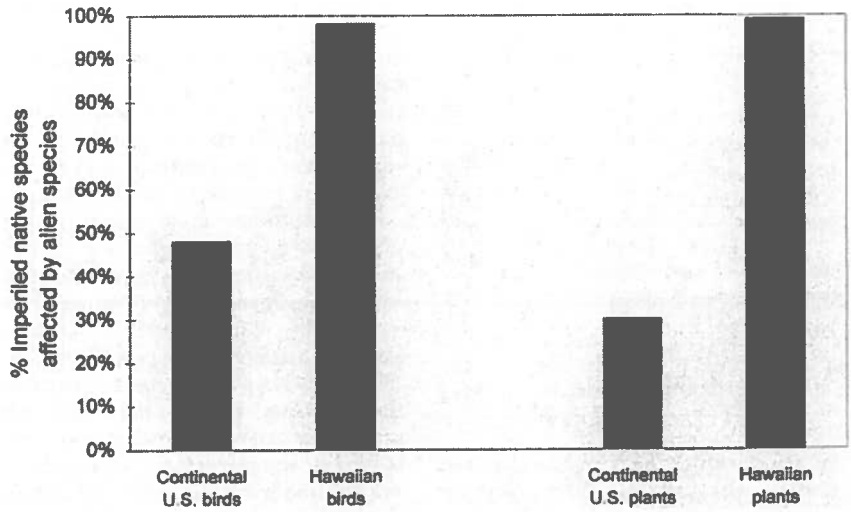

Figure 2. A comparison of the impacts of alien species on imperiled birds and plants in Hawaii and in the continental United States. A much higher proportion of Hawaiian birds and plants than continental birds and plants is threatened by alien species (chi-square = 27.60, d.f. = 1, P <<0.001 for birds; chi-square = 484.28, d.f. = 1, P<<0.001 for plants). Data are taken from Table 3.

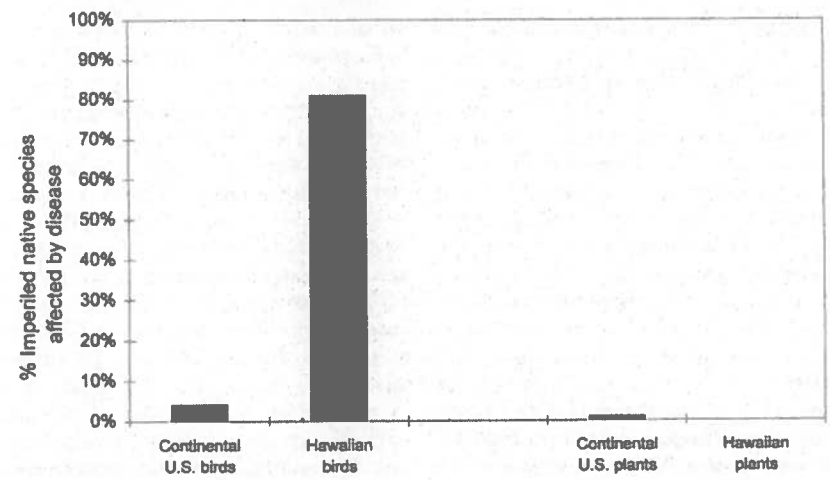

Figure 3. A comparison of the impacts of disease on imperiled birds and plants in Hawaii and in the continental United States. A much higher proportion of Hawaiian birds than continental birds is threatened by disease (chi-square = 62.03, d.f. = 1, P<<0.001). By contrast, similar proportions of Hawaiian and continental plants are affected by disease (although the difference is statistically significant: chi-square = 4.02, d.f. = 1, P = .045).

respect to the data in this phase of the analysis. Species added to the endangered list prior to 1980 (238 species) tended to have fewer threats delineated in the listing notices than species listed in later years. Although there may be a biological basis for this difference, we strongly suspect that it reflects the less controversial nature of endangered species protection at that time. Before 1980, USFWS probably was under less pressure to produce detailed justifications for its listing decisions. We do not know how this pattern may have influenced our results. Also, as noted in our coarse-scale analysis, assessments of the threats to individual species are often based on the subjective opinions of knowledgeable individuals, rather than experimental evidence or quantitative data.

Ranking the causes of habitat destruction. The most overt and widespread forms of habitat alteration were, as might be expected, the leading threats to species that are either listed or proposed for listing (hereafter referred to collectively as "endangered" species), as measured by the number of species they affect (Table 4). These forms include agriculture (affecting 38% of endangered species), commercial development (35%), water development (30% when agricultural diversion is included; 17% for just dams, impoundments, and other barriers), and infrastructure development (17%). Not surprisingly, the impacts of water development are felt most acutely by aquatic species. Ninety-one percent of endangered fish and 99% of endangered mussels are affected by water development, in contrast to 10% of mammals and 22% of birds. Within the category of infrastructure development, roads affect a wide array of species (15% of all endangered species), confirming their reputation as "a leading threat to biodiversity" (Noss and Cooperrider 1994).

Outdoor recreation also harms a large number of endangered species (27%). It affects a significantly higher proportion of plants than animals (33% vs. 17%; chi square = 39.03, d.f. = 1, P<<0.001). Within the category of outdoor recreation, the use of off-road vehicles is implicated in the demise of approximately 13% of endangered species.

Among extractive land uses, logging, mining, and grazing have contributed to the demise of 12%, 11%, and 22%, respectively, of the endangered species we analyzed. Both logging and mining are especially serious threats to freshwater mussels, probably because they result in increased amounts of silt, in the cases of both logging and mining, and of toxic pollutants, in the case of mining. Livestock grazing, on the other hand, is particularly harmful to plants, affecting 33% of endangered plant species compared to 14% of endangered animals; the difference is highly significant (chi square = 51.95, d.f. = 1, P<<0.001).

Finally, 168 species (14%) are threatened by disruption of fire regimes in the ecosystems in which they live. Of these, 85 (7%) are

threatened by fire suppression and 83 (7%) are threatened by controlled or uncontrolled fires.

Comparisons with other studies

Flather et al. (1994, 1998) catalogued the threats to US endangered species based on information from the *Federal Register*, the USFWS *Endangered Species Technical Bulletin*, recovery plans for individual species, federal agency reports, and consultations with USFWS biologists and state Natural Heritage Program scientists. Their analysis covered 667 species, subspecies, and populations protected by the ESA as of August 1992; it did not include species proposed for listing.

Although the way in which Flather et al. categorized threats was not identical to our approach, the major findings from the two studies can still be compared. These authors also identified habitat loss and alien species as the two most widespread threats to endangered species, affecting more than 95% and 35% of listed species, respectively. (Comparable figures from our study are 85% for habitat destruction and 49% for alien species.) The smaller percentage of species affected by exotics in Flather et al.'s study probably reflects the large number of Hawaiian species that were included in our study but were not on the endangered species list at the time Flather et al. conducted theirs. Flather et al. (1998) also point out that the relative frequency of particular threats to species varies geographically.

Two previous studies have focused on threats to aquatic species. Williams et al. (1989) catalogued threats to 364 species and subspecies of imperiled fish from Canada, the United States, and Mexico; Richter et al. (1997) surveyed aquatic biologists to identify the threats to 135 imperiled freshwater fishes, crayfishes, dragonflies and damselflies, mussels, and amphibians in the United States. Narrowing the scope of Williams et al. to imperiled US and Canadian fishes (254 species), we can compare their results with ours. The findings of the two studies are similar: Williams et al. identified habitat destruction and degradation as the most widespread threat to imperiled fishes, affecting 96% of the species (versus 94% in our study; Table 2). Next in significance was an amalgamated category of hybridization, alien species, predation, and competition, which affected 39% of the fish species (versus our tally of 53% for alien species, which probably covers most of the same threats). Finally, Williams et al. found that overharvest and disease affected 4% and 2%, respectively, of the fishes (versus 13% and 1% in our study).

Richter et al. (1997) concluded that the three leading threats to aquatic species nationwide were agricultural nonpoint pollution (e.g., siltation and nutrient inputs), alien species, and altered hydrologic regimes due to dams and impoundments. This conclusion is consistent with our findings from the fine-scale analysis, which identified pollution and impoundments (including dams) as significant threats to fish and mus-

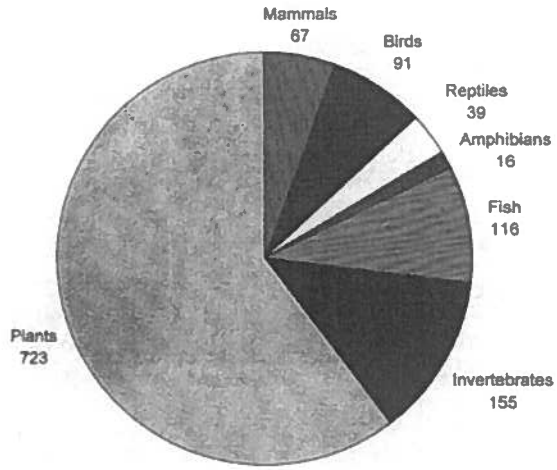

Figure 4. Taxonomic breakdown of the species, subspecies, and populations used in the fine-scale analysis. The 1207 species, subspecies, and populations include those that are listed as endangered or threatened under the Endangered Species Act or are proposed for listing.

The major categories of habitat destruction used in this analysis

- Agriculture (including agricultural practices, land conversion and water diversion for agriculture, pesticides and fertilizers; excluding livestock grazing)
- Livestock grazing (including range management activities)
- Mining, oil and gas, and geothermal exploration and development (including roads constructed for and pollutants generated by these activities)
- Logging (including impacts of logging roads and forest management practices)
- Infrastructure development (including bridges, dredging for navigation, and road construction and maintenance)
- Road construction and maintenance specifically (including logging and mining roads)
- Military activities
- Outdoor recreation (including swimming, hiking, skiing, camping, and off-road vehicles)
- Off-road vehicles specifically
- Water development (including diversion for agriculture, livestock, residential use, industry, and irrigation; dams, reservoirs, impoundments, and other barriers to water flow; flood control; drainage projects; aquaculture; navigational access and maintenance)
- Dams, impoundments, and other barriers to water flow specifically
- Pollutants (including siltation and mining pollutants)
- Land conversion for urban and commercial development
- Disruption of fire ecology (including fire suppression)

sels (Table 4). Our coarse-scale analysis, which included a larger pool of imperiled species than the fine-scale analysis, also highlighted the importance of alien species as a threat to US fish.

Richter et al. (1997) point out that there are important geographic differences in the nature of the threats facing aquatic species. Aquatic species in the eastern United States are experiencing particular harm from agricultural nonpoint pollution; in the West, the dominant threat is alien species, followed by habitat degradation and altered hydrologic regimes. Richter et al. attribute these differences to differences in both land use patterns in the East versus the West and in the ecological sensitivities of eastern versus western species.

Using information from USFWS recovery plans, Schemske et al. (1994) identified the primary cause of endangerment for each of 98 US plant species protected under the ESA. These authors did not distinguish between historical and contemporary threats, and they listed only one (i.e., the primary) threat per species, although they acknowledged that most species experience more than one threat. The top six threats in their study (in terms of frequency of appearance) were development (affecting 20.4% of the species); grazing (10.2%); collecting (10.2%); water control (8.2%); oil, gas, and mining (8.2%); and trampling (8.2%). By contrast, our coarse-scale analysis identified habitat destruction and alien species as the two most widespread threats to imperiled plants, affecting 81% and 57% of species, respectively. Moreover, in our fine-scale analysis of habitat destruction, the top five threats to imperiled plants protected under the ESA were land conversion (i.e., development; 36%), agriculture (33%), grazing (33%), outdoor recreation (33%), and disruption of fire ecology (20%).

The consistently higher percentages for all threats in our study compared to that of Schemske et al. (1994) undoubtedly stem from our practice of tallying multiple threats per species. Perhaps the most noticeable difference between the two studies lies in their assessments of the importance of alien species as a threat to rare plants. Schemske et al. (1994) considered alien species the primary threat to only 6.1% of the plants they studied, whereas we found that 57% of endangered plants were affected by alien species. Their lower percentage stems in part from the small number of Hawaiian plants that had been listed as endangered or threatened at the time of their study. Our results do indicate that alien species are a frequent threat to continental plants as well (Table 3), but they are not necessarily the primary threat, which may account for the remainder of the difference.

Collar et al. (1994) identified the primary threat to each of 1111 bird species they regarded as imperiled. Because they evaluated endangered birds worldwide, focused on primary threats only, and categorized the

Table 4. Percentages of federal endangered, threatened, or proposed species, subspecies, or populations that are harmed by various types of habitat destruction and degradation. Categories are nonexclusive and therefore do not sum to 100.

Cause	Overall (n = 1207)	Vertebrates (n = 329)	Invertebrates (n = 155)	Plants (n = 723)	Mammals (n = 67)	Birds (n = 91)	Reptiles (n = 39)	Amphibians (n = 16)	Fish (n = 116)	Insects (n = 39)	Arachnids (n = 4)	Crustaceans (n = 20)	Mollusks (n = 23)	Mussels (n = 69)
Agriculture	38	40	57	33	25	42	33	63	45	56	75	55	35	64
Livestock grazing	22	17	10	33	19	20	8	19	16	15	0	30	9	1
Mining, oil and gas, geothermal	11	12	31	11	2	3	13	13	23	10	0	0	17	58
Logging	12	16	25	7	12	18	13	19	19	5	25	5	13	46
Infrastructure development (including roads)	17	16	12	20	9	8	28	38	17	23	25	10	9	6
Road construction and maintenance	15	15	10	17	8	8	23	38	16	18	25	5	9	6
Military activities	4	2	1	5	2	3	5	0	0	0	0	5	4	0
Outdoor recreation (including ORVs)	27	16	19	33	18	15	31	25	9	41	0	30	26	4
Off-road vehicles	13	6	12	16	6	7	13	13	1	31	0	25	4	0
Water development (including dams, etc.)	30	47	66	15	10	22	28	63	91	21	0	70	48	99
Dams, impoundments, and other barriers	17	28	54	5	3	9	15	13	64	15	0	15	35	96
Pollutants	20	27	66	7	5	10	21	25	55	26	75	55	48	97
Land conversion for commercial development	35	30	42	36	31	33	56	44	16	67	75	65	13	29
Disruption of fire ecology	14	5	6	20	7	8	5	6	0	18	25	0	4	0

threats differently than we did, their results are not directly comparable to ours. Nonetheless, it is worth noting that both studies identified habitat loss as the most widespread threat. In Collar et al.'s study, the next most important threats, in order of decreasing frequency, were small range or population, overhunting, and alien species. In our study, the next most important threats, also in order of decreasing frequency, were alien species, disease, overhunting, and pollution. The higher rankings accorded alien species and diseases in our analysis are probably due to the Hawaiian avifauna, which constitutes a large fraction of endangered birds in the United States and is profoundly affected by these threats. In our study, we did not classify small range per se as a threat.

Changes in threats over time

As human activities and customs change over time, one would expect to see corresponding changes in the threats to biodiversity. Because our study does not distinguish between historical and contemporary threats, it is not well suited to test this hypothesis. For example, the relatively large percentage of species affected by overexploitation (17%) includes a variety of animals that were once hunted but are now reasonably well protected from this threat (e.g., the whooping crane [*Grus americana*] and the California condor [*Gymnogyps californianus*]). Similarly, pesticide pollution is listed as the primary threat to the bald eagle (*Haliaeetus leucocephalus*) and to North American populations of the peregrine falcon (*Falco peregrinus*), but the primary pollutant harming both species—DDT—has been banned in the United States since 1972 (although it continues to be used in other countries where peregrines spend the winter). Thus, our study may overestimate the number of animals that are currently harmed by overexploitation and pollutants.

There are no accurate figures on the total number of alien species now established in the United States, although the Office of Technology Assessment [OTA] (1993) has estimated that there are at least 4500 (a number that OTA acknowledges is probably an underestimate). What is indisputably clear, however, is that the cumulative number of alien species in the United States has skyrocketed since the late 18th century (Sailer 1978, OTA 1993); this pattern holds for all types of species, from plants, to insects, to vertebrates. Given that the cumulative number of alien species is increasing over time, one may confidently predict that alien species will pose an ever-increasing threat to native flora and fauna.

A somewhat more complicated question is whether the *rate* of alien introductions has increased over time, which would indicate a rapidly worsening situation for imperiled species. The data from published studies are ambiguous on this point. Reviewing the numbers of alien terrestrial vertebrates, fishes, mollusks, and plant pathogens added to the United States per decade over the past 50 years, OTA (1993) found no consistent increase for any of the groups. The greatest numbers of terrestrial vertebrates and fishes were added during the 1950s and 1960s, whereas the 1970s saw the greatest increase in the numbers of mollusks and plant pathogens. On the other hand, a detailed study of alien species in the San Francisco Estuary shows that there have been more introductions in recent years than in earlier years (Cohen and Carlton 1995).

Many factors influence the rate at which alien species are introduced into the United States, so the lack of a consistent increase in that rate over time should not be surprising. Species can be brought into the country and released intentionally, or their release can occur as an unintentional byproduct of cultivation, commerce, tourism, or travel. Each new development in the field of transportation creates new opportunities for the transport of alien species, from the first sailing ships to reach US shores, to the building of the nation's road and highway system, to the advent of jet airplanes. As transporation technology changes, so do the opportunities for alien stowaways. Empty cargo ships arriving in the United States, for example, used to carry dry ballast in the form of rocks and soil, which was then off-loaded around wharves to provide cargo space. Numerous insects and plants were accidentally introduced into the United States in this dry ballast, including fire ants (*Solenopsis invicta* and *Solenopsis richteri*) and purple loosestrife (*Lythrum salicaria*). Today, ships use water for ballast instead of dry material, thus ending the spread of alien species via dry ballast. However, the release of ballast water into US waterways has been implicated in the introduction of at least eight alien species since 1980, including the zebra mussel, *Dreissena polymorpha* (OTA 1993). Finally, the public's growing infatuation with ornamental plants, tropical fish, and tropical birds has led to numerous unintentional releases of alien species, including over 300 plants in California alone (McClintock 1985).

Looking ahead, as the human population of the United States continues to grow, one might predict an increase in the frequency of biodiversity threats associated with urbanization, such as infrastructure development, water development, and land conversion. Comparable increases in the proportion of species affected by agriculture are also a possibility. There is, in fact, good reason to suspect that a growing human population in the United States will disproportionately affect this nation's imperiled species. Dobson et al. (1997) have shown that most endangered species in the United States are clustered in a relatively small number of areas, particularly in Hawaii, Southern California, and Florida. The human populations in all three states are projected to increase at rates well beyond the national average. Thus, whereas the population of the United States as a whole is expected to grow by 14% between 1995 and 2010, the populations of Hawaii, California, and Florida are projected to increase by 27%, 27%, and 22%, respectively (US Bureau of the Census 1995).

Although climate change was not listed as a current threat to any species in our databases, it is almost certain to become one in the foreseeable future due to increasing concentrations of greenhouse gases from fossil-fuel use, land-use changes, and agriculture. Climate models developed by the Intergovernmental Panel on Climate Change predict a 0.9–

3.5 °C increase in global mean temperature over the course of the next century (Houghton et al. 1995). That increase will cause a rise in sea levels of 15–95 cm and significant changes in the frequencies of severe floods and droughts.

These changes are likely to affect a broad array of imperiled species. For example, Morse et al. (1993) estimate that 7–11% of North America's vascular plant species would no longer encounter a suitable climatic regime ("climate envelope") within their present ranges in the event of a 3 °C increase in temperature. Due to their small ranges and weak dispersal abilities, imperiled plants would be disproportionately affected. Morse et al. (1993) also estimate that 10–18% of North America's rare plants could be excluded from their climate envelope due to climate change.

In another well-publicized study, Britten et al. (1994) noted that relictual populations of the critically endangered Uncompahgre fritillary butterfly (*Boloria acrocnema*) living atop a few peaks in the San Juan Mountains of southwestern Colorado were extremely vulnerable to unusual weather events. They further hypothesized that a regional warming trend (as might occur due to global climate change) could eliminate all of the butterfly's habitat, essentially pushing it off of the mountains and into extinction. Indirect support for this hypothesis comes from a recent study of another butterfly. Parmesan (1996) censused populations of the Edith's checkerspot (*Euphydryas editha*) throughout its known range (Baja California, the western United States, and western Canada) and found significant latitudinal and altitudinal differences in the proportion of populations (in suitable habitat) that had become extinct. Populations in Mexico were four times more likely to have vanished than those in Canada, a North–South gradient in survival that is consistent with the predicted impacts of global warming on species' ranges.

Conservation implications

The major findings of this study confirm what most conservation biologists have long suspected: Habitat loss is the single greatest threat to biodiversity, followed by the spread of alien species. However, the discovery that nearly half of the imperiled species in the United States are threatened by alien species—combined with the growing numbers of alien species—suggests that this particular threat may be far more serious than many people have heretofore believed. The impact of alien species is most acute in the Hawaiian Islands, as demonstrated by the fact that nearly 100% of the archipelago's imperiled plants and birds are threatened by alien species, compared with 30% and 48%, respectively, for mainland plants and birds (Table 3). This finding is also consistent with numerous other studies that have highlighted the unique vulnerability of island communities to alien species (Culliney 1988, Simberloff 1995).

Pollution (including siltation) ranks well below alien species as a threat to imperiled species in general, but it exceeds alien species as a threat to aquatic taxa. As Richter et al. (1997) point out, the pollutants affecting the largest number of aquatic species are agricultural pollutants, such as silt and nutrients, that enter lakes and rivers as runoff from farming operations. These nonpoint source pollutants have proved to be exceedingly difficult to regulate and control (Young and Congdon 1994).

Finally, this study and one by Wilcove and Chen (in press) raise troubling questions about the future of imperiled species in the United States. Both studies found that a high proportion of imperiled species is threatened by either fire suppression within their fire-maintained habitats or alien species. Both types of threats must be addressed through active, "hands-on" management of the habitat, such as pulling up alien plants and trapping alien animals or using prescribed fire to regenerate early successional habitats. Although the ESA prohibits actions that directly harm listed animals and, to a lesser extent, listed plants, it does not require landowners to take affirmative actions to maintain or restore habitats for listed species. Thus, a landowner is under no obligation to control exotic weeds, undertake a program of prescribed burning, or do any of the other things that may be absolutely necessary for the long-term survival of many imperiled species. In fact, it may be possible for a landowner to rid himself of an endangered species "problem" by literally doing nothing and waiting until the habitat is no longer suitable for the species in question. Even those landowners who care deeply about endangered species and wish to protect them face a daunting burden: The costs of undertaking these management actions can be considerable and, at present, are usually not tax deductible.

With a growing list of species in need of attention and less money to spend per species (Wilcove et al. 1996), the USFWS cannot hope to cover the necessary management costs for most of the plants and animals it aspires to protect. Nor can it count on the goodwill of landowners to contribute their own money or labor for actions they are not obligated to perform and that ultimately may result in restrictions on the use of their property. As a nation, therefore, we are incurring a growing "management debt" associated with efforts to protect imperiled species. To address this problem, it will be necessary to supplement the regulatory controls of the ESA and other wildlife protection laws with a wide array of incentives to reward landowners who wish to manage their property to benefit endangered species (Wilcove et al. 1996). Without such incentives, the United States stands to lose a large proportion of its imperiled plants and animals.

Acknowledgments

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merson, Bruce Stein, David Braun, and Brian Richter, for which we are grateful. We thank Jane Lubchenco, Margaret McMillan, and three anonymous reviewers for their helpful reviews of earlier versions of this paper. E. Losos and A. Phillips would like to thank The Wilderness Society for its support of their work on this project.

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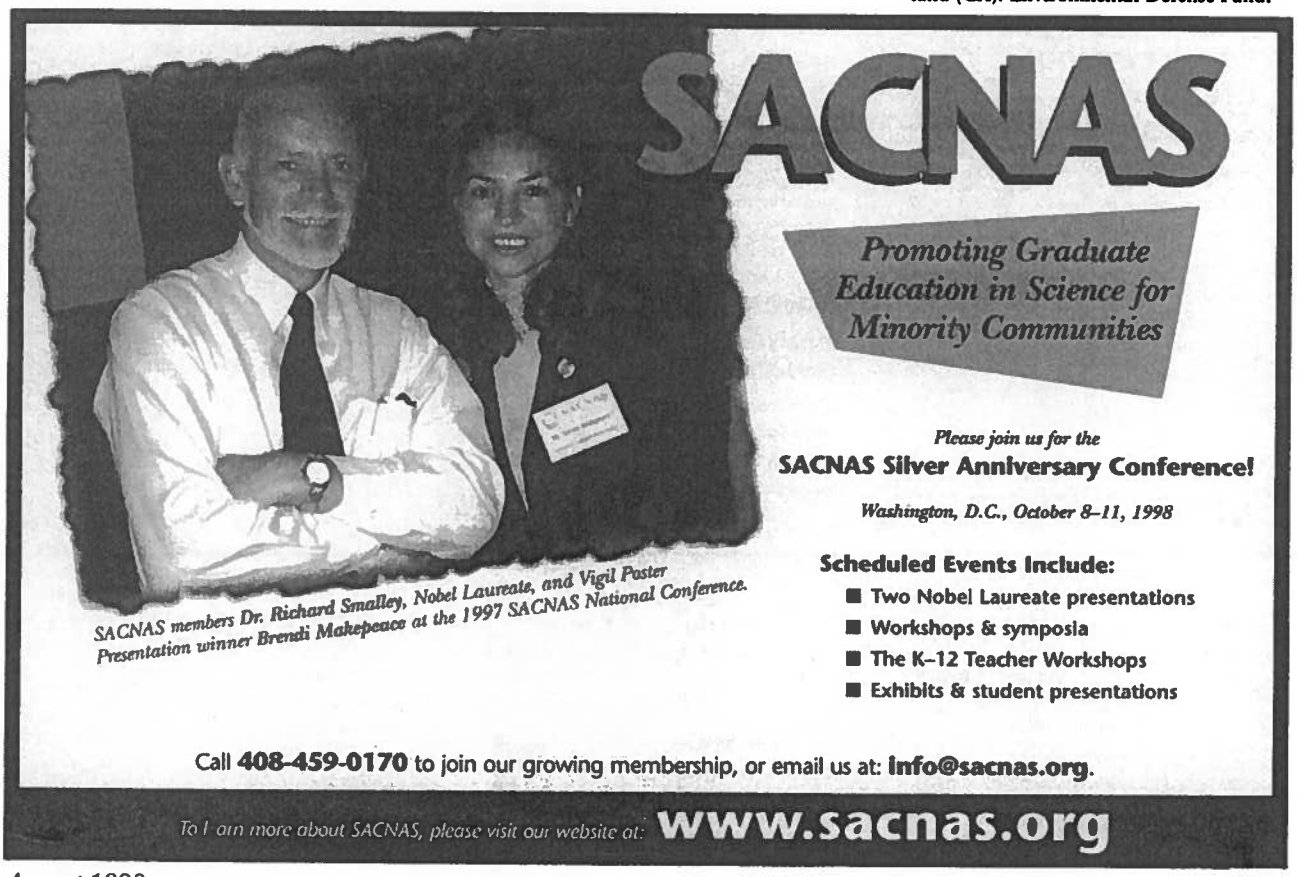

EXHIBIT B

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Casa Diablo IV Geothermal Development Project (CACA 11667)

Toward a safe, clean energy future: The proposed Casa Diablo Geothermal Energy Project has recently started the environmental review and public participation process required by Federal law. The project would be built on Inyo National Forest lands and private lands.

Casa Diablo (CACA 11667)
- Fact Sheet
- Federal Process & Documents

Vitals

Proposed Location: Mammoth Pacific, L.P. (MPLP) has submitted an application to the BLM to build and operate the Casa Diablo IV Geothermal Development Project in the immediate vicinity of the existing MPLP geothermal projects near the intersection of California State Route 203 and U.S. Highway 395 approximately 3 miles east of Mammoth Lakes, California. The proposed project would be located on Inyo National Forest lands and adjacent private lands within portions of Federal geothermal leases CACA-11667, CACA-11672 and CACA-14408.

Electricity Production Capacity: 33 net megawatts

Company: Mammoth Pacific, L.P. (MPLP)

Acreage: 100 acres

Status: Notice of Intent published in the Federal Register 3/25/11

Public Comment: Scoping period ended 5/9/11

Public Scoping Meetings:

- Scoping meeting presentation

Electrictrical Transmission Connection: A 500-foot transmission line is proposed to interconnect the new power plant to the existing Southern California Edison (SCE) substation at Substation Road.

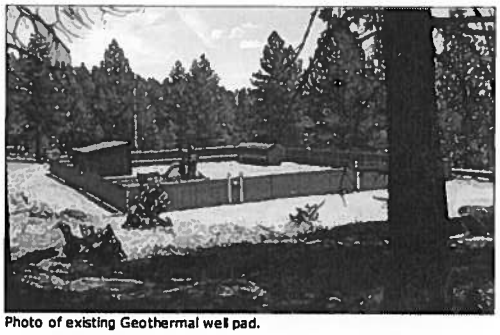

Photo of existing Geothermal well pad.

Last updated: 04-11-2012

EXHIBIT C

SWAPE Technical Consultation, Data Analysis and Litigation Support for the Environment

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September 11, 2012

Christina Caro
Lozeau | Drury LLP
410 12th Street, Suite 250
Oakland, CA 94607

Subject: **Comments on the Hudson Ranch Power II and Simbol Calipatria II Projects, Imperial County**

Dear Ms. Caro:

We have reviewed August 2012 Final Environmental Impact Report (FEIR) for the Hudson Ranch Power II and Simbol Calipatria II projects which would involve: (1) construction of the Hudson Ranch Power II Geothermal Project, a 49.9 MW geothermal power plant and well field; and (2) construction of the Simbol Calipatria Plant II, a commercial lithium carbonate production plant ("Projects").

The 52-acre Geothermal Project (HR-2 Plant) would involve:

- Drilling and development of up to eight geothermal wells and up to four injection wells;
- Construction of a stormwater retention basin, wastewater treatment plant, and potable water treatment plant;
- Construction of a geothermal flash power plant consisting of a brine production facility, a turbine generator facility, control room, office, maintenance shop, supporting geothermal production and injection wells, and associated pipelines; and
- Well abandonment if a well does not have commercial potential.

The 48-acre Lithium Carbonate Project (SmCP–2 Plant) would include:

- Construction of facilities to extract lithium, manganese, zinc from geothermal brine to produce commercial quantities of lithium, hydrochloric acid, manganese, and zinc products;
- Construction and operation of brine pipelines connected to the HR-2 plant; and

- Construction of a power distribution line. (FEIR. pp. 1-2, 1-3.)

The FEIR fails to: (1) identify current baseline soil conditions at the Project sites which may pose hazards to construction workers; (2) adequately describe waste handling from brine production; (3) potential impacts to the Salton Sea from conversion of agricultural lands; (4) consider the potential for induced seismic activity; and (5) adequately evaluate air impacts during construction. The FEIR needs to be supplemented to adequately disclose and mitigate these impacts, if significant, prior to certification of the FEIR.

Hazards and Hazardous Materials

Current baseline soil and groundwater conditions at the Project sites are unknown. Land use, which has included agriculture, may have resulted in soil contamination from pesticide use which may pose risks to workers involved in construction activity.

1. A Phase I Environmental Site Assessment (ESA) was prepared for the Geothermal Project in August 2009 (Appendix H-1). The Phase I is unreliable because it was prepared more than three years ago. Standard industry practices dictate that a Phase I ESA is invalid after a year.[1] Prior to certification of the FEIR, a new Phase I ESA should be completed to ensure hazardous conditions do not exist on the Geothermal Project site.

2. A Phase I ESA has not been prepared for the 48-acre Lithium Carbonate Project. The August 2009 Phase I Environmental Site Assessment was prepared only for 52-acre Geothermal Project. The FEIR mistakenly states:

   > Simbol, Inc. has conducted a Phase 1 environmental site assessment (Appendix H-2) and no recognized environmental conditions were identified within 1 mile of the proposed Project site

Instead, Appendix H-2 is only an Agency Database Record Search (completed in March 2012). A records search is only one component of a Phase I ESA which includes a review of historical site activities, an inspection, and interviews with landowners. Prior to FEIR certification, a new Phase I ESA should be prepared for the Geothermal Project site and a Phase I should be prepared for the Lithium Carbonate Project site to ensure that conditions, which may include pesticide contamination, do not pose hazards to construction workers.

Brine Handling

Spent fluid or brine produced following heat extraction from the geothermal wells will be sent to the Lithium Carbonate Plant by a brine delivery pipeline. Once the brine has been processed, it will be sent for disposal to the injection wells. Solids produced from evaporation at the brine pond will be classified as hazardous waste (p. 3-31). Chemical compounds in the brine include high concentration of sulfate, sodium, and chloride (Table 3-7). Handing of the brine will likely require a Report of Waste Discharge

[1] http://blog.augustmack.com/blog/environmental-considerations-for-real-estate/phase-i-esa-update

(ROWD) from the Colorado River Regional Water Quality Control Board (RWQCB), a report not included in the FEIR.

The Hudson Ranch I Geothermal Exploration Project, which broke ground in May 2010[2], required a Report of Waste Discharge and issuance of Waste Discharge Requirements from the RWQCB to address well drilling and brine handling practices.[3] The Waste Discharge Requirements govern the handling of drilling wastes and brine handling and include information regarding:

- the chemical characteristics of the brine and the drilling mud and rock cuttings drilling waste containment units;
- drilling waste disposal;
- surface water in the area of exploration;
- regional and local groundwater;
- the RWQCB Basin Plan, including information on beneficial uses of groundwater and surface water; and
- stormwater management during construction.

Waste Discharge Requirements specify:

- waste containment at all times;
- capacity of sumps and containment basins;
- analytical testing requirements for contaminants in brine which may include sodium, chloride calcium and potassium; and
- a prohibition on the release of pollutants, or waste constituents in a manner that could cause or contribute to a condition of contamination, nuisance, or pollution.

Poor waste management practices for other geothermal projects in the area have led to enforcement actions by the RWQCB at other geothermal facilities. In 2006, the RWQCB filed an administrative action against a group of geothermal operators in the area of the Hudson II project for failure to improve brine filter cake storage areas and to take measures to including to prevent filter cake from being released or disposed during transport.[4]

The FEIR includes measures for the Geothermal Plant to "minimize or avoid hydrology and/or water quality impacts" but does not include a ROWD and, in fact makes no specific reference for the need of a

[2] http://latimesblogs.latimes.com/money_co/2010/05/hudson-ranch-geothermal-power-facility-underway-in-imperial-valley.html
[3] http://www.swrcb.ca.gov/rwqcb7/board_decisions/adopted_orders/orders/2007/42_hudson_wdr.pdf
[4] http://www.dtsc.ca.gov/HazardousWaste/Projects/upload/CAL_ENERGY_ENF_FinalJudgmnt.pdf

ROWD, stating only that the Projects could violate water quality standards or waste discharge requirements (p. 4.8-20) and identifying measures to address these impacts. Without the preparation of a ROWD and RWQCB review, the effectiveness of these measures is unknown. The FEIR should not be certified until it includes a draft ROWD and documentation that the RWQCB will review and issue a Waste Discharge Requirement permit.

Hydrology

Agricultural runoff from Imperial County accounts for 75% of inflows to the Salton Sea.[5] Construction of the Projects will convert agricultural lands which will lead to a reduction in inflows and, consequently, lake levels, leading to potential water quality degradation. Additionally, the FEIR does not address the potential that dust emissions might result from reductions in water inflows to the Salton Sea from the Project construction.

The HR-2 Plant will convert 52 acres of farmland for 30 years over the Project life span while the SmCP-2 Plant will convert 48 acres of farmland for the 30 year life span (FEIR, p. 5-18). Agricultural water use in Imperial County is 5.6 acre-feet per acre per year.[6] The Project's conversion of 100 acres, therefore, will reduce inflows to the Salton Sea by 16,800 acre-feet over their lifespan.

The FEIR identifies 26 other projects in Imperial County that will also convert agricultural land. These 26 projects, together with the HR-2 Plant and SmCP-2 Plant, will convert 17,047 acres of farmland (FEIR, p. 5-20). Conversion of this farmland will result in a decrease of approximately 95,500 acre-feet of water per year to the Salton Sea.[7] The Salton Sea Restoration Program estimates median inflows to the Salton Sea to be 717,000 acre-feet per year for 2018-2078.[8] Conversion of 17,047 acres of farmland will result in a 13% reduction[9] of inflows to the Salton Sea per year – an undisclosed cumulative impact.

The level of the Salton Sea will be further lowered from reductions of inflows under the Quantification Settlement Agreement (QSA). The QSA was approved in 2003 and requires the Imperial Irrigation District to conserve 303,000 acre-feet per year of water by 2026 for transfer to San Diego and 103,000 acre-feet per year of water to the Coachella Valley Water District.[10]

As agricultural inflows to the Salton Sea decrease, salts and nutrients become more concentrated and threaten ecologic habitat which has been designated a National Wildlife Refuge and is a critical stop on the Pacific Flyway for migrating birds, including several state and federal listed endangered and threatened species.[11] The Regional Water Quality Control Board has characterized the Salton Sea to be in "serious trouble" and that it "may be unable to support ... beneficial uses in the future".[12]

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[5] http://www.waterboards.ca.gov/coloradoriver/water_issues/programs/salton_sea/index.shtml
[6] Imperial County Farm Bureau. Imperial County Agriculture. http://www.icfb.net/countyag.html
[7] 17,047 acres * 5.6 acre-feet/year = 95,463. 2 acre-feet per year
[8] http://www.water.ca.gov/saltonsea/historicalcalendar/wg/01.18.2006/Hydrology_Report_Draft.pdf, p. 52
[9] (95,463.2 acre-feet/year)/(717,000 acre-feet/year)* 100 = 13.3%
[10] http://www.iid.com/Modules/ShowDocument.aspx?documentid=3445, p. 2
[11] http://www.waterboards.ca.gov/coloradoriver/water_issues/programs/salton_sea/index.shtml
[12] http://www.waterboards.ca.gov/coloradoriver/water_issues/programs/salton_sea/index.shtml

Reductions of inflows from lowered Salton Sea lake levels will result in the exposure of formerly submerged shoreline areas, increasing dust generation potential. A commission formed to evaluate the effects of the lowering of the Salton Sea concluded:

> The overall consensus of the workshop panel is that episodes of windblown dust should be expected if there is a significant reduction in Salton Sea water levels.[13]

Generation of dust from lowered levels in other arid lake basins, like Owens Lake, have led to significant PM emissions and have required extensive mitigation. Water diversions by the Los Angeles Department of Water and Power since early in the 20th century cut Owens Lake from its natural sources of water, causing lake level declines. Frequent winds in the Owens Valley generate dust from former wetted lake bed soils and cause the PM10 violations. Emissions from Owens Lake contributed to reclassification of the southern Owens Valley as a "serious nonattainment" area for PM10. Extensive mitigation has resulted in attempt to improve air quality for residents over 50 miles away.[14]

The FEIR should not be certified until the potential for Project-related reductions of inflows to the Salton Sea, along with cumulative reductions, to include all projects that propose conversion of agricultural land, can be evaluated for impacts on water quality and PM generation.

Injection Induced Seismicity

The FEIR describes a high potential for a magnitude 7.4 to 7.9 earthquake along the San Andreas Fault, located 14 miles northwest of the Project sites. Since 1987, 70 earthquakes with a magnitude greater than 5.0 have been reported within 100 miles of the Project sites. A maximum earthquake of magnitude 6.4 is also possible along the Brawley seismic zone approximately 2.6 miles southwest of the Project sites. (p. 4.6-2). Although the FEIR adequately describes the seismic setting of the Projects, the FEIR does not consider the potential for seismicity to be induced by injection of geothermal fluids.

Induced seismicity has been documented in association with number of operating geothermal fields in the United States and globally. The Geysers and the Coso geothermal fields in California have a well-known association of geothermal production and induced seismicity, producing thousands of earthquakes annually. Most are small and are not perceived by humans, but some earthquakes of up to magnitude 4 have been documented.[15]

Communities near geothermal fields have expressed concerned about damage from single seismic events and cumulative effects. Concerns include the potential for structural damage and that small events may trigger larger events.[16]

These well-known concerns are not identified in the FEIR. Potential structural damage impacts in communities, including Niland which is located 2.3 miles northeast, are not considered in the FEIR. The

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[13] http://www.usbr.gov/lc/region/saltnsea/pdf_files/Final_Air_Quality_Paper.pdf
[14] http://www.gbuapcd.org/airqualityplans.htm
[15] http://esd.lbl.gov/research/projects/induced_seismicity/egs/history.html

[16] http://esd.lbl.gov/research/projects/induced_seismicity/egs/local_outreach.html

FEIR should be revised to include a thorough discussion about the potential for induced seismicity from development of the Geothermal Project. Mitigation should also be considered in the FEIR, including establishment of a monitoring network to determine any increases in seismic activity resulting from Project operation. Mitigation should also include a program for outreach to inform nearby communities of the potential relationship between geothermal development and seismic activity.

Air Impacts

Emissions of NOx during construction are estimated to be significant only for approximately two months during overlap of construction of the Lithium Carbonate Plant and the Geothermal Project in 2015 (p. 4.3-33). Our review has shown that construction emissions of NOx would potentially exceed the Imperial County Air Pollution Control District threshold during other construction in 2013 and 2014, at a minimum.

NOx emissions from the FEIR for the Geothermal Project are estimated to be just below thresholds for 2013 and 2014 (below).

These estimates are after mitigation – Attachment P to Appendix C, p. 2 includes the following table which shows the basis for the estimates above.

August - October 2013

Grading						
August through October 2013 - Unmitigated Winter						
Winter Unmitigated	Emission Rate (lbs/day)					
	ROG	NOx	CO	SO2	PM10	PM2.5
Total	18.77	157.13	73.85	0.17	37.30	12.32
ICAPCD Significance	75.00	100.00	550.00	150.00	150.00	
CEQA Significant?	No	Yes	No	No	No	
September through October 2013 - Unmitigated Summer						
Summer Unmitigated	Emission Rate (lbs/day)					
	ROG	NOx	CO	SO2	PM10	PM2.5
Total	18.86	157.14	74.66	0.17	37.30	12.32
ICAPCD Significance	75.00	100.00	550.00	150.00	150.00	
CEQA Significant?	No	Yes	No	No	No	
September through October 2013 - Mitigated Winter						
Winter Mitigated	Emission Rate (lbs/day)					
	ROG	NOx	CO	SO2	PM10	PM2.5
Total	5.57	96.57	93.29	0.17	19.79	8.62
ICAPCD Significance	75.00	100.00	550.00	150.00	150.00	
CEQA Significant?	No	No	No	No	No	
September through October 2013 - Mitigated Summer						
Summer Mitigated	Emission Rate (lbs/day)					
	ROG	NOx	CO	SO2	PM10	PM2.5
Total	5.66	96.58	94.10	0.17	19.79	8.62
ICAPCD Significance	75.00	100.00	550.00	150.00	150.00	
CEQA Significant?	No	No	No	No	No	

The table above shows unmitigated emissions for grading from August through October 2013 to be 157 lbs/day, in excess of the Imperial County threshold of 100 lbs/day. The mitigated emissions are reduced to an estimate of 97 lbs/day (the figure cited in Table 4.3-7 in the FEIR for 2013), just below the Imperial County threshold of 100 lbs/day.

No substantiation of the effectiveness of the mitigation is provided in the FEIR. Even if mitigation effectiveness can be demonstrated, the estimate of emissions of NOx at 97 pounds per day in 2013 (Table 4.3-7 in the FEIR – just three pounds less than the Imperial County threshold -- is not defensible. Modeling estimates are just that: estimates. They may be higher or lower based on the values used for input parameters. In the case of the geothermal plant construction, Appendix C acknowledges that geothermal projects are not a project that is contemplated by the model used in the analysis, CalEEMod. Therefore, estimates of project construction emissions of NOx should be considered even more imprecise and an estimate of 97 pounds per day should be considered a significant impact.

Additional mitigation for construction NOx emissions during the entire construction period should be incorporated into the FEIR prior to certification. The FEIR identifies Mitigation Measure AQ-2.1 to address what was identified as a NOx threshold exceedence only during concurrent construction of the Geothermal Plant and the Lithium Carbonate Plant (p. 4.3-35).

- Utilize all Tier 3 or Tier 4 construction equipment.
- Prohibit idling of equipment not in use; for equipment in use reduce idling time to a maximum of 5 minutes.
- Where feasible replace fossil fuel burning equipment with electrically driven equivalents provided they are not powered via a portable generator.
- Register all portable engines 50 horse power or greater with the ICAPCD.
- Submit to the Air District prior to any earthmoving activity a complete list of all construction equipment to be utilized during the construction phase identifying Make, Model, Year, and estimated hours of usage.
- In the event NOx emissions are calculated to exceed ICAPCD thresholds for construction, the Permittee shall provide for "off-site" mitigation or comply with Policy Number 5. Policy Number 5 allows a project to pay in-lieu impact fees utilizing the most current

Because construction NOX emissions estimates are so close to thresholds the FEIR should not be certified until these measures are incorporated for application to the entire project construction period.

Sincerely,

Matt Hagemann, P.G., C.Hg.

Uma Bhandaram

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Geologic and Hydrogeologic Characterization
Industrial Stormwater Compliance
CEQA Review
Investigation and Remediation Strategies
Litigation Support and Testifying Expert

Education:

M.S. Degree, Geology, California State University Los Angeles, Los Angeles, CA, 1984.
B.A. Degree, Geology, Humboldt State University, Arcata, CA, 1982.

Professional Certification:

California Professional Geologist
California Certified Hydrogeologist
Qualified SWPPP Developer and Practitioner

Professional Experience:

Matt has 25 years of experience in environmental policy, assessment and remediation. He spent nine years with the U.S. EPA in the RCRA and Superfund programs and served as EPA's Senior Science Policy Advisor in the Western Regional Office where he identified emerging threats to groundwater from perchlorate and MTBE. While with EPA, Matt also served as a Senior Hydrogeologist in the oversight of the assessment of seven major military facilities undergoing base closure. He led numerous enforcement actions under provisions of the Resource Conservation and Recovery Act (RCRA) while also working with permit holders to improve hydrogeologic characterization and water quality monitoring.

Matt has worked closely with U.S. EPA legal counsel and the technical staff of several states in the application and enforcement of RCRA, Safe Drinking Water Act and Clean Water Act regulations. Matt has trained the technical staff in the States of California, Hawaii, Nevada, Arizona and the Territory of Guam in the conduct of investigations, groundwater fundamentals, and sampling techniques.

Positions Matt has held include:

- Founding Partner, Soil/Water/Air Protection Enterprise (SWAPE) (2003 – present);
- Geology Instructor, Golden West College, 2010 – present;
- Senior Environmental Analyst, Komex H2O Science, Inc (2000 -- 2003);

- Executive Director, Orange Coast Watch (2001 – 2004);
- Senior Science Policy Advisor and Hydrogeologist, U.S. Environmental Protection Agency (1989–1998);
- Hydrogeologist, National Park Service, Water Resources Division (1998 – 2000);
- Adjunct Faculty Member, San Francisco State University, Department of Geosciences (1993 – 1998);
- Instructor, College of Marin, Department of Science (1990 – 1995);
- Geologist, U.S. Forest Service (1986 – 1998); and
- Geologist, Dames & Moore (1984 – 1986).

Partner, SWAPE:

With SWAPE, Matt's responsibilities have included:

- Lead analyst and testifying expert in the review of numerous environmental impact reports under CEQA that identify significant issues with regard to hazardous waste, water resources, water quality, air quality, greenhouse gas emissions and geologic hazards.
- Stormwater analysis, sampling and best management practice evaluation at industrial facilities.
- Lead analyst and testifying expert in the review of environmental issues in license applications for large solar power plants before the California Energy Commission.
- Technical assistance and litigation support for vapor intrusion concerns.
- Manager of a project to evaluate numerous formerly used military sites in the western U.S.
- Manager of a comprehensive evaluation of potential sources of perchlorate contamination in Southern California drinking water wells.
- Manager and designated expert for litigation support under provisions of Proposition 65 in the review of releases of gasoline to sources drinking water at major refineries and hundreds of gas stations throughout California.
- Expert witness on two cases involving MTBE litigation.
- Expert witness and litigation support on the impact of air toxins and hazards at a school.
- Expert witness in litigation at a former plywood plant.

With Komex H2O Science Inc., Matt's duties included the following:

- Senior author of a report on the extent of perchlorate contamination that was used in testimony by the former U.S. EPA Administrator and General Counsel.
- Senior researcher in the development of a comprehensive, electronically interactive chronology of MTBE use, research, and regulation.
- Senior researcher in the development of a comprehensive, electronically interactive chronology of perchlorate use, research, and regulation.
- Senior researcher in a study that estimates nationwide costs for MTBE remediation and drinking water treatment, results of which were published in newspapers nationwide and in testimony against provisions of an energy bill that would limit liability for oil companies.
- Research to support litigation to restore drinking water supplies that have been contaminated by MTBE in California and New York.
- Expert witness testimony in a case of oil production-related contamination in Mississippi.
- Lead author for a multi-volume remedial investigation report for an operating school in Los Angeles that met strict regulatory requirements and rigorous deadlines.
- Development of strategic approaches for cleanup of contaminated sites in consultation with clients and regulators.

Executive Director:

As Executive Director with Orange Coast Watch, Matt led efforts to restore water quality at Orange County beaches from multiple sources of contamination including urban runoff and the discharge of wastewater. In reporting to a Board of Directors that included representatives from leading Orange County universities and businesses, Matt prepared issue papers in the areas of treatment and disinfection of wastewater and control of the dischrge of grease to sewer systems. Matt actively participated in the development of countywide water quality permits for the control of urban runoff and permits for the discharge of wastewater. Matt worked with other nonprofits to protect and restore water quality, including Surfrider, Natural Resources Defense Council and Orange County CoastKeeper as well as with business institutions including the Orange County Business Council.

Hydrogeology:

As a Senior Hydrogeologist with the U.S. Environmental Protection Agency, Matt led investigations to characterize and cleanup closing military bases, including Mare Island Naval Shipyard, Hunters Point Naval Shipyard, Treasure Island Naval Station, Alameda Naval Station, Moffett Field, Mather Army Airfield, and Sacramento Army Depot. Specific activities were as follows:

- Led efforts to model groundwater flow and contaminant transport, ensured adequacy of monitoring networks, and assessed cleanup alternatives for contaminated sediment, soil, and groundwater.
- Initiated a regional program for evaluation of groundwater sampling practices and laboratory analysis at military bases.
- Identified emerging issues, wrote technical guidance, and assisted in policy and regulation development through work on four national U.S. EPA workgroups, including the Superfund Groundwater Technical Forum and the Federal Facilities Forum.

At the request of the State of Hawaii, Matt developed a methodology to determine the vulnerability of groundwater to contamination on the islands of Maui and Oahu. He used analytical models and a GIS to show zones of vulnerability, and the results were adopted and published by the State of Hawaii and County of Maui.

As a hydrogeologist with the EPA Groundwater Protection Section, Matt worked with provisions of the Safe Drinking Water Act and NEPA to prevent drinking water contamination. Specific activities included the following:

- Received an EPA Bronze Medal for his contribution to the development of national guidance for the protection of drinking water.
- Managed the Sole Source Aquifer Program and protected the drinking water of two communities through designation under the Safe Drinking Water Act. He prepared geologic reports, conducted public hearings, and responded to public comments from residents who were very concerned about the impact of designation.

- Reviewed a number of Environmental Impact Statements for planned major developments, including large hazardous and solid waste disposal facilities, mine reclamation, and water transfer.

Matt served as a hydrogeologist with the RCRA Hazardous Waste program. Duties were as follows:

- Supervised the hydrogeologic investigation of hazardous waste sites to determine compliance with Subtitle C requirements.
- Reviewed and wrote "part B" permits for the disposal of hazardous waste.
- Conducted RCRA Corrective Action investigations of waste sites and led inspections that formed the basis for significant enforcement actions that were developed in close coordination with U.S. EPA legal counsel.
- Wrote contract specifications and supervised contractor's investigations of waste sites.

With the National Park Service, Matt directed service-wide investigations of contaminant sources to prevent degradation of water quality, including the following tasks:

- Applied pertinent laws and regulations including CERCLA, RCRA, NEPA, NRDA, and the Clean Water Act to control military, mining, and landfill contaminants.
- Conducted watershed-scale investigations of contaminants at parks, including Yellowstone and Olympic National Park.
- Identified high-levels of perchlorate in soil adjacent to a national park in New Mexico and advised park superintendent on appropriate response actions under CERCLA.
- Served as a Park Service representative on the Interagency Perchlorate Steering Committee, a national workgroup.
- Developed a program to conduct environmental compliance audits of all National Parks while serving on a national workgroup.
- Co-authored two papers on the potential for water contamination from the operation of personal watercraft and snowmobiles, these papers serving as the basis for the development of nation-wide policy on the use of these vehicles in National Parks.
- Contributed to the Federal Multi-Agency Source Water Agreement under the Clean Water Action Plan.

Policy:

Served senior management as the Senior Science Policy Advisor with the U.S. Environmental Protection Agency, Region 9. Activities included the following:

- Advised the Regional Administrator and senior management on emerging issues such as the potential for the gasoline additive MTBE and ammonium perchlorate to contaminate drinking water supplies.
- Shaped EPA's national response to these threats by serving on workgroups and by contributing to guidance, including the Office of Research and Development publication, Oxygenates in Water: Critical Information and Research Needs.
- Improved the technical training of EPA's scientific and engineering staff.
- Earned an EPA Bronze Medal for representing the region's 300 scientists and engineers in negotiations with the Administrator and senior management to better integrate scientific principles into the policy-making process.
- Established national protocol for the peer review of scientific documents.

Geology:

With the U.S. Forest Service, Matt led investigations to determine hillslope stability of areas proposed for timber harvest in the central Oregon Coast Range. Specific activities were as follows:

- Mapped geology in the field, and used aerial photographic interpretation and mathematical models to determine slope stability.
- Coordinated his research with community members who were concerned with natural resource protection.
- Characterized the geology of an aquifer that serves as the sole source of drinking water for the city of Medford, Oregon.

As a consultant with Dames and Moore, Matt led geologic investigations of two contaminated sites (later listed on the Superfund NPL) in the Portland, Oregon, area and a large hazardous waste site in eastern Oregon. Duties included the following:

- Supervised year-long effort for soil and groundwater sampling.
- Conducted aquifer tests.
- Investigated active faults beneath sites proposed for hazardous waste disposal.

Teaching:

From 1990 to 1998, Matt taught at least one course per semester at the community college and university levels:

- At San Francisco State University, held an adjunct faculty position and taught courses in environmental geology, oceanography (lab and lecture), hydrogeology, and groundwater contamination.
- Served as a committee member for graduate and undergraduate students.
- Taught courses in environmental geology and oceanography at the College of Marin.

Matt currently teaches Physical Geology (lecture and lab) to students at Golden West College in Huntington Beach, California.

Invited Testimony, Reports, Papers and Presentations:

Hagemann, M.F., 2008. Disclosure of Hazardous Waste Issues under CEQA. Presentation to the Public Environmental Law Conference, Eugene, Oregon.

Hagemann, M.F., 2008. Disclosure of Hazardous Waste Issues under CEQA. Invited presentation to U.S. EPA Region 9, San Francisco, California.

Hagemann, M.F., 2005. Use of Electronic Databases in Environmental Regulation, Policy Making and Public Participation. Brownfields 2005, Denver, Coloradao.

Hagemann, M.F., 2004. Perchlorate Contamination of the Colorado River and Impacts to Drinking Water in Nevada and the Southwestern U.S. Presentation to a meeting of the American Groundwater Trust, Las Vegas, NV (served on conference organizing committee).

Hagemann, M.F., 2004. Invited testimony to a California Senate committee hearing on air toxins at schools in Southern California, Los Angeles.

Brown, A., Farrow, J., Gray, A. and **Hagemann, M.**, 2004. An Estimate of Costs to Address MTBE Releases from Underground Storage Tanks and the Resulting Impact to Drinking Water Wells. Presentation to the Ground Water and Environmental Law Conference, National Groundwater Association.

Hagemann, M.F., 2004. Perchlorate Contamination of the Colorado River and Impacts to Drinking Water in Arizona and the Southwestern U.S. Presentation to a meeting of the American Groundwater Trust, Phoenix, AZ (served on conference organizing committee).

Hagemann, M.F., 2003. Perchlorate Contamination of the Colorado River and Impacts to Drinking Water in the Southwestern U.S. Invited presentation to a special committee meeting of the National Academy of Sciences, Irvine, CA.

Hagemann, M.F., 2003. Perchlorate Contamination of the Colorado River. Invited presentation to a tribal EPA meeting, Pechanga, CA.

Hagemann, M.F., 2003. Perchlorate Contamination of the Colorado River. Invited presentation to a meeting of tribal repesentatives, Parker, AZ.

Hagemann, M.F., 2003. Impact of Perchlorate on the Colorado River and Associated Drinking Water Supplies. Invited presentation to the Inter-Tribal Meeting, Torres Martinez Tribe.

Hagemann, M.F., 2003. The Emergence of Perchlorate as a Widespread Drinking Water Contaminant. Invited presentation to the U.S. EPA Region 9.

Hagemann, M.F., 2003. A Deductive Approach to the Assessment of Perchlorate Contamination. Invited presentation to the California Assembly Natural Resources Committee.

Hagemann, M.F., 2003. Perchlorate: A Cold War Legacy in Drinking Water. Presentation to a meeting of the National Groundwater Association.

Hagemann, M.F., 2002. From Tank to Tap: A Chronology of MTBE in Groundwater. Presentation to a meeting of the National Groundwater Association.

Hagemann, M.F., 2002. A Chronology of MTBE in Groundwater and an Estimate of Costs to Address Impacts to Groundwater. Presentation to the annual meeting of the Society of Environmental Journalists.

Hagemann, M.F., 2002. An Estimate of the Cost to Address MTBE Contamination in Groundwater (and Who Will Pay). Presentation to a meeting of the National Groundwater Association.

Hagemann, M.F., 2002. An Estimate of Costs to Address MTBE Releases from Underground Storage Tanks and the Resulting Impact to Drinking Water Wells. Presentation to a meeting of the U.S. EPA and State Underground Storage Tank Program managers.

Hagemann, M.F., 2001. From Tank to Tap: A Chronology of MTBE in Groundwater. Unpublished report.

Hagemann, M.F., 2001. Estimated Cleanup Cost for MTBE in Groundwater Used as Drinking Water. Unpublished report.

Hagemann, M.F., 2001. Estimated Costs to Address MTBE Releases from Leaking Underground Storage Tanks. Unpublished report.

Hagemann, M.F., and VanMouwerik, M., 1999. Potential Water Quality Concerns Related to Snowmobile Usage. Water Resources Division, National Park Service, Technical Report.

VanMouwerik, M. and **Hagemann, M.F.** 1999, Water Quality Concerns Related to Personal Watercraft Usage. Water Resources Division, National Park Service, Technical Report.

Hagemann, M.F., 1999, Is Dilution the Solution to Pollution in National Parks? The George Wright Society Biannual Meeting, Asheville, North Carolina.

Hagemann, M.F., 1997, The Potential for MTBE to Contaminate Groundwater. U.S. EPA Superfund Groundwater Technical Forum Annual Meeting, Las Vegas, Nevada.

Hagemann, M.F., and Gill, M., 1996, Impediments to Intrinsic Remediation, Moffett Field Naval Air Station, Conference on Intrinsic Remediation of Chlorinated Hydrocarbons, Salt Lake City.

Hagemann, M.F., Fukunaga, G.L., 1996, The Vulnerability of Groundwater to Anthropogenic Contaminants on the Island of Maui, Hawaii. Hawaii Water Works Association Annual Meeting, Maui, October 1996.

Hagemann, M. F., Fukanaga, G. L., 1996, Ranking Groundwater Vulnerability in Central Oahu, Hawaii. Proceedings, Geographic Information Systems in Environmental Resources Management, Air and Waste Management Association Publication VIP-61.

Hagemann, M.F., 1994. Groundwater Characterization and Cleanup at Closing Military Bases in California. Proceedings, California Groundwater Resources Association Meeting.

Hagemann, M.F. and Sabol, M.A., 1993. Role of the U.S. EPA in the High Plains States Groundwater Recharge Demonstration Program. Proceedings, Sixth Biennial Symposium on the Artificial Recharge of Groundwater.

Hagemann, M.F., 1993. U.S. EPA Policy on the Technical Impracticability of the Cleanup of DNAPL-contaminated Groundwater. California Groundwater Resources Association Meeting.

Hagemann, M.F., 1992. Dense Nonaqueous Phase Liquid Contamination of Groundwater: An Ounce of Prevention... Proceedings, Association of Engineering Geologists Annual Meeting, v. 35.

Other Experience:

Selected as subject matter expert for the California Professional Geologist licensing examination, 2009-2011.

EXHIBIT E

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November 13, 2012

Via Electronic Mail and Hand Delivery

Ms. Vikki Magee-Bauer, Chair
and Honorable Members of the
Mono County Board of Supervisors
c/o Lynda Roberts, Clerk of the Board
Annex I
74 North School Street
Bridgeport, CA 93517
Email: lroberts@mono.ca.gov

With Hand Delivery to Board of Supervisors Meeting:
Mono County Courthouse
278 Main
2nd Floor Board Chambers
Bridgeport, CA 93517

Re: Item 10(b): Appeal of Planning Commission Approval Mammoth Pacific I ("MP-I") Replacement Project (State Clearinghouse No: 2011022020); approval of Final Environmental Impact Report; Clarifying General Plan Amendment 12-003(b); Condition Use Permit 12-004; Variance 12-002, Reclamation Plan 12-001, and Notice of Decision.

Chair Magee-Bauer and Honorable Members of the Mono County Board of Supervisors:

This letter is submitted on behalf of Laborers International Union of North America, Local Union 783, and its members living in Mono County (collectively "LIUNA" or "Commenters") in support of LIUNA's appeal of the October 11, 2012 Planning Commission approval of the Final Environmental Impact for the Mammoth Pacific I (MP-1) Replacement Project (State Clearinghouse No: 2011022020), Clarifying General Plan Amendment 12-003(b), Conditional Use Permit ("CUP") 12-004, Variance 12-002 & Reclamation Plan 12-001, and Notice of Decision (collectively "Project" or "Mammoth Project").

We write in response to the Board of Supervisors ("Board") Agenda Report ("Staff Report"), made available on November 8, 2012. This letter supplements LIUNA's prior comments on the Final Environmental Impact Report ("FEIR")[1] and related Project

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[1] Citation to FEIR documents: The Mammoth Pacific I Final EIR consists of the DEIR, RDEIR, and RDEIR2, as well as all comments received on the DEIR, RDEIR, and RDEIR2, the County's Responses to Comments, and all Appendices Exhibits thereto. These documents

approvals submitted on October 11, 2012. After reviewing the Staff Report, it is clear that the County staff's responses to LIUNA's prior comments ("Staff Responses") fail to properly respond to several comments, fail to resolve the significant deficiencies raised in LIUNA's October 11, 2012 comment letter, fail to rebut the substantial evidence presented by expert comments, and fail to provide for recirculation of the FEIR to analyze all significant impacts of the Project and to identify and impose feasible mitigation measures to reduce the Project's impacts, as requested in LIUNA's prior comment letters. Provision of additional responses to comments less than 10 days prior to the Board's proposed certification of the FEIR also violates the 10-day notice requirement of Pub. Res. Code ("PRC") section 21092.5.

It is clear that the Planning Commission failed to comply with the California Environmental Quality Act, Public Resources Code § 21000 et seq. ("CEQA"), in all aspects of its Project approvals, and that the Board and the County will further abuse its discretion and violate CEQA if it affirms the Planning Commissions' Project approvals. The Staff Responses contain numerous errors and omissions that continue to preclude an accurate analysis of the Project. The EIR fails to implement all feasible mitigations, including those proposed by Commenters and other members of the public, to reduce the significant environmental impacts of the Project to a level of insignificance. As a result of these inadequacies, the Project will result in significant environmental impacts on animal and plant populations, air quality and water quality, among other impacts.

The County is unable, and has failed, to support its proposed findings that the Project's impacts will be adequately mitigated, with substantial evidence, and as a result, is unable to adopt either a finding of no significant unmitigated impacts or a statement of overriding considerations to support its approvals despite the Project's significant environmental impacts. LIUNA therefore requests that the Board grant this Appeal, and require the County to go back and prepare and circulate a legally adequate Supplemental Draft Environmental Impact Report ("SEIR") to address the issues raised in this and other comments, and to require implementation of feasible mitigations and alternatives required by law.

In particular, the Project will have the following adverse impacts that remain inadequately mitigated and to which the Staff Report fails to adequately respond:

Impacts on Biological Resources:

- The Staff Report fails to adequately assess respond to comments raised regarding potentially significant impacts on mule deer resulting from Project construction and operations, including:

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and their content constitute the FEIR on the proposed Project. Citations herein may refer to "DEIR" pages, "RDEIR pages", "RDEIR2" pages, or "FEIR" pages. All references are intended as citations to the Final EIR.

- Failure to mitigate significant impacts on mule deer migration patterns during the spring season, when pregnant does are particularly sensitive to habitat disturbance while recovering from condition lost from winter.

- The County and the Applicant have failed to conduct spring surveys of mule deer to properly assess use of the area in spring, and have failed to recognize and analyze the differences between spring and fall deer migration patterns.

- Construction will result in the loss of 3.5 acres of quality habitat for mule deer that is dominated by bitterbrush, an important browse species for mule deer. The FEIR fails to mitigate for this loss, and the Staff Report fails to adequately respond to this issue.

- Significant cumulative impacts of the loss of mule deer habitat have not been properly addressed or mitigated. In order to adequately minimize the cumulative impacts of the M-I replacement Project in conjunction with other habitat-destructive development in and around the County, the Project should return the existing MP-I plant to natural habitat once the M-I plant is fully operational, rather than retain the existing MP-I footprint as a storage facility and overflow parking lot.

- The Staff Report fails to address issues raised in prior comments about the unproven effectiveness of proposed Bio Protection Measure 8, which proposes to mitigate for linear barriers erected for the Project by constructing 10m earthen ramp connections, despite the fact that the efficacy of these ramps is unproven and doubtful for use by mule deer.

- The Staff Report fails to address inconsistencies and conflict between Bio Protection Measure 7, which purportedly prohibits the erection of "any linear barriers to movement of deer or other wildlife in the area between the existing MP-I plant site and the replacement M-I plant site," and other components of the Project, such as RDEIR schematics and project description which provide for construction of new linear pipelines and interconnection lines, and Bio Protection Measure 2, which requires mitigations during installation of "above ground pipeline and transmission lines," precisely the type of linear barriers that are prohibited under Measure 7.

- The Staff Report fails to adequately respond to issues raised by expert comments on potentially significant impacts on the Owens Tui Chub.

General Plan Inconsistency:

- The Project remains inconsistent with the Mono County General Plan ("General Plan") in that it requires the County to amend the Mono County General Plan to authorize the Applicant to develop geothermal facilities within 500 feet of a watercourse within the Hot Creek Buffer Area. To remedy this inconsistency, the FEIR proposed a General Plan amendment to allow geothermal development in areas that were previously prohibited in the County. The amendment is both facially inconsistent with the Plan's Conservation and Open Space Element, which requires the County to minimize impacts of geothermal energy production on water resources in the Casa Diablo area, and opens the door for new geothermal projects to develop facilities within this previously protected, sensitive habitat.

Inaccurate Project Description:

- The Project description in the FEIR remains inaccurate and legally insufficient in that it:
  - Fails to describe the Project in light of the proposed General Plan Amendments identified for the first time in the RDEIR2.
  - The Project, as described in the FEIR and in Staff Responses, would continue to violate its own proposed mitigation measures for impacts to biological resources, including in particular rendering either the Project description, or its mitigation measures, inaccurate and facially inconsistent with each other.

Inadequate Cumulative Impacts Analysis:

- The Staff Report fails to adequately respond to prior comments regarding the FEIR's failure to adequately analyze cumulative impacts resulting from planned construction of the Casa Diablo IV geothermal power plant and facilities, wells, and pipelines, currently undergoing joint NEPA and CEQA review by the U.S Bureau of Land Management ("BLM") and the Great Basin Air Pollution and Control District ("GBAPCD"), including but not limited to:
  - **Hydrology**: The FEIR fails to adequately analyze cumulative impacts on the geothermal aquifer and nearby surface waterways.
  - **Seismic Activity**: Enhanced geothermal systems can trigger earthquakes as part of hydraulic fracturing. The FEIR fails entirely to analyze the cumulative impacts of Project-generated seismic activity, combined with that of the proposed Casa Grande IV facility on nearby communities and existing structures.
  - **Biological Resources**: The FEIR fails to adequately analyze cumulative impacts on fisheries dependent on Hot Creek. The FEIR also fails to

analyze the incrementally significant impact of the Project on interruption of mule deer habitat and migration corridors.

Air Quality:

- The Staff Report fails to respond to the comments of LIUNA and other members of the public regarding the following air quality issues, in particular during the overlapping 2-year period of simultaneous operations of the existing MP-I and replacement M-I plant until M-I becomes fully operational:
    - NOx: Project construction will have significant air quality impacts from excess emissions of nitrogen oxides produced during combustion (NOx) that the County has failed to properly analyze and mitigate due to reliance on inappropriately high significant thresholds borrowed from Imperial County.
    - DPM: The FEIR fails to analyze diesel particulate matter ("DPM") emissions from Project construction.
    - Baseline: The FEIR relies on a legally improper baseline for operational emissions, given the new location of the proposed M-1 plant and the simultaneous operations of both the MP-1 and M-1 plants for up to 2 years during the M-I startup period.
    - VOCs: The EIR fails to adequately disclose and document the basis for its calculations of estimated operational emissions of Volatile Organic Compounds ("VOCs") from both the existing MP-I plant (and the M-I Replacement plant. The FEIR estimates a total of 205 lb /day of VOC emissions (from n-pentane motive fluid) from the new M-I plant, and 500 lb /day of VOC emissions (from isobutane gaseous motive fluid) from the existing MP-I plant, yet fails to identify methods used to calculate emissions based on historical plant purchase records, fails to discuss the applicability of the average emission factors for refineries from the USEPA's document to the Project's equipment. As a result, the Project's VOC emissions may be significantly underestimated, resulting in actual VOC emissions far above the GBAPCD's VOC BACT significant threshold of 205 lb / day. The EIR fails to mitigated these potentially significant impacts.

Expert Comments and Prior Comments

These comments are supported by the expert comments of expert Wildlife Ecologist Luke Macauley, M.S. Mr. Macauley is an expert wildlife biologist and ecologist who has expertise in the areas of rare and special status plants, animal density and distribution, habitat selection, habitat restoration, interactions between wildlife and human infrastructure and activities, conservation of rare and endangered species, and on the ecology of invading species, and other species impacts relevant to this Project. His comments and curriculum vitae are attached hereto as Exhibit A and are

incorporated by reference in their entirety. These expert comments are incorporated herein in full.

LIUNA expressly adopts and incorporates by reference its own prior comments on the Project, as well as all other prior comments on the Project, including but not limited to comments on the Notice of Preparation, Draft EIR, Revised Draft EIR, Second Revised Draft EIR, and Final EIR, including but not limited to the following:

- March 15, 2012 letter of David Marcus, Consultant, regarding reported capacity, and output generation of existing geothermal plant;
- March 22, 2012 letter of Matt Hagemann, P.G., C.Hg., *Comments on the Proposed Mammoth Pacific I Replacement Project Revised Draft Environmental Impact Report*;
- March 22, 2012 letter of James Clark, Ph.D., Clark & Associates, *Comment Letter on Proposed Mammoth Pacific MP-I Plant Replacement Revised Draft Environmental Impact Report (RDEIR)*;
- March 23, 2012 letter of Scott Cashen, M.S., Senior Biologist, *Comments on Revised Draft Environmental Impact Report for Mammoth Pacific I Replacement Project;*
- March 30, 2012 letter of Jan. M. Zimmerman. P.G., Environmental Geologic, Lahontan Regional Water Quality Control Board, *Comments on the Revised Draft Environmental Impact Report (EIR) for the Mammoth Pacific I Replacement Project, Mammoth Lakes, Mono County;*
- October 17, 2012 letter of Dr. Petra Pless, D.Env., *Comments on Final Environmental Impact Report for Mammoth Pacific I Replacement Project*;
- October 18, 2012 letter of Matt Hagemann, P.G., C.Hg., *Comments on the Proposed Mammoth Pacific I Replacement Project Final Environmental Impact Report*;
- October 18, 2012 letter of Scott Cashen, M.S., *Comments on Final Environmental Impact Report for Mammoth Pacific I Replacement Project.*

Statement of Interest

LIUNA Local 783 recognizes that the development of reliable renewable energy sources is critical for California's future. LIUNA supports the development of clean, renewable energy technology, including the use of geothermal power generation where feasible. All geothermal and related mineral extraction extraction projects must be properly analyzed and carefully planned to minimize impacts on the environment. Geothermal and mineral extraction projects should avoid impacts to sensitive species and habitats, and should take all feasible steps to ensure that the production of renewable energy is not done at the expense of the State's natural resources, and dependent species. Only by maintaining the highest standards in these and other ways can energy supply development be truly sustainable. Unfortunately, the Project falls short in these and other ways. As a consequence, an SEIR is required to analyze the Project impacts discussed above, including impacts raised by other commenters and not adequately addressed by the County, and to propose feasible mitigation measures to bring the Project in compliance with applicable laws.

LIUNA supplements its prior comments on the Final EIR with the following.

I. BACKGROUND.[2]

The proposed Project approvals include approval of a Final EIR and related CEQA findings; Conditional Use Permit; approval of a variance from the 100-foot property-line and 500-foot stream setbacks applicable to geothermal development, authorization for the placement of an aboveground transmission pipeline, and a recommendation that the Board of Supervisors add clarifying language to the Mono County General Plan related to the 500-foot stream setback.

The County prepared an Environmental Impact Report "(EIR") pursuant to CEQA for the Project. On October 11, 2012, the Mono County Planning Commission held a public hearing on the Project, Final EIR, and approvals, and approved the Conditional Use Permit, granted the requested variance, approved the Reclamation Plan, and recommended that the Board of Supervisors approve the General Plan amendment. LIUNA appeals from these approvals.

II. THE PROPOSED CEQA FINDINGS ARE INADEQUATE AND UNSUPPORTED BY SUBSTANTIAL EVIDENCE.

A. The EIR Fails To Provide Substantial Evidence To Support the Proposed Findings that the Project Will Have No Unavoidable Significant Environmental Effects After Mitigation.

CEQA requires that a lead agency's findings for the approval of a project be supported by substantial evidence in the administrative record. CEQA further requires that a lead agency provide an explanation of how evidence in the record supports the conclusions it has reached. When an EIR identifies significant environmental impacts that may result from a project, the lead agency must make one or more specific findings for those impacts. Under PRC § 21081 and 14 CCR § 15091, the lead may find that:

> Changes or alterations have been required in, or incorporated into, the project that avoid or substantially lessen the significant environmental effects identified in the EIR.
>
> Such changes or alterations are within the responsibility and jurisdiction of another public agency that has adopted, or can and should adopt, such changes.
>
> Specific economic, social, legal, technological, or other considerations make infeasible the mitigation measures or project alternatives identified in the EIR. (PRC § 21081; 14 CCR § 15091)

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2 LIUNA hereby incorporate the Project background from its October 11, 2012 letter, and adds the following procedural background related to the appeal.

One or more of these findings must be made for each significant environmental impact identified in the EIR. (PRC § 21081; 14 CCR §§ 15091(a), 15121(b)) Each finding must be accompanied by an adequate explanation of the rationale for the finding. (14 CCR §15091(a); see Village Laguna of Laguna Beach v. Bd. Of Supervisors (1982) 134 CA3d 1022, 1034) And any finding that proposed mitigation measures will avoid or substantially reduce a significant impact must be supported by substantial evidence in the record of the agency's proceedings. (14 CCR § 15091(b)) Reliance on clearly inadequate or unsupported studies to support proposed mitigation measures is prohibited by CEQA. (*Laurel Heights Improvement Ass'n v. Regents of Univ. of Cal.* (1988) 47 Cal.3d 376, 409, n12) The County will violate CEQA if it adopts the CEQA findings proposed in the Staff Report because they are inadequate as a matter of law in that they are not supported by substantial evidence in the record.

The Staff Report and EIR erroneously conclude that the Project will have no unavoidable significant environmental effects, and that all potentially significant environmental effects will be mitigated to below a level of significance. (See Draft Resolution 12-0005, Exh. A. Part II). This conclusion is unsupported by the evidence in the Project record, and is rebutted by the expert evidence cited herein.

The County simply cannot meet its burden of finding that all significant impacts of the Project have been adequately mitigated where, as here, the County has failed to disclose, analyze and mitigate numerous significant impacts. The Board should decline to adopt the County's proposed CEQA findings.

B. The EIR Also Fails To Provide Substantial Evidence To Support a Finding of Overriding Considerations.

The Staff Report erroneously concludes that the Project will not have any potentially significant, unmitigated environmental impacts. In fact, and as evidenced by the extensive expert comments filed by LIUNA and other members of the public during the Project's CEQA review process, the Project will, in fact, have significant, unmitigated environmental impacts, particularly in the areas of biological resources and air quality. As a result, the County will need to adopt a statement of overriding considerations. Under CEQA, when an agency approves a project with significant environmental impacts that will not be fully mitigated, it must adopt a "statement of overriding considerations" finding that, because of the project's overriding benefits, it is approving the project despite its environmental harm. (14 Cal.Code Regs. §15043; Pub. Res. Code §21081(B); *Sierra Club v. Contra Costa County* (1992) 10 Cal.App.4th 1212, 1222). A statement of overriding considerations expresses the "larger, more general reasons for approving the project, such as the need to create new jobs, provide housing, generate taxes and the like." (*Concerned Citizens of South Central LA v. Los Angeles Unif. Sch. Dist.* (1994) 24 Cal.App.4th 826, 847).

A statement of overriding considerations must be supported by substantial evidence in the record. (14 Cal.Code Regs. §15093(b); *Sierra Club v. Contra Costa Co.* (1992) 10 Cal.App.4th 1212, 1223)). The agency must make "a fully informed and

publicly disclosed" decision that "specifically identified expected benefits from the project outweigh the policy of reducing or avoiding significant environmental impacts of the project." (15 Cal.Code Regs. §15043(b)). As with all findings, the agency must present an explanation to supply the logical steps between the ultimate finding and the facts in the record. (*Topanga Assn. for a Scenic Community v. County of Los Angeles* (1974) 11 Cal.3d 506, 515).

Key among the findings that the lead agency *must* make is that:

> "Specific economic, legal, social, technological, or other considerations, including ***the provision of employment opportunities for highly trained workers,*** make infeasible the mitigation measures or alternatives identified in the environmental impact report...[and that those] benefits of the project outweigh the significant effects on the environment."

(Pub. Res. Code §21081(a)(3), (b)).

Thus, the County must make specific findings, supported by substantial evidence, concerning both the environmental impacts of the Project, and the economic benefits including "the provision of employment opportunities for highly trained workers" created. The EIR and its supporting documents fails to provide substantial evidence to support a statement of overriding considerations.

In short, the County cannot find that the economic benefits of the Project outweigh the environmental costs if it does not know what the economic benefits will be. A revised EIR, Fiscal Analysis and Statement of Overriding Considerations is required to provide this information.

III. THE STAFF REPORT FAILS TO RESPOND TO COMMENTS REGARDING THE EIR'S FAILURE TO ANALYZE AND MITIGATED ALL POTENTIALLY SIGNIFICANT IMPACTS OF THE PROJECT TO BIOLOGICAL RESOURCES.

CEQA requires that an agency analyze the potential environmental impacts of its proposed actions in an environmental impact report ("EIR") (except in certain limited circumstances). (*See, e.g.*, Pub. Res. Code § 21100.) The EIR is the very heart of CEQA. (*Dunn-Edwards v. BAAQMD* (1992) 9 Cal.App.4th 644, 652.) "The 'foremost principle' in interpreting CEQA is that the Legislature intended the act to be read so as to afford the fullest possible protection to the environment within the reasonable scope of the statutory language." (*Communities for a Better Environment v. Calif. Resources Agency* (2002) 103 Cal. App. 4th 98, 109.)

CEQA requires public agencies to avoid or reduce environmental damage when "feasible" by requiring "environmentally superior" alternatives and all feasible mitigation measures. (CEQA Guidelines § 15002(a)(2) and (3); See also, *Berkeley Jets*, 91 Cal. App. 4th 1344, 1354; *Citizens of Goleta Valley v. Board of Supervisors* (1990) 52 Cal.3d 553, 564) The EIR serves to provide agencies and the public with information about the environmental impacts of a proposed project and to "identify ways that environmental damage can be avoided or significantly reduced." (Guidelines §15002(a)(2)) If the project will have a significant effect on the environment, the agency may approve the project only if it finds that it has "eliminated or substantially lessened all significant effects on the environment where feasible" and that any unavoidable significant effects

on the environment are "acceptable due to overriding concerns." (Pub.Res.Code § 21081; 14 Cal.Code Regs. § 15092(b)(2)(A) & (B))

A prejudicial abuse of discretion occurs "if the failure to include relevant information precludes informed decisionmaking and informed public participation, thereby thwarting the statutory goals of the EIR process." (*San Joaquin Raptor/Wildlife Rescue Center v. County of Stanislaus* (1994) 27 Cal. App. 4th 713, 722]; *Galante Vineyards v. Monterey Peninsula Water Management Dist.* (1997) 60 Cal. App. 4th 1109, 1117; *County of Amador v. El Dorado County Water Agency* (1999) 76 Cal. App. 4th 931, 946)

Expert wildlife biologist Mr. Macauley reviewed the Staff Responses to his October 11, 2012 comments regarding the FEIR, and has concluded that Staff failed to adequately respond to his comments, and that the EIR fails to adequately analyze and mitigate impacts to mule deer.

Mr. Macauley states:

The following is a list of issues that have not been adequately responded to or addressed by the Applicant:

1. Applicant has not conducted spring surveys of mule deer to properly assess use of the area in spring. The Applicant cannot adequately address impacts of the project without this information.
2. Applicant has still not addressed clear differences between spring and fall deer migration patterns. Because of this, the Applicant cannot conclusively describe the deer use on the site, especially for spring migrating deer.
3. Construction will result in the loss of 3.5 acres of quality habitat for mule deer that is dominated by bitterbrush, an important browse species for mule deer.
    a. The Applicant states that Bio Protection Measures 7 -12 are applicable to the proposed project and would address potential direct project effects on mule deer and wildlife. However none of these measures addresses the loss of 3.5 acres of quality habitat for mule deer.
    b. In a very general sense, this project will result in the net gain of an overflow parking lot and storage yard in the Project Area. Since the project will be moving an existing power plant to a new site, to keep impacts to less than significant, the Applicant should decommission the old site and restore it to quality habitat for mule deer and other impacted wildlife species. Instead, as the project now stands, the project will result in the old decommissioned site being converted to a fenced storage yard and overflow parking facility. This does not appear to be essential to the goals of the

project, and fails to mitigate for the loss of habitat by new construction.

4. Significant cumulative impacts have not been adequately addressed.
    a. Cumulative Bio Mitigation Measure 1 calls for others to conduct baseline deer studies and monitoring deer use. Conducting studies and monitoring for deer use do not qualify as mitigation.
    b. Bio Mitigation Measure 1 does not include any mitigation for cumulative impacts of habitat loss, which is one of the primary threats to mule deer in the area.
5. Construction schedule interferes with migrating deer.
    a. During early construction, an average of seven truck deliveries a day (resulting in 14 trips) and 60 workers on the construction site will likely overlap with part of the spring migration of mule deer, causing significant impact to pregnant does that are recovering from condition lost from winter.
6. Bio Protection Measure 8 remains unproven and vague.
    a. The Applicant has failed to provide any evidence that earthen ramps like the one proposed in Bio Protection Measure 8 are used by deer and provide effective mitigation.
    b. While expert testimony noted that the new site would provide better connectivity than the current configuration of the site, this is not clear based on basic width measurements. Currently the site has three gaps of approximately 20m, 8 m, and 44 m (see Figure 32). Under option 1 the first two smaller gaps would be eliminated. Resulting in a loss of total width of connectivity paths by approximately 39%. The proposed ramp would create a 10m connection, but the efficacy of these ramps is unproven and doubtful. Even if this ramp constituted effective connectivity for deer, there would still be a loss of approximately 25% of width of connectivity corridors from pre-construction levels. This reduction constitutes a significant impact to connectivity for a migrating deer herd that is already undergoing serious declines.
    c. Furthermore, the Applicant has still failed to describe the slope of the ramp to be built and how they will build such a ramp without blocking the road that is adjacent to the ramp crossing area.
    d. The Applicant notes in response to comments that the pipelines cannot be buried due to hot soils. However, the pipelines cross underground at road crossing and it is unclear why hot soils are not a problem at these points. Additional information on the presence of hot soils and reasons for not burying pipelines are necessary to show that avoidance of connectivity impacts is not possible.

The Applicant's response to comments raises additional inconsistencies and creates confusion by taking citations out of context:

7. In response to the comment about the Applicant violating their own Bio Protection Measure 7, the Applicant notes that new pipelines would be constructed at "ground level." This is in conflict with Figure 11 in the FDEIR, which notes the pipelines will be 2-3 feet in height and 6 inches in diameter.
    a. While I acknowledge that deer can likely pass over or below this pipeline, the definition of a barrier includes objects that can hinder movement, and it is likely that these new pipelines create some hindrance to movement by deer, especially migrating deer that will not be acclimated to the pipelines. The construction of approximately 2000 feet of new pipelines and transmission lines does represent a new linear barrier, which violates the Applicant's Bio Protection Measure 7.
8. The Applicant misreads and confuses citations to Kucera 1987. The citations are provided to show evidence of biological characteristics and timing of fall and spring deer migrations. They are not an endorsement of the final conclusions of the report. Furthermore, the final conclusions of this report were written 26 years ago. In the last 26 years the population of the Round Valley deer herd has seen dramatic losses, and the conclusions of the report must be viewed in the context of which they were written – before dramatic losses of this deer population. While the decline of migratory deer has makes the conclusions of this report outdated, the biological assessments of deer migration patterns remain relevant.

(See Exh. A at pp. 1-3)

An EIR may not avoid studying impacts to biological resources by proposing future study or mitigation based on future studies unless the mitigation measures and performance standards are explicit in the EIR. (*San Joaquin Raptor Rescue Center v. County of Merced* (2007) 149 Cal.App.4th 645, 671)

The Project's FEIR fails to assess impacts to wildlife, especially sensitive species and plants, and the Staff Report fails to respond to the substantial evidence raised by LIUNA's experts about the inadequacy of proposed mitigation measures to mitigated these impacts. Where impacts are identified, the FEIR impermissibly relies on vague, unenforceable and deferred mitigation measures, most of which lack a foundation in science and performance standards. Consequently, the FEIR must be revised to reassess impacts to biological resources and, where appropriate, propose adequate mitigation measures with definite terms and verifiable performance standards.

IV. THE STAFF REPORT FAILS TO AEQUATELY RESPOND TO COMMENTS REGARDING INCONSISTENCIES WITH THE COUNTY'S GENERAL PLAN.

As discussed in LIUNA's prior comments, the Project is inconsistent with the Mono County General Plan ("General Plan") in that it requires the County to amend the Mono County General Plan to authorize the Applicant to develop geothermal facilities within 500 feet of a watercourse within the Hot Creek Buffer Area. To remedy this inconsistency, the FEIR proposed, and the Planning Commission approved, a General Plan amendment to allow geothermal development in areas that were previously prohibited in the County. The amendment is both facially inconsistent with the Plan's Conservation and Open Space Element, which requires the County to minimize impacts of geothermal energy production on water resources in the Casa Diablo area, and opens the door for new geothermal projects to develop facilities within this previously protected, sensitive habitat. The Staff Report dismisses this comment with no meaningful response.

It is well-established that the elements, data, assumptions and projections used in various parts of a general plan must be consistent with one another. (Gov. Code §65300.5; *see Concerned Citizens of Calaveras County*, 166 Cal. App. 3d at 96-97; *Sierra Club*, 126 Cal. App. 3d at 704) Additionally, general plan inconsistencies are, themselves, also potentially significant impacts under CEQA. (*See Pocket Protectors v. City of Sacramento* (2004) 124 Cal. App. 4th 903, 930, 934 (requiring project's conflicts with land use policies adopted to avoid environmental effects to be discussed in an EIR))

Here, General Plan Land Use Element, Development Standards section 15.070(B)(1)(d) expressly prohibits geothermal development within 500 feet of surface waters. It provides in relevant part:

> No geothermal development located within the Hot Creek Buffer Zone shall occur within 500 feet on either side of a surface watercourse (as indicated by a solid or broken blue line on U.S. Geological Survey 7.5- or 15-minute series topographic maps). (General Plan at LU- II-263)

Additionally, Conservation / Open Space Element, Goal 7 provides, in relevant part:

> **GOAL 7:** Minimize the visual and environmental impacts of electrical transmission lines and fluid conveyance pipelines....
> **Objective B**
> Transmission and distribution lines shall not adversely impact wildlife or fisheries.
> Policy 1: New transmission or distribution lines shall avoid open expanses of water and wetland, particularly those heavily used by birds. They shall also avoid nesting and rearing areas.
> Policy 2: Avoid the placement of transmission or distribution lines through crucial wildlife habitats, such as deer fawning and migration areas. (See Conservation/Open Space Element at V-47 to V-49)

Nevertheless, the Project proposes two variances to exempt it from critical elements of the General Plan's Land Use Element and Conservation/Open Space Element:

- A Variance for setback reductions from property line(s); setback reductions from streams designated by a blue line on USGS topographic maps for structures within the 5.7-acre proposed M-1 plant site; and for grading of the existing MP-I plant site for use as an equipment storage area;
- A Variance to construct an aboveground electrical transmission line. (RDEIR2 at p. 29)

The FEIR incorrectly concludes that the Project is consistent with the General Plan under its proposed Clarifying General Plan Amendment. The RDEIR2 proposed a General Plan Amendment to relieve the Project from the General Plan 500-foot setback requirement contained in Land Use Element Section 15.070(B)(1)(d) that will amend the Conservation/Open Space Element to authorize development of geothermal facilities within 500 feet of a watercourse within the Hot Creek Buffer Zone, as follows:

Conservation and Open Space Element
Energy Resources, Objective D, Policy 1
Action 1.13: ~~No geothermal development located within the Hot Creek Buffer Zone shall occur~~ Adoption of land development regulations for geothermal development within 500 feet on either side of a surface watercourse (as indicated by a solid or broken blue line on U.S. Geological Survey 7.5- or 15-minute series topographic maps) within the Hot Creek Buffer Zone (See Mono County Land Development Regulations, Chapter 15, section 15.070(B)(1)(d).)

(RDEIR2 at p. 34)

The amendment was included for the first time in the RDEIR2, in subsection 4.10 of the document, and was not included in the Project description in either the RDEIR2 or the FEIR's updated Project Location or Project Summary. (RDEIR2 at pp. 33-34; FEIR at pp. 1-4) On its face, the proposed amendment would render Section 15.070(B)(1)(d) of the General Plan facially inconsistent with Objective D, Policy 1 of the Conservation / Open Space Element, which provides in relevant pat:

Policy 1: Geothermal exploration and development projects shall be sited, carried out and maintained by the permit holder in a manner that best protects hydrologic resources and water quality and quantity.

(See Conservation/Open Space Element at V-41)

If approved, the Clarifying General Plan Amendment will render these General Plan provisions internally inconsistent with one another. The County would be exceeding its authority if it were to issue permits or variances related to the Project as described in the FEIR, based on the proposed amendment or otherwise, because the Project is inconsistent with the County's General Plan, particularly its Land Use and Conservation/ Open Space Elements. (*See Neighborhood Action Group v. County of*

Calaveras (1984) 156 Cal.App.3d 1176, 1184) In *Neighborhood Action Group*, the Court of Appeal held that "a use permit is struck from the mold of the zoning law....the zoning law must comply with the adopted general plan...[and] the adopted general plan must comply with state law." (*Id.* at 1184) The general plan delimits the authority of the permit-issuing agency; thus, where an agency issues a permit that is inconsistent with the general plan, it exceeds its legal authority and the permit is invalid. (*Id.*)

V. THE PROJECT DESCRIPTION IN THE FEIR AND STAFF REPORT REMAINS INACCURATE AND IMCOMPLETE.

"An accurate, stable and finite project description is the sine qua non of an informative and legally adequate EIR." (*County of Inyo v. City of Los Angeles* (1977) 71 Cal.App.3d 185, 192; *Berkeley Jets*, 91 Cal. App. 4th 1344, 1354; *Sacramento Old City Assn. v. City Council* (1991) 229 Cal. App. 3d 1011, 1023; *Stanislaus Natural Heritage Project v. County of Stanislaus* (1996) 48 Cal. App. 4th 182, 201) "[A] curtailed or distorted project description," on the other hand, "may stultify the objectives of the reporting process. Only through an accurate view of the project may affected outsiders and public decision-makers balance the proposal's benefit against its environmental costs, consider mitigation measures, assess the advantage of terminating the proposal (i.e., the "no project" alternative) and weigh other alternatives in the balance." (*Id.;* see also, 14 CCR § 15124) As one analyst has noted:

> The adequacy of an EIR's project description is closely linked to the adequacy of the EIR's analysis of the project's environmental effects. If the description is inadequate because it fails to discuss the complete project, the environmental analysis will probably reflect the same mistake. (Kostka and Zischke, "Practice Under the California Environmental Quality Act," p. 474 (8/99 update); *see also Santiago County Water Dist. v. County of Orange* (1981) 188 Cal. App. 3d 818, 829)

A "rigorous analysis" is required to dispose of an impact as insignificant. (*Kings County Farm Bureau v. City of Hanford* (1990) 221 Cal.App.3d 692) Such a rigorous analysis is not possible is not possible if the project description is inaccurate, inconsistent, or misleading.

The Staff Report fails to respond to comments regarding inaccuracies in the Project description due to both (1) the General Plan amendments discussed above, which were disclosed for the first time in a subsection of the RDEIR2 and were not included in either the original or updated Project description contained in the various CEQA documents prepared for the Project, and (2) the Project, as described, would continue to violate its own proposed mitigation measures for impacts to biological resources, rendering either the Project description, or its mitigation measures, inaccurate and facially inconsistent with each other.

A. The Proposed General Plan Amendment to Relieve the Project from the General Plan's 500-Foot Surface Water Setback Requirement Was Not Included in the Project Description, and Its Impacts Have Not Been Analyzed.

The RDEIR2 proposed a General Plan Amendment to relieve the Project from the General Plan 500-foot setback requirement contained in Land Use Element Section 15.070(B)(1)(d), discussed in Section IV.A above, by amending the Conservation/Open Space Element to authorize development of geothermal facilities within 500 feet of a watercourse within the Hot Creek Buffer Zone, as follows:

> **Conservation and Open Space Element**
> **Energy Resources, Objective D, Policy 1**
> Action 1.13: ~~No geothermal development located within the Hot Creek Buffer Zone shall occur~~ Adoption of land development regulations for geothermal development within 500 feet on either side of a surface watercourse (as indicated by a solid or broken blue line on U.S. Geological Survey 7.5- or 15-minute series topographic maps) within the Hot Creek Buffer Zone (See Mono County Land Development Regulations, Chapter 15, section 15.070(B)(1)(d).)

(RDEIR2 at p. 34)

The amendment was included for the first time in the RDEIR2, in subsection 4.10 of the document, and was not included in the Project description in either the RDEIR2 or the FEIR's updated Project Location or Project Summary. (RDEIR2 at pp. 33-34; FEIR at pp. 1-4) The FEIR fails to adequately respond to this issue, raised in prior Comment Letter 12. Including a significant land use change in a subsection of the RDEIR2, and not amending the overall Project Description to both describe the Project revision and evaluate its environmental impacts, fails to satisfy CEQA's requirement to describe all aspects of the Project which may result in potentially significant environmental impacts. (14 CCR § 15124) As a result of the surface water setback reduction, the Project may result in significant surface water impacts within the Hot Creek Buffer Zone that have not been properly disclosed or analyzed in the EIR. (*See County of Inyo v. City of Los Angeles* (1981) 124 Cal. App. 3d 1, 7 (revised EIR that fails to describe or analyze surface water impacts is legally insufficient as a CEQA document))

B. The Project Description Is Inaccurate Because It is Facially Inconsistent With Bio Protection Measure 7, and In the RDEIR, Authorizes Construction of Linear Barriers to Deer Migration, While In Proposed Mitigation Measures, Expressly Prohibits Such Barriers.

The Project, as described in the FEIR, will install approximately 2000 feet of linear barriers in the area between the existing MP-I plant site and the replacement M-1 plant site. Specifically, the project will construct 500 feet of interconnection injection fluid pipeline and about 1,500 feet of interconnection transmission line. (FEIR, p. 4-65)

This component of the Project is directly inconsistent with Bio Protection Measure 7, which calls for no additional linear barriers to be constructed:

> "The Project shall not erect any linear barriers to movement of deer or other wildlife in the area between the existing MP-I plant site and the replacement M-1 plant site. During M-1 plant site construction, no temporary fencing or pipeline

racks shall be erected in this same area during the normal periods of mule deer migration, from April 1st to May 30th or from September 15th through November 15th." (FEIR, p.4-73)

As discussed by expert Macauley, "the pipelines that would be constructed appear to be permanent, and would violate this mitigation measure. While the Applicant notes that wildlife could move both over and beneath the interconnection pipeline and transmission line conduit, it is nonetheless an additional linear barrier that clearly violates the Applicant's own proposed mitigation measures." (Exh. A; see also Macauley comments of October 11, 2012 at p. 8)

CEQA requires that an EIR's project description must provide "enough information to ascertain the project's environmentally significant effects, assess ways of mitigating them, and consider project alternatives." (*Sierra Club v. County of Orange* (2008) 163 Cal. App. 4th 523) The Mammoth Project description does exactly the opposite here. The inconsistency between the Project's described transmission lines and its required Bio Measure 7 create a presumption of a per se significant impact that was not properly disclosed or analyzed in the EIR.

The Project description must be amended, and the FEIR revised and recirculated, to correct these deficiencies.

VI. INCONSISTENCY BETWEEN PROPOSED MITIGATION MEASURES RENDERS THEM INFEASIBLE.

As discussed above, the Staff Report fails to respond to inconsistencies and conflicts between Bio Protection Measure 7, which purportedly prohibits the erection of "any linear barriers to movement of deer or other wildlife in the area between the existing MP-I plant site and the replacement M-I plant site," and Bio Protection Measure 2, which requires mitigations during installation of "above ground pipeline and transmission lines," precisely the type of linear barriers that are prohibited under Measure 7. The inconsistency between these two mitigation measures renders them inherently infeasible and thus, inadequate to support a finding that the Project will have no unmitigated significant impacts.

It is well settled that mitigation measures must be feasible, enforceable and effective. A public agency may not rely on mitigation measures of uncertain efficacy or feasibility. (*Kings County Farm Bureau v. City of Hanford* (1990) 221 Cal.App.3d 692, 727 (finding groundwater purchase agreement inadequate mitigation measure because no record evidence existed that replacement water was available).) "Feasible" means capable of being accomplished in a successful manner within a reasonable period of time, taking into account economic, environmental, legal, social and technological factors. (14 CCR § 15364.) Mitigation measures must be fully enforceable through permit conditions, agreements or other legally binding instruments. (14 CCR § 15126.4(a)(2).)

Here, Bio Measure 7 can never be accomplished **at all**, let alone in a reasonable period of time, because it is facially inconsistent with elements of Project design and other Mitigation Measures, such as Bio Measure 2, which provide for erection of linear

barriers that will impede deer migration. As such, at a minimum, Measure 7 is infeasible, and therefore the County cannot find that this Measure serves to mitigate any significant impact of the Project, not make a finding to such effect in any contemplated Project approvals.

VII. THE STAFF REPORT FAILS TO RESPOND TO COMMENTS REGARDING AN INADEQUATE CUMULATIVE IMPACTS ANALYSIS, AND FAILS TO RESOLVE THESE ISSUES BY PREPARING A SUPPLEMENTAL EIR.

As discussed in prior comments, the Mammoth Project is one of several existing and planned geothermal projects within the Casa Grande geothermal complex and the Great Basin Valleys Air Basin, which air basin encompasses Mono, Inyo and Alpine counties. (RDEIR at p. 4-37, 4-378) The EIR and Staff Report fail to include an adequate analysis of the Project's cumulative impacts on hydrology, seismicity, and biological resources, among other issues, as together with the existing MP-I, MP-II, PLES-I, and Basalt Canyon Pipeline facilities, and, in particular, the proposed 33 MW Casa Diablo IV Project, including its proposed wellfield expansion of up to 14 additional wells. (See Exhibit B, Casa Grande IC BLM Project webpage; see Exhibit A, Macauley comments; see also October 18, 2012 letter of Matt Hagemann, P.G., C.Hg. submitted by CURe)

An EIR must discuss significant cumulative impacts. (CEQA Guidelines § 15130(a)) This requirement flows from CEQA section 21083, which requires a finding that a project may have a significant effect on the environment if "the possible effects of a project are individually limited but cumulatively considerable. . . . 'Cumulatively considerable' means that the incremental effects of an individual project are considerable when viewed in connection with the effects of past projects, the effects of other current projects, and the effects of probable future projects." (*See also* 14 Cal. Code Regs. § 15130(a))"Cumulative impacts" are defined as "two or more individual effects which, when considered together, are considerable or which compound or increase other environmental impacts." (*Id.* § 15355(a)) "[I]ndividual effects may be changes resulting from a single project or a number of separate projects." (*Id.*) Incremental contributions must be assessed "when viewed in connection with the effects of past projects, the effects of other current projects, and the effects of probably foreseeable projects." (14 Cal. Code Regs. § 15065(a)(3))

"The cumulative impact from several projects is the change in the environment which results from the incremental impact of the project when added to other closely related past, present, and reasonably foreseeable probable future projects. Cumulative impacts can result from individually minor but collectively significant projects taking place over a period of time." (*Communities for a Better Environment v. Cal. Resources Agency ("CBE v. CRA")*, (2002) 103 Cal.App.4th 98, 117) A legally adequate cumulative impacts analysis views a particular project over time and in conjunction with other related past, present, and reasonably foreseeable probable future projects whose impacts might compound or interrelate with those of the project at hand. "Cumulative impacts can result from individually minor but collectively significant projects taking place over a period of time." (CEQA Guidelines § 15355(b))

As the court recently stated in *CBE v. CRA,* 103 Cal. App. 4th at 114:

> Cumulative impact analysis is necessary because the full environmental impact of a proposed project cannot be gauged in a vacuum. One of the most important environmental lessons that has been learned is that environmental damage often occurs incrementally from a variety of small sources. **These sources appear insignificant when considered individually, but assume threatening dimensions when considered collectively with other sources with which they interact.**

(Citations omitted)

The Staff Report and EIR fail to adequately analyze cumulative impacts resulting from planned construction of the Casa Diablo IV geothermal power plant and facilities, wells, and pipelines, currently undergoing joint NEPA and CEQA review by the U.S Bureau of Land Management ("BLM") and the Great Basin Air Pollution and Control District ("GBAPCD"). The Casa Diablo IV Project, proposed by Mammoth Project Applicant MPLP, is to be located in the immediate vicinity of the existing MPLP geothermal projects, near the intersection of California State Route 203 and U.S. Highway 395, approximately 3 miles east of Mammoth Lakes, California, and may construct up to 14 additional geothermal wells. (Exhibit B; RDEIR p. S-17)

The Staff Report and EIR also fail to adequately analyze cumulative impacts resulting from incremental reduction of mule deer habitat from multiple development projects in the vicinity of the Mammoth Pacific I Project.

As discussed by wildlife expert Mr. Macauley, the Staff Report fails to adequately respond to his comments regarding cumulative impacts on mule deer.

Mr. Macauley states:

> 4. Significant cumulative impacts have not been adequately addressed.
> a. Cumulative Bio Mitigation Measure 1 calls for others to conduct baseline deer studies and monitoring deer use. Conducting studies and monitoring for deer use do not qualify as mitigation.
> b. Bio Mitigation Measure 1 does not include any mitigation for cumulative impacts of habitat loss, which is one of the primary threats to mule deer in the area.

(Exh. A at pp. 2-3; see also Macauley October 11, 2012 comments at pp. 3-5)

This is precisely the type of cumulatively considerable impact that must be properly analyzed and mitigated under CEQA. The EIR's failure to analyze reasonably forseeable cumulative impacts of other development projects on mule deer render the EIR legally deficient as a matter of law.

VIII. THE COUNTY SHOULD PREPARE AND RECIRCULATE A SUPPLEMENTAL FEIR.

Recirculation of an EIR prior to certification, as here, is addressed in CEQA § 21092.1, and CEQA Guidelines §15088.5. "When significant new information is added to an environmental impact report after notice has been given pursuant to Section 21092 ... ***but prior to certification***, the public agency shall give notice again pursuant to Section 21092, and consult again pursuant to Sections 21104 and 21153 before certifying the environmental impact report." PRC § 21092.1.

"Significant new information" includes:

> (1) A new significant environmental impact would result from the project or from a new mitigation measure proposed to be implemented.
>
> (2) A substantial increase in the severity of an environmental impact would result...
>
> (3) A feasible project alternative or mitigation measure considerably different from others previously analyzed would clearly lessen the significant environmental impacts of the project...
>
> (4) The draft EIR was so fundamentally and basically inadequate and conclusory in nature that meaningful public review and comment were precluded.
>
> 14 CCR §15088.5; *Mountain Lion Coal. v. Fish and Game Comm'n* (1989) 214 Cal.App.3d 1043.

In *Mountain Lion,* the court held that when a detailed project analysis is not prepared until the FEIR, then the document must be recirculated for public comment.

> If we were to allow the deficient analysis in the draft EID[3] to be bolstered by a document that was never circulated for public comment ... we would be subverting the important public purposes of CEQA. Only at the stage when the draft EID is circulated can the public and outside agencies have the opportunity to analyze a proposal and submit comment. No such right exists upon issuance of a final EID unless the project is substantially modified or new information becomes available. (See Cal. Code Regs., tit. 14, § 15162.) To evaluate the draft EID in conjunction with the final EID in this case would only countenance the practice of releasing a report for public consumption that hedges on important environmental issues while deferring a more detailed analysis to the final EID that is insulated from public review.

Mountain Lion, 214 Cal.App.3d at 1052.

In *Laurel Heights Impr. Assn. v. Reg. of Univ. of Cal.* (1993) 6 Cal. 4th 1112 ("*Laurel Heights II,* the Supreme Court explained that Section 21092 favors EIR recirculation prior to certification. The Court stated:

> ***Section 21092.1 was intended to encourage meaningful public comment.*** (See State Bar Rep., supra, at p. 28.) Therefore, new information that demonstrates that an EIR commented upon by the public was so fundamentally

[3] EID is essentially the same as an EIR since the Dept. of Fish and Game had a certified environmental program.

> and basically inadequate or conclusory in nature that public comment was in effect meaningless triggers recirculation under section 21092.1. (See, *Mountain Lion Coalition v. Fish & Game Com., supra*, 214 Cal.App.3d 1043.)

Laurel Heights II, 6 Cal.4th at 1130 (emph. added).

Here, the FEIR has failed to properly analyze cumulative impacts of the Project in conjunction with both existing and reasonably forseeable future projects in the Casa Grande geothermal basin, has failed entirely to analyze cumulative seismic impacts the Projects, and fails to adequately analyze or mitigate impacts to biological resources.

The FEIR must be revised to address these many impacts. Unless the FEIR is revised to address these deficiencies and unless that FEIR is recirculated for further public review, the public and decision makers will be deprived of an opportunity for full input and informed decision making.

IX. CONCLUSION

The Project FEIR fails to analyze and mitigate all significant impacts of the Project. As such, the FEIR remains wholly inadequate and requires significant revision, recirculation and review. The Project as proposed would result in too many unmitigated adverse impacts on the environment to be justified in its present form. California is in need of renewable energy. However, that energy cannot be obtained at the expense of other resources of the State. The Mammoth Project will result in significant that have not been adequately considered, creating the potential for great harm to humans and the natural environment. All of these considerations weigh against approval of the project as proposed.

For the foregoing reasons, the County may not approve the Project as currently proposed. LIUNA respectfully urges the Board to grant this Appeal, and require the County to go back and perform legally adequate environmental review for the Project, and properly mitigate its significant impacts. Thank you for your attention to these comments.

Sincerely,

Richard T. Drury
Christina M. Caro
Lozeau Drury LLP
Attorneys for Laborers' International Union of North America (LIUNA), Local Union No. 783

Cc: Dan Lyster, Mono County Planner (via email only: dyster@mono.ca.gov)

EXHIBIT A

November 12, 2012

Ms. Christina Caro
Lozeau | Drury LLP
410 12th Street, Suite 250
Oakland, CA 94607

Subject: Comments on the Staff Responses for the Mammoth Pacific I Replacement Project

Dear Ms. Caro,

In this letter I briefly outline the areas where the Applicant has not fully responded to or addressed previous comments to the FEIR. The points raised below detail areas of significant environmental impact that have not been adequately addressed in the FEIR. In the few areas where the Applicant did respond to comments, the Applicant has created additional inconsistencies with the FEIR and cause confusion by misreading the intention of citations. The second part of this letter will respond to those issues.

The following is a list of issues that have not been adequately responded to or addressed by the Applicant:

1. Applicant has not conducted spring surveys of mule deer to properly assess use of the area in spring. The Applicant cannot adequately address impacts of the project without this information.
2. Applicant has still not addressed clear differences between spring and fall deer migration patterns. Because of this, the Applicant cannot conclusively describe the deer use on the site, especially for spring migrating deer.
3. Construction will result in the loss of 3.5 acres of quality habitat for mule deer that is dominated by bitterbrush, an important browse species for mule deer.
    a. The Applicant states that Bio Protection Measures 7 -12 are applicable to the proposed project and would address potential direct project effects on mule deer and wildlife. However none of these measures addresses the loss of 3.5 acres of quality habitat for mule deer.
    b. In a very general sense, this project will result in the net gain of an overflow parking lot and storage yard in the Project Area. Since the project will be moving an existing power plant to a new site, to keep impacts to less than significant, the Applicant should decommission the old site and restore it to quality habitat for mule deer and other impacted wildlife species. Instead, as the project now stands, the project will result in the old decommissioned site being converted to a fenced storage yard and overflow parking facility. This does not appear to be essential to the goals of the project, and fails to mitigate for the loss of habitat by new construction.
4. Significant cumulative impacts have not been adequately addressed.

a. Cumulative Bio Mitigation Measure 1 calls for others to conduct baseline deer studies and monitoring deer use. Conducting studies and monitoring for deer use do not qualify as mitigation.
b. Bio Mitigation Measure 1 does not include any mitigation for cumulative impacts of habitat loss, which is one of the primary threats to mule deer in the area.

5. Construction schedule interferes with migrating deer.
   a. During early construction, an average of seven truck deliveries a day (resulting in 14 trips) and 60 workers on the construction site will likely overlap with part of the spring migration of mule deer, causing significant impact to pregnant does that are recovering from condition lost from winter.
6. Bio Protection Measure 8 remains unproven and vague.
   a. The Applicant has failed to provide any evidence that earthen ramps like the one proposed in Bio Protection Measure 8 are used by deer and provide effective mitigation.
   b. While expert testimony noted that the new site would provide better connectivity than the current configuration of the site, this is not clear based on basic width measurements. Currently the site has three gaps of approximately 20m, 8 m, and 44 m (see Figure 32). Under option 1 the first two smaller gaps would be eliminated. Resulting in a loss of total width of connectivity paths by approximately 39%. The proposed ramp would create a 10m connection, but the efficacy of these ramps is unproven and doubtful. Even if this ramp constituted effective connectivity for deer, there would still be a loss of approximately 25% of width of connectivity corridors from pre-construction levels. This reduction constitutes a significant impact to connectivity for a migrating deer herd that is already undergoing serious declines.
   c. Furthermore, the Applicant has still failed to describe the slope of the ramp to be built and how they will build such a ramp without blocking the road that is adjacent to the ramp crossing area.
   d. The Applicant notes in response to comments that the pipelines cannot be buried due to hot soils. However, the pipelines cross underground at road crossing and it is unclear why hot soils are not a problem at these points. Additional information on the presence of hot soils and reasons for not burying pipelines are necessary to show that avoidance of connectivity impacts is not possible.

The Applicant's response to comments raises additional inconsistencies and creates confusion by taking citations out of context:

7. In response to the comment about the Applicant violating their own Bio Protection Measure 7, the Applicant notes that new pipelines would be constructed at "ground

level." This is in conflict with Figure 11 in the FDEIR, which notes the pipelines will be 2-3 feet in height and 6 inches in diameter.

a. While I acknowledge that deer can likely pass over or below this pipeline, the definition of a barrier includes objects that can hinder movement, and it is likely that these new pipelines create some hindrance to movement by deer, especially migrating deer that will not be acclimated to the pipelines. The construction of approximately 2000 feet of new pipelines and transmission lines does represent a new linear barrier, which violates the Applicant's Bio Protection Measure 7.

8. The Applicant misreads and confuses citations to Kucera 1987. The citations are provided to show evidence of biological characteristics and timing of fall and spring deer migrations. They are not an endorsement of the final conclusions of the report. Furthermore, the final conclusions of this report were written 26 years ago. In the last 26 years the population of the Round Valley deer herd has seen dramatic losses, and the conclusions of the report must be viewed in the context of which they were written – before dramatic losses of this deer population. While the decline of migratory deer has makes the conclusions of this report outdated, the biological assessments of deer migration patterns remain relevant.

Sincerely,

Luke Macaulay, M.S.

EXHIBIT F

Comment Letter 9C

Technical Consultation, Data Analysis and Litigation Support for the Environment

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Newport Beach, California 90405
Fax: (949) 717-0069

Matt Hagemann
Tel: (949) 887-9013
Email: mhagemann@swape.com

March 22, 2012

Elizabeth Klebaner
Adams Broadwell Joseph & Cardozo
601 Gateway Boulevard, Suite 1000
South San Francisco, CA 94080-7037

Subject: **Comments on the Proposed Mammoth Pacific I Replacement Project Revised Draft Environmental Impact Report**

Dear Ms. Klebaner:

I have reviewed the February 2012 Revised Draft Environmental Impact Report (RDEIR) for the proposed Mammoth Pacific I Replacement Project (Project) to replace an existing geothermal power plant (MP–I) with a new plant (M–1) in the vicinity of Mammoth Lakes, California. The proposed M–1 plant would be capable of generating approximately 18.8 MW of electricity. Both the new and the existing plants would operate over a two year transition period until the new plant is at full generating capacity. Currently, power is being produced from three plants, MP-I, MP-II, and PLES-1. An additional power generating facility, Casa Diablo IV (CD–4), has been proposed for the area and would produce an additional 33 MW of electricity.

My review has focused on cumulative impacts to water resources. I have found that the RDEIR fails to adequately evaluate cumulative impacts that could result from the operation of the plant in conjunction with other future projects. Because cumulative impacts were not properly evaluated, they are unmitigated.

9C-01 The proposed CD-4 facility includes the drilling of up to 14 new production wells over the life of the plant (RDEIR, p. S-17). The RDEIR includes a map (Fig. 40) that shows a total of three existing production wells. Therefore, addition of CD-4 to the Casa Diablo geothermal complex will increase, by more than four times, the number of production wells in the wellfield. With the addition of the 33 MW CD-4 facility, the expansion of the well field is matched by an equally substantial increase in power generation at the Casa Diablo geothermal complex. Section S, Cumulative Effects, provides no analysis of the combined effects of MP-I, MP-II, and PLES-1 and CD-4 on the geothermal aquifer and the discharge to

9C-01 Cont.

Hot Creek Headsprings. No analysis is provided to determine if the operation of the wells for M-1 along with the operation of the 16 proposed CD-4 wells will potentially deplete the thermal qualities of the geothermal aquifer and alter the discharge from the Hot Creek Headsprings.

9C-02

Monitoring is in place for the existing three wells to determine impacts to Hot Creek; however, it is my opinion that the monitoring would be inadequate to mitigate the combined impacts from the MP-I, MP-II, PLES-I, CD-4 facilities and the proposed M-1 facility. Because of the greatly expanded area and volume of geothermal fluid extraction, a new monitoring plan is necessary to mitigate the impact on thermal resources from existing and proposed power production activities at the Casa Diablo geothermal complex.

The RDEIR needs to be revised to include an analysis of the impacts on geothermal resources from the operation of all existing and proposed generating facilities at the Casa Diablo complex and to include any measures necessary to mitigate those impacts.

Sincerely,

Matt Hagemann, P.G., C.Hg.

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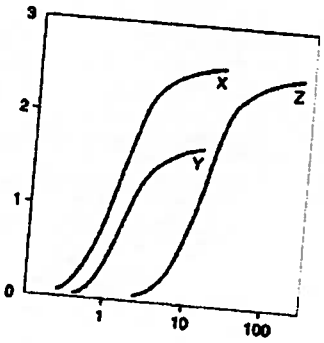
Comment Letter 9D



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March 22, 2012

Adams Broadwell Joseph & Cardozo
601 Gateway Boulevard, Suite 1000
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Attn: Ms. Elizabeth Klebaner

Subject: Comment Letter on Proposed Mammoth Pacific MP-1 Plant Replacement Revised Draft Environmental Impact Report (RDEIR)

Dear Ms. Klebaner:

At the request of Adams Broadwell Joseph and Cardozo (ABJC), Clark and Associates (Clark) has reviewed materials related to the above referenced project, including the Revised Draft Environmental Impact Report (RDEIR) prepared for Mono County. The proponent, Mammoth Pacific, L.P. (MPLP), is proposing to replace an existing geothermal plant with a new geothermal plant. Clark's review of the materials in no way constitutes a validation of the conclusions or materials contained within the plan. If we do not comment on a specific item, this does not constitute acceptance of the item.

Project Description

MPLP operates an existing geothermal development complex northeast of the junction of US Highway 395 and State Route 203, and located about 2.5 miles east of the Town of Mammoth Lakes in Mono County, California[1]. The Casa Diablo geothermal complex includes

[1] 2012. Mammoth Pacific I Replacement Project Revised Draft Environmental Impact Report, California Clearinghouse Number 2011022020. February 2012.

multiple generating stations including the 14 megawatt (MW) Mammoth Pacific I unit (MP-1), the 15 MW Mammoth Pacific II unit ("MP-II"), and the 15 MW PLES-I unit ("PLES-I") – totaling 44 MW in net generating capacity at the site. MPLP is proposing to replace the existing Mammoth Pacific I (MP-I) geothermal power plant with new plant designated as "M-1."

The existing MP-I plant and the replacement M-1 plant would each be located on a 90-acre parcel of private land owned by MPLP.[2] The replacement M-1 plant would be built approximately 500 feet northeast of the existing MP-I plant. The new M-1 plant and associated structures and equipment would occupy a little more than 3 acres. The existing entrances to the MPLP geothermal complex would provide access to the new M-1 plant site.

The MP-I plant was the first geothermal power plant to be built at the Casa Diablo geothermal complex, commencing operation in 1984.[3] The MP-I plant uses a binary cycle technology (i.e., the use of a secondary motive fluid to extract heat from geothermal fluid to generate electricity). The design capacity of the existing MP-I plant is 14 "net" megawatts (MW).[4] The MP-I plant itself (without surrounding supporting shops, pumps, wells, etc., none of which would be altered by the proposed project) occupies about 2.5 acres.

The design capacity of the M-1 plant would be approximately 18.8 MW (net).[5] According to the Proponent,[6] no new geothermal wells would

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[2] County of Mono. 2011. Initial Study Mammoth Pacific-1 (MP-1) Replacement Project. February 2011.

[3] County of Mono. 2011. Initial Study Mammoth Pacific-1 (MP-1) Replacement Project. February 2011.

[4] County of Mono. 2011. Initial Study Mammoth Pacific-1 (MP-1) Replacement Project. February 2011.

[5] CAJA. 2012. Mammoth Pacific I Replacement Project Revised Draft Environmental Impact Report, California Clearinghouse Number 2011022020. February, 2012. Pg 2-2

be constructed for the replacement plant; it would use the same geothermal fluid from the existing geothermal wells that currently supply MP-I. According to the RDEIR, the total brine flow for the MPLP complex would not increase beyond what is currently permitted.

The proposed binary technology uses both high and moderate temperature geothermal resources to extract heat energy from geothermal fluid.[7] With this process geothermal fluids are produced from production wells either by artesian flow or by pumping. Once delivered to the power plant, the heat in the geothermal fluid is transferred to the "motive" fluid in multiple stage non-contact heat exchangers. The motive fluid currently used in MP-I is isobutane. Isobutane or methylpropane is a commonly used refrigerant (also known as R-600a). Isobutane is a colorless gas with gasoline-like odor. Isobutane is flammable and there are reports of explosions with the use of isobutene as a refrigerant.

9D-01

The geothermal heat vaporizes the motive fluid and turns the binary turbine. The vaporized motive fluid exits the turbine and is condensed in an air-cooled condenser system that uses large fans to pull air over the tubes carrying the motive fluid. The condensed motive fluid is then pumped back to the heat exchangers for re-heating and vaporization, completing the closed cycle. The cooled geothermal fluid from the heat exchangers is pumped under pressure to the geothermal injection wells.

The existing MP-I plant uses isobutane as the binary motive fluid. The new M-1 plant would use n-pentane as the binary motive fluid. Pentane is also a flammable gas. Bulk quantities of n-pentane would be stored in pressure vessels and bulk storage containers on the M-1 power plant site.

9D-02

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[6] CAJA. 2012. Mammoth Pacific I Replacement Project Revised Draft Environmental Impact Report, California Clearinghouse Number 2011022020. February, 2012. Pg 2-2

[7] County of Mono. 2011. Initial Study Mammoth Pacific-1 (MP-1) Replacement Project. February 2011.

According to the proponent, a new 12.47 kV substation/switching station would be constructed adjacent to the M-1 plant and would be connected to an existing transmission line on the site via a new interconnection line. All of the proposed new geothermal facilities would be located on the same private parcel on which the existing MP-I plant is located.

During M-1 plant startup operations, the existing MP-I plant would continue to operate until the new M-1 plant becomes commercial, after which time MPLP would close and dismantle the old MP-I plant. According to the RDEIR, the transition period during which both MP-I and M-1 operations would overlap is two years, or until the M-1 plant is commissioned.[8] Thereafter, the MP-I power plant facilities would be removed from the site; plant foundations and above ground pipeline would be removed; and a retention pond on the MP-I site would be removed. The former MP-I site would then be graded and the pad covered with gravel to provide an all weather surface for continuing MPLP operations on the site.

The M-1 replacement plant would operate 24 hours per day, 7 days per week. Plant and well field operations would be integrated via a computer link to the existing power plant control room. The expected life of the proposed M-1 replacement power plant would be a nominal 30 years. The existing MPLP staff would continue to operate the replacement M-1 plant. No new operational staff would be needed for the M-1 plant.

9D-03 Up to 200 people may be temporarily employed during M-1 plant construction.

[8] CAJA. 2012. Mammoth Pacific I Replacement Project Revised Draft Environmental Impact Report, California Clearinghouse Number 2011022020. February, 2012. Pg 2-2

The County has released a Revised DEIR for the proposed project. According to the RDEIR[9], "supplemental environmental information was compiled and analyzed, including:

1. A revised and supplemented construction air emission analysis (see Appendix G);
2. A supplemented emergency generator air emission analysis (see Appendix H); "

This RDEIR was issued prematurely without considering the serious flaws in the Proponent's analysis of the project, and these flaws are replicated in the RDEIR. The flaws include:

1. a failure to document the operational emissions for the existing and proposed projects;
2. a failure to provide technical specifications for the vapor recovery unit (VRU) which proponents claim will reduce ROG emissions;
3. a failure to estimate the impacts from the co-operation of the new and existing plants during the proposed 2 year period for start up of the new plant; and
4. a failure to determine the cumulative impacts from the existing and future projects on air quality in the basin.

I. Failure To Document The Operational Emissions For The Existing And Proposed Projects

9D-04

According to the RDEIR,[10] "after abatement the annual potential fugitive emissions of n-pentane from the Project would be about 37.4 tons annually, based on the estimated daily losses. According to the RDEIR,

[9] CAJA. 2012. Mammoth Pacific I Replacement Project Revised Draft Environmental Impact Report, California Clearinghouse Number 2011022020. February, 2012.

[10] CAJA. 2012. Mammoth Pacific I Replacement Project Revised Draft Environmental Impact Report, California Clearinghouse Number 2011022020. February, 2012.

9D-04 Cont.

this would represent about a 60 percent decrease in fugitive reactive organic gases (ROG) emissions from the MP-I Project as the aging MP-I plant has fugitive losses of up to 500 pounds per day (91.3 tons per year) of isobutane. The RDEIR does not provide documentation validating the current emission estimates or the claimed reduction in operational emissions in the RDEIR or the RDEIR appendices. The proponents must provide clear documentation of their claims for operational emissions at the site in a revised RDEIR.

II. Failure To Provide Technical Specifications For The Vapor Recovery Unit (VRU) Which Proponents Claim Will Reduce ROG Emissions

9D-05

According to the RDEIR, "the Proponent has estimated that up to 205 pounds per day of fugitive n-pentane emissions would be released to the atmosphere from very tiny leaks of n-pentane through valves, flanges, seals, and other connections. Air leaked into the n-pentane condensers would be captured in the proposed OEC Unit vapor recovery units (VRU). Some n-pentane vapors would be discharged to the atmosphere from the OEC Unit, VRU and from maintenance VRU during OEC Unit maintenance activities." [11]

The RDEIR does not include a description of the VRU in the RDEIR text, and no manufacturer's guarantee or verifiable emission control efficiency information for the VRU is provided in the Appendices to the RDEIR. The proponent's claims regarding reductions in n-pentane emissions cannot be validated. The proponent must provide VRU technical specifications in order to validate any claims for ROG emission reductions in a revised DEIR.

[11] CAJA. 2012. Mammoth Pacific I Replacement Project Revised Draft Environmental Impact Report, California Clearinghouse Number 2011022020. February, 2012.

III. Failure To Estimate The Impacts From Co-Operation Of The New And Existing Plants During The Proposed 2 Year Period For Start Up Of The New Plant

9D-06

The RDEIR's air quality analysis is deficient and does not include an analysis of the co-operation of the new and existing plants during the 2-year period of start up for the proposed M-1 plant. As noted in the DEIR and RDEIR, "*The transition period during which both MP-I and M-1 operations would overlap may be up to a maximum of two years after the M-1 plant is commissioned*"[12] *(emphasis added).* No air quality analysis is presented wherein both plants are operational (per the DEIR[13] and RDEIR[14]).

9D-07

The RDEIR does not include a condition proponent requiring the proponent to limit operations of the two facilities such that there is no net increase in emissions during the period of co-operation. In addition, the RDEIR does not exclude the proponent from extending the period in which both plants are operating together. Unless the proponent is willing to be held to those conditions, estimates of potential air quality emission reductions are meaningless.

9D-08

IV. Failure To Determine The Combined Impacts From The Existing And Future Projects On Air Quality In The Basin

Evaluations of proposed projects under the California Environmental Quality Act (CEQA) must consider the broad impacts on

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[12] County of Mono. 2011. Initial Study Mammoth Pacific-1 (MP-1) Replacement Project. February 2011.

[13] County of Mono. 2011. Initial Study Mammoth Pacific-1 (MP-1) Replacement Project. February 2011.

[14] CAJA. 2012. Mammoth Pacific I Replacement Project Revised Draft Environmental Impact Report, California Clearinghouse Number 2011022020. February, 2012.

9D-08 Cont.

air quality for an air basin. According to the RDEIR[15], "the proposed MP–I Replacement Project would be located among the other existing geothermal projects which comprise the Casa Diablo geothermal complex." The proponent[16] claims that the Casa Diablo geothermal complex is not a single project rather a series of independent geothermal power plant projects with separate power purchase agreements, separate agency approvals, and the capability to operate independently. The proponent then states that the projects share a "common control room and other facilities for economy and operational efficiencies." The proponent's description clearly details a single project with multiple inputs.

9D-09

Based upon the proponent's previous analyses of the Casa Diablo geothermal complex, it is clear that the cumulative ROG emissions from the complex exceed the Imperial County Air Pollution Control District's (ICAPCD's) Daily CEQA Significance Threshold of the 55 lbs per day of ROG. According to the RDEIR, the current ROG emissions from the MP-1 plant are 500 lbs per day (91.3 tons/year). The replacement plant, M-1, is assumed to release 205 lbs per day of ROG (37.4 tons per year). Co-operation of the MP-I and M-I plants at 50% capacity could result in the emission of approximately 350 lbs per day of ROG. The cumulative analysis presented in the RDEIR reflects that emissions from M-1, MP-I (combined emissions 350 lbs/day), MP-II, PLES-I and the proposed CD-4 project will total 1,336 lbs of ROG per day (244 tons per year). The combined emissions from existing projects (MP-I at 50% capacity, MP-II, and PLES-1), reasonably foreseeable future projects (CD-4) and the Project (M-1) are significantly higher than the ICAPCD Daily CEQA

[15] CAJA. 2012. Mammoth Pacific I Replacement Project Revised Draft Environmental Impact Report, California Clearinghouse Number 2011022020. February, 2012.

[16] CAJA. 2012. Mammoth Pacific I Replacement Project Revised Draft Environmental Impact Report, California Clearinghouse Number 2011022020. February, 2012.

9D-09 Cont.

Threshold, amounting to 1686 lbds/day. The Project's contribution to combined emissions is significant, accounting for 350 lbs/day of uncontrolled ROG emissions.

9D-10

Following the decommissioning of MP-I and the commissioning of M-1, the cumulative emissions from the Casa Diablo Geothermal Complex would be more than 1,000 lbs per day, well in excess of the ICAPCD's Daily CEQA Significance Threshold of the 55 lbs per day of ROG. The Project's contribution to combined emissions would be significant, accounting for 205 lbs/day of uncontrolled ROG emissions.

A recirculated RDEIR should include a proper cumulative analysis detailing the impacts of all pollutants on a region that is in non-attainment under an applicable federal or state ambient air quality standard.

Conclusion

A revised DEIR should be prepared that addresses the above analytical deficiencies. This concludes my comments.

Sincerely,

James Clark, Ph.D.

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Comment Letter I14

Comment Letter 9A

Scott Cashen, M.S.—Independent Biological Resources and Forestry Consultant

March 23, 2012

Ms. Elizabeth Klebaner
Adams Broadwell Joseph & Cardozo
601 Gateway Boulevard, Suite 1000
South San Francisco, CA 94080

Subject: Comments on the Revised Draft Environmental Impact Report for the Mammoth Pacific I Replacement Project

Dear Ms. Klebaner:

This letter contains my comments on the Revised Draft Environmental Impact Report ("RDEIR") prepared for Mammoth Pacific Limited Partnership's ("Applicant") proposed Mammoth Pacific I Replacement Project. The project involves replacing the aging Mammoth Pacific Unit I (MP–I) power plant with a new, more modern and efficient binary power plant (M–1), while maintaining the existing geothermal wellfield, pipeline system and ancillary facilities. The RDEIR analyzes two potential locations for the M-1 power plant. The "proposed" location is on private land approximately 500 feet northeast of the existing MP-I facility, whereas the "alternative" location is on public land approximately one-quarter mile north of MP-I. Based on the information provided in the RDEIR, I assume the project would be constructed at the "proposed" location. Hereafter, I refer to the project at the proposed location as the "Project." However, many of the issues discussed herein would also apply to a project at the alternative location.

I am an environmental biologist with 20 years of professional experience in wildlife ecology, forestry, and natural resource management. To date, I have served as a biological resources expert for over 35 projects, the majority of which have been renewable energy facilities. My experience in this regard includes testifying before the California Energy Commission and assisting various clients with evaluations of biological resource issues. My educational background includes a B.S. in Resource Management from the University of California at Berkeley, and a M.S. in Wildlife and Fisheries Science from Pennsylvania State University.

I have gained particular knowledge of the biological resource issues associated with the Project through my work on other projects in the Sierra Nevada. The comments contained herein are based on this knowledge, as well as my review of the environmental documents prepared for the Projects, a review of scientific literature pertaining to biological resources known to occur in Mono County, consultations with numerous biological resource experts, and the knowledge and experience I have acquired during more than 20 years of working in the field of natural resources management. In addition, the comments pertaining to mule deer were prepared after several consultations with Dr. Vernon Bleich, a recognized expert on mule deer, and a former senior environmental scientist with the California Department of Fish and Game.

The RDEIR Relies on Inadequate Baseline Data on Deer Use of the Project Region

9A-01 The RDEIR relies on two deer studies that were conducted in the Project area: (1) Paulus's *Fall 2011 Resident Deer Survey for the Casa Diablo, Basalt Canyon, and Upper Basalt Geothermal Areas*; and (2) Paulus's *Fall 2011 Migratory Deer Survey for the M-1 Project Site at the Casa Diablo Geothermal Area.*[1] I have the following comments pertaining to these two studies:

9A-02 1. Migration, particularly that which occurs over long distances, is one of the most threatened biological phenomena. Research has demonstrated a marked decrease in the proportion of deer migrating from Round Valley to the west side of the Sierra Crest.[2] Clearly, there are two cohorts of migrants: those that move west of the crest, and those that remain on the east side. The cause of the shift in the proportion of animals that moved to the west side in 1985 (84%) versus the current proportion that moves to the west side (~55%) has not been adequately investigated. However, the shift demonstrates that there are ongoing (likely anthropogenic) impacts to deer that use the Project area. The deer studies (and RDEIR) prepared for the Project fail to: (a) disclose the aforementioned information; or (b) discuss the importance of the Project site in maintaining migratory processes exhibited by the Round Valley deer herd.

9A-03 2. Neither study examined deer use of the project areas during the spring. It is possible that springtime conditions would dictate different movement corridors, or strategies for deer, compared to those in the fall. As a result, the analyses presented in the RDEIR are based on incomplete information and Project impacts to deer during spring cannot be assessed (including the estimated number of deer and migratory corridors that would be impacted).

9A-04 3. The biologist surveyed deer tracks along several transects. The way "transects" were selected, and their alignments (i.e., along roads) has a potentially confounding effect on the results, rendering them unreliable. For example, "Transect GG" was established parallel to the anticipated deer movement pattern, whereas "Transect AA" was established perpendicular to the anticipated movement pattern.[3] This inconsistency skews the results of the surveys considerably because a transect perpendicular to a linear movement corridor is more apt to show evidence of use than one running parallel to such a corridor.

9A-05 4. Statistical comparisons between transects, across time, or the interaction thereof, cannot be made with the data that are presented in the reports. For example, the transects varied in length. Because data obtained from the transects were not standardized (e.g., number of tracks per mile of transect), the calculations, and much of the analyses presented in the report, are impossible to interpret. Moreover, the sampling effort was inconsistent. For example, transects were surveyed twice per week during part of the study period, but only

[1] Paulus J. 2011 Dec 29. Fall 2011 Migratory Deer Survey for the M-1 Project Site at the Casa Diablo Geothermal Area. *See also* Paulus J. 2011 Oct 30. Fall 2011 Resident Deer Survey for the Casa Diablo, Basalt Canyon, and Upper Basalt Geothermal Areas.

[2] Monteith KM, VC Bleich, TR. Stephenson, BM Pierce, MM Conner, RW Klaver, RT Bowyer. 2011 Timing of seasonal migration in mule deer: effects of climate, plant phenology, and life-history characteristics. Ecosphere 2(4):art47. doi:10.1890/ES10-00096.1 (Attachment A)

[3] Paulus J. 2011 Dec 29. Fall 2011 Migratory Deer Survey for the M-1 Project Site at the Casa Diablo Geothermal Area, Figure 1.

9A-05 Cont.

once per week during the other part of the study period. To help rectify these issues, to enable meaningful interpretation of the results, and to provide the opportunity to detect changes in the index of deer use between seasons and among transects (and across years, as specified in the general plan), data from the studies need to be expressed in a manner that allows such comparisons. Thus, the investigator should consider expressing data in the context of tracks encountered/transect unit/survey day, or in some other manner that will facilitate the aforementioned comparisons; the assistance of an applied statistician would prove helpful in resolving this issue.

9A-06

5. The author described the location of "Transect GG" as "a reliable location for monitoring crossing frequency and timing."[4] This conclusion appears to be arbitrary, because it does not appear that any evaluation, other than a subjective one, was completed before deriving the conclusion. Moreover, transects were not established randomly, but were tied to existing roads. Thus, the data provide a track-count index specific to each of the roads (transects), rather than a track-count index that reflects the abundance of deer in the study area. Consequently, the author's inferences can be applied to the roads only, rather than to the entire study area.

9A-07

6. Although the number of deer tracks detected in the study area is an index of deer use, the number of tracks may not accurately reflect the number of deer using the study area. Although the author acknowledges this limitation, he subsequently applies the data beyond their capability. For example, the author concluded that the main use of the Project area by deer is as a movement corridor.[5] The data obtained in the studies cannot be used to derive this conclusion for several reasons. First, the author had no way of knowing whether tracks were deposited by migrating deer or resident deer. At best, the author would have been forced to make assumptions on the class of deer that deposited the tracks based on the time of year, and perhaps the direction of the tracks. Such assumptions would be extremely tenuous due to the overlap in the categories of deer present during the sampling period (i.e., migrating and resident deer were both present). Second, even if one assumes tracks can be linked to a specific category of deer (i.e., migratory or resident), any comparisons must necessarily rely on the assumption that bias is constant. It is unlikely that this assumption was met due to differences in behavior between migratory and resident categories of deer. For example, migratory deer are likely to exhibit directional movement, whereas resident deer are more likely to exhibit random movement. If this occurred in the study area, one can assume most migrating deer crossed a transect once, whereas there is a much greater probability that most resident deer crossed multiple times. Because this difference was not (nor could it have been given the resources available to the investigator) quantified (or approximated), the data cannot be used to support the conclusion that deer use the Project area primarily as a movement corridor.

[4] Id, Figure 2.

[5] [BRA] Paulus J. 2011 Dec 20. Assessment of Biological Resources M-1 Replacement Power Plant at Casa Diablo Mono County, California. RDEIR, Appendix D, p. 24.

9A-08 7. The author alludes to the movement by deer to water, but such movements should not be the only ones of concern.[6] Moreover, it is unclear how he concluded that movement to water was the primary reason deer were using the study area.

8. My ability to interpret the results of the studies is inhibited by:

9A-09
a. the author's inconsistent use of the terms resident, migratory, and "residency;"[7]
b. omission of the statistical methods that were used to answer the objectives of the studies; and
c. the lack of an adequate description of the study methodology such that the results could be interpreted in a meaningful manner.

9A-10 9. The study methods are so poorly stated that anyone attempting to replicate the study would not be able to do so. This is problematic given the requirement in the RDEIR for additional deer monitoring studies that can be used to evaluate deer use of the Project area in relation to the baseline.

The Project Will Result in Potentially Significant Impacts to Mule Deer

The Project site is used by mule deer during the spring and fall when deer are transitioning between their winter and summer ranges.[8] Mule deer also occupy the Project area during summer or winter, or as year-round residents.[9] The mule deer is an important game species, and the impacts of geothermal development on the Round Valley and Casa Diablo deer herds have been a longstanding management concern of both the California Department of Fish and Game ("CDFG") and Mono County.

9A-11 The Mono County General Plan states: "[d]evelopment may be prevented in any part of a deer migration zone upon a finding that it will interfere with adopted regulations of the California Department of Fish and Game and the goals of the CDFG deer herd management plans."[10] The RDEIR does not provide a discussion of the compatibility between the Project and CDFG's deer herd management plans. Similarly, because the RDEIR does not make reference to or describe the goals of the deer management plans, I cannot independently assess the Project's compliance with the Mono County General Plan.

9A-12 The Project would result in the partial closure of a migration route used by deer.[11] The RDEIR states: "[t]he biological survey assessment of deer movement through the existing MP-I project

[6] Paulus J. 2011 Dec 29. Fall 2011 Migratory Deer Survey for the M-1 Project Site at the Casa Diablo Geothermal Area, p. 8.
[7] For example, *See* Paulus J. 2011 Dec 29. Fall 2011 Migratory Deer Survey for the M-1 Project Site at the Casa Diablo Geothermal Area, p. 8. In this case the term "residency" applies to deer that were *present* in the Project area in December, but not necessarily "resident" deer according to the operational definition.
[8] County of Mono Community Development Department. 2010. Mono County General Plan. Bridgeport, CA. (Drafted July 1997 and Revised 2010). Conservation /Open Space Element-2010, Figure 1.
[9] Paulus J. 2011 Dec 29. Fall 2011 Migratory Deer Survey for the M-1 Project Site at the Casa Diablo Geothermal Area, p. 8. *See also* Ferranto SP. 2006. Conservation of mule deer in the eastern Sierra Nevada. M.S. Thesis, University of Nevada, Reno. 129 pp.
[10] RDEIR, p. 4-53.
[11] BRA, p. 25.

9A-12 Cont.

area concludes that partial closure of the movement corridors located between the existing MP-I and MP-II/PLES-I plant sites for the proposed M-1 plant site would not substantially change the use of the movement corridor by resident deer."[12] The RDEIR lacks the basis for this conclusion. As the RDEIR subsequently acknowledges, "[t]here are not sufficient data to speculate how migrating deer would respond to the proposed change from partial blockage by a pipeline rack to partial blockage by a power plant."[13]

9A-13

The RDEIR ultimately concludes the Project would not have a significant impact on mule deer or mule deer movement through the Casa Diablo area.[14] This conclusion is not supported by information provided in the RDEIR and in other sources.

First, the RDEIR indicates "[i]f movement patterns of either resident or migratory deer are thwarted by the increase in noise, lighting and traffic at this corridor, the animals could be redirected to the west of MP-I fencing and possibly onto U.S. Highway 395 with increased frequency."[15] In this regard, the Town of Mammoth Lakes concluded "indirect impacts including an increased incidence of deer kills on U.S. Highway 395, would in the cumulative context of other regional developments, be *significant and unavoidable*."[16]

9A-14

Second, researchers examining habitat selection of mule deer before and during development of a natural gas field observed shifts in the distribution of deer toward less-preferred and presumably less-suitable habitats as development progressed.[17] The researchers concluded (a) the avoidance of, or lower use of, areas near development creates indirect losses of habitat that are substantially larger in size than the direct losses; (b) that these habitat losses have the potential to reduce carrying capacity and result in population-level effects (i.e., survival or reproduction); and (c) deer did not acclimate or habituate to well pads.[18] The results of the aforementioned study indicate the Project could indirectly impact habitat use by deer, and that this impact would be potentially significant. The deer survey report that was prepared for the Project provides additional evidence that the Project could cause the deer to shift to less-preferred habitat. The report states: "it will not be tenable to assume these animals can simply move to a nearby similarly scrub-covered or forested area. Habitat that loses nightly accessibility to Mammoth Creek and Murphy Gulch, or is too far from these resources, would be very different from the habitat now being used."[19] Although the RDEIR discusses the indirect impacts that could occur to deer movement corridors, it does not analyze the consequences of deer being displaced to potentially less-suitable habitats as a result of the Project.

9A-15

Third, Polfus (2011) concluded that any increase in development has the potential to

[12] RDEIR, p. 4-66.
[13] Id.
[14] Id, p. 4-67.
[15] Id.
[16] Town of Mammoth Lakes. 2007 May. Final Environmental Impact Report: Town of Mammoth Lakes 2005 General Plan Update, p. 5-10.
[17] Sawyer H, RM Nielson, F Lindzey, LL McDonald. 2006. Winter Habitat Selection of Mule Deer Before and During Development of a Natural Gas Field. Journal of Wildlife Management 70(2):396-403. (Attachment B)
[18] Id.
[19] Paulus J. 2011 Oct 30. Fall 2011 Resident Deer Survey for the Casa Diablo, Basalt Canyon, and Upper Basalt Geothermal Areas, p. 11.

9A-15 Cont.

significantly affect mule deer migrations, and that migration corridors can be negatively impacted by even small amounts of development.[20] These conclusions were based on a comprehensive review of scientific literature.

Finally, the conclusions in the RDEIR contradict, and are unsupported by, the conclusions made by the Applicant's deer expert. The Applicant's expert concluded the following:

1. The removal of forage, or the restriction of movement corridors (especially to water), could reduce the fitness of deer and affect survivorship.[21]
2. "[t]he likelihood that these [aforementioned adverse] effects will occur *is plausible*."[22]
3. "[a]dditional human activity and operational lighting and noise associated with power plant operation, power plant decommissioning, and storage yard activities could potentially discourage resident deer use of the corridor between MP-I and MP-II/PLES-I for nightly movement to water."[23]

9A-16

4. "[d]eer attempting to overwinter would be sensitive to any project elements that would function as barriers to night movement between forest (forage and cover) resources and heated refuge areas that are of course very limited in extent."[24]
5. "[m]igratory deer that presumably are less adapted to local developments may be thwarted in their movement along traditional paths that pass through the existing corridor between MP-I and MP-II/PLES-I."[25]
6. "[t]he new noise and activity at the M-1 power plant could potentially reduce [deer] usage of the SCE easement that it abuts."[26]

The aforementioned issues provide considerable evidence that the Project will cause potentially significant impacts on mule deer. Moreover, those impacts could be different between "resident" animals (defined here as those that include the project area within their home ranges on a year-round basis) and migratory individuals (defined here as those that occupy the project site on a seasonal, or transitory basis).

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[20] Polfus JL. 2011. Literature review and synthesis on the effects of residential development on ungulate winter range in the Rocky Mountain West. Report prepared for Montana Fish, Wildlife and Parks. Helena, MT. Available at: fwp.mt.gov/fwpDoc.html?id=51645, p. 47. (Attachment C).
[21] Id.
[22] Id.
[23] Paulus J. 2011 Dec 29. Fall 2011 Migratory Deer Survey for the M-1 Project Site at the Casa Diablo Geothermal Area, p. 8.
[24] Id, p. 9.
[25] Id.
[26] Id.

The Project Will Result in Potentially Significant Impacts on Tree Kills and Wildlife

Since 2006 the U.S. Geological Survey ("USGS") has collected data at tree-kill areas near Casa Diablo. The data reveal the tree-kill areas have elevated CO_2 and soil temperature levels, both of which can directly or indirectly (i.e., through stress) kill trees.[27]

Tree kills have broad implications on sensitive resources and the ecology of the Project region. In addition to modifying habitat, elevated CO_2 levels at the tree-kill sites pose a hazard to wildlife, particularly species that occur at or below ground level. Indeed, smoke cartridges that produce carbon monoxide and carbon dioxide gases are commonly used to kill gophers and other "pest" species.[28] Although the effects of elevated CO_2 levels on wildlife have not been studied at the Casa Diablo sites, I believe it is likely that elevated CO_2 levels have caused heightened
9A-17 mortality among select taxa (e.g., reptiles and small mammals). Heightened mortality among these taxa could have implications on the entire ecological community.

The RDEIR provides scant discussion of the tree kills near Casa Diablo. It simply refers to the tree kills as "natural surface manifestations that change over time."[29] The RDEIR then states:

> there has been speculation that use of the geothermal resource in the Casa Diablo area may affect vegetation (Bergfeld and Evans 2011). A cause and effect relationship has not been established, but the issue should be studied with respect to future projects that would increase utilization of the resource or expand wellfield development. However, the proposed MP-I Replacement Project would not change the utilization of the existing geothermal wellfield or expand wellfield development. Therefore, the Project would have no adverse incremental cumulative impacts on the geothermal resource and would not add to the impacts of geothermal operations on vegetation, if any are established.[30]

These statements do not accurately disclose the relationship between the Project and tree kills.

First, the information provided in Bergfeld and Evans (2011) should not be characterized as "speculation." Bergfeld and Evans are senior scientists employed by the U.S. Geological Survey ("USGS"). These scientists have been studying tree kills at the Long Valley Caldera since 2006. Their research has led them to the following inferences and conclusions:

1. "[m]any of these kills occurred during the mid-1990s and were associated with early power-plant operations at Casa Diablo (Bergfeld and others, 2006)."[31]
2. "[o]ur findings indicate that the [new tree-kill] areas have developed as a response to changes in the shallow hydrologic system. Some of the changes are likely related to fluid

[27] Bergfeld D, WC Evans. 2011, Monitoring CO2 emissions in tree kill areas near the resurgent dome at Long Valley Caldera, California: U.S. Geological Survey Scientific Investigations Report 2011-5038, 22 p. (Attachment D).
[28] Engeman RM, GW Witmer. 2000. Integrated management tactics for predicting and alleviating pocket gopher (*Thomomys* spp.) damage to conifer reforestation plantings. USDA National Wildlife Research Center - Staff Publications. Paper 180. http://digitalcommons.unl.edu/icwdm_usdanwrc/180
[29] RDEIR, p. 5-11.
[30] Id.
[31] Bergfeld D, WC Evans. 2011, Monitoring CO_2 emissions in tree kill areas near the resurgent dome at Long Valley Caldera, California: U.S. Geological Survey Scientific Investigations Report 2011-5038, p. 5.

production at the power plant, but at distal sites the changes are more likely related to seismicity and uplift of the dome."[32]

3. "changes in the size of kill zones, increases in soil temperatures or steam discharge, and changes in CO_2 emissions most likely reflect the response of the shallow hydrothermal system to geothermal fluid production at the Casa Diablo power plant."[33]
4. "[o]ur early work (Bergfeld and others, 2006) indicated that about 8.7 metric tonnes of CO_2 per day (t/d) were emitted from these kill zones, with the highest discharge occurring in areas within a few km of the Casa Diablo geothermal power plant, and that most of the kill zones developed as a response to changing conditions in the shallow hydrothermal system."[34]
5. "[w]ithout sufficient pressure support, the shallow hydrothermal system [at Shady Rest] would respond to the 2006 onset of fluid production at the 5725 and 6625 wells. Variations in CO_2 emissions since that time may reflect adjustments in the shallow reservoir to the fluid production."[35]

9A-17 Cont.

6. "[t]he presence of isobutane in gas samples at Basalt Canyon shows that volatiles from the injectate have reached the underlying area. The pressure support provided by the injectate would stabilize the depth of boiling in the reservoir and, consequently, would control the upflow of steam and CO_2, producing more constant CO_2 emissions."[36]
7. "[t]he presence of isobutane in gas samples from sites in and around Basalt Canyon suggests that geothermal fluid production directly effects fluid upflow in the region close to the power plant."[37]
8. "[t]he appearance of this gas [H_2S] at the surface may signal increased drawdown of water levels near the geothermal productions wells."[38]

Second, the statement in the RDEIR that a cause and effect relationship has not been established is misleading. The tree-kill sites have elevated CO_2 and soil temperature levels, both of which can directly or indirectly (i.e., through stress) kill trees. Thus, the cause (i.e., high CO_2 and soil temperatures) and effect (i.e., tree mortality) can be inferred with relative certainty.

Because the information presented in the RDEIR conflicts with information published by the USGS, I solicited additional information from the USGS scientists (i.e., Bergfeld and Evans) that have been studying the tree-kill sites near Casa Diablo. The scientists provided the following statements addressing the discrepancies between the information presented in their publications and the information in the RDEIR:

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[32] Bergfeld D, WC Evans, JF Howle, CD Farrar. 2006. Carbon Dioxide Emissions from Vegetation-Kill Zones Around the Resurgent Dome of Long Valley Caldera, Eastern California USA. Journal of Volcanology and Geothermal Research 152 (2006): 140-156. Abstract available at: www.sciencedirect.com/science/article/pii/S0377027305003550. (Attachment E)

[33] Bergfeld D, WC Evans.2011, Monitoring CO_2 emissions in tree kill areas near the resurgent dome at Long Valley Caldera, California: U.S. Geological Survey Scientific Investigations Report 2011-5038, p. 1.

[34] Id.

[35] Id, p. 9.

[36] Id, p. 8.

[37] Id, p. 1.

[38] Id.

9A-17 Cont.

1. "[w]e stand behind the wording in our published reports, including: 'The high concentration of thermal and diffuse CO_2 degassing areas around the power plant leaves little doubt that some areas owe their existence to the geothermal operations.' This is more inference than speculation."[39]
2. "[w]e have not pinpointed the exact cause of tree death, nor do we attribute every dead tree to geothermal operations, but the relation between the overall timing and pattern of vegetation kill and changes in geothermal operations is clear. We stand behind: '...changes in the size of kill zones, increases in soil temperatures or steam discharge, and changes in CO_2 emissions most likely reflect the response of the shallow hydrothermal system to geothermal fluid production at the Casa Diablo power plant.' The formation of steaming ground is a well-known impact of development at geothermal sites world-wide. The cause and effect relation is largely established even if the precise mechanism by which the trees die is not established."[40]
3. "[t]he size of the kill areas is expanding under the current production regime. However, a relocation of the power plant that does not involve changes to the fluid production/injection scheme would not be expected to speed up or otherwise alter this process."[41]

Based on the information provided above, there is ample scientific evidence that the Project would contribute to additional tree kills. Specifically, because the continued expansion of the tree-kill areas has been highly correlated with geothermal operations, one can infer that the Project would contribute to additional expansions of the tree-kills over the course of its 30-year operational life. The RDEIR lacks baseline information on the Project's contribution to tree-kills, and because it circumvents any analysis of the issue, the magnitude of the issue cannot be properly evaluated.

The Project's Impact on Mule Deer is Cumulatively Considerable

9A-18

The Project, in conjunction with other projects, has the potential to cause cumulatively considerable impacts to deer, especially with the addition of the CD-4 facility to the Casa Diablo geothermal complex. However, the analysis in the RDEIR of cumulative impacts to deer from the Project and CD-4 is limited to the statement that:

> The addition of the proposed M-1 plant site and CD-4 project would expand the affected area of development east of U.S. Highway 395 near Casa Diablo Hot Springs and impinge on the remaining corridors for wildlife movement through the area. Constraints on wildlife movement through the area could be cumulatively significant if future development is undertaken in a manner which prevents wildlife to readily pass north-south between Mammoth Creek and the habitat north of the Casa Diablo geothermal complex.[42]

The analysis presented in the RDEIR is insufficient for several reasons. First, the RDEIR fails to establish the context of the impact such that it cannot be adequately interpreted. Specifically, the

[39] 2012 Mar 19 email communication from WC Evans to S Cashen. (Attachment F)
[40] Id.
[41] Id.
[42] RDEIR, p. 5-11.

RDEIR does not (a) use existing information on the currently proposed CD-4 to assess whether the two projects combined would hinder movement to and from Mammoth Creek; (b) identify corridors that would remain on the landscape under the cumulative impacts scenario; or (c) provide evidence that supports an inference that any remaining corridors would be viable.

Second, the RDEIR lacks any analysis of impacts to other types of deer movement (i.e., besides movement to and from Mammoth Creek). These include movement among foraging resources, cover, and reproductive sites; and movement between summer and winter ranges.

9A-18 Cont.

Third, potentially significant cumulative impacts to deer are not limited to impacts on movement. They also include permanent habitat loss, loss of forest cover, loss of special use areas, stress (e.g., from disturbance), and altered predator-prey relationships. The RDEIR provides no analysis of the Project's contribution to these potentially significant cumulative impacts.

Fourth, existing development already has had a detrimental impact on the Round Valley deer herd.[43] Consequently, analysis conducted for the Project needs to consider the cumulative impacts that all past, present and probable future projects are likely to have on the entire Round Valley deer herd. The RDEIR did not take this approach, but instead focused on impacts to the subset of the herd that was present on the Project site during the latter half of 2011.[44]

Nutritional limits on survival and recruitment of deer in Round Valley clearly indicate "bottom-up" limitation on deer dynamics.[45] Consequently, further restrictions on use of habitat, or additional destruction of habitat, would have an additive effect in terms of decreasing the number of deer that comprise the population. This conclusion is supported by the deer study that was conducted for the Project, and by other mule deer studies.[46]

Based on the issues identified above, the RDEIR lacks adequate analysis of the Project's contribution to cumulative impacts to deer. Moreover, it is my professional opinion that the Project's impacts to deer may be cumulatively considerable given the CD-4 project.

The RDEIR Fails to Propose Effective Mitigation Measures to Reduce the Project's Potentially Significant Impacts to All Sensitive Biological Resources

9A-19

A. Tree-Kills

The RDEIR lacks any mitigation for impacts to tree-kills despite the clear relationship to geothermal operations. To be consistent with Mono County's General Plan, the Applicant needs

[43] Ferranto SP. 2006. Conservation of mule deer in the eastern Sierra Nevada. M.S. Thesis, University of Nevada, Reno, p. 50.
[44] BRA, p. 25.
[45] A bottom-up limitation is one in which population dynamics are limited by nutrient supply and productivity. *See* Monteith KL, VC Bleich, TR Stephenson, BM Pierce. 2009. Population Dynamics of Mule Deer in the Eastern Sierra Nevada: Implications of Nutritional Condition. Available at: mcbadeer.com/DFG_ROUND_VALLEY_STUDY.pdf
[46] Id. *See also* Paulus J. 2011 Oct 30. Fall 2011 Resident Deer Survey for the Casa Diablo, Basalt Canyon, and Upper Basalt Geothermal Areas, p. 11. *See also* USDA Forest Service, Pacific Northwest Research Station. 2012 Mar. Seasonal Neighbors: Residential Development Encroaches on Mule Deer Winter Range in Central Oregon. Science Findings 140. Available at: www.fs.fed.us/pnw/sciencef/scifi140.pdf. (Attachment G).

9A-19 Cont.

to prepare a written analysis of the impacts that the Project and other development projects may individually or cumulatively have on tree-kills.[47] The Applicant should then develop a monitoring plan subject to review by the County, CDFG, USGS, and other relevant resource agencies. As was done for hydrologic resources in the Project area, specific triggers for additional mitigation should be established in conjunction with the monitoring plan. Once Project operations commence, the tree-kills should be monitored to determine the extent of additional impacts to vegetation and other biological resources. If the monitoring indicates geothermal operations have contributed to additional tree kills, then Mono County should take the actions necessary to reduce any adverse effects to less-than-significant levels.

B. Deer

I have the following comments pertaining to the mitigation measures that have been proposed for impacts to mule deer:

9A-20

1. Mitigation proposed in the RDEIR includes the following: "[c]onstraints to wildlife movement through the Casa Diablo Hot Springs area shall be evaluated as part of any new development project proposed in the area."[48] Proposed mitigation also includes: "[c]onducting baseline deer studies of proposed projects in the Casa Diablo Hot Springs area and monitoring deer use within and near a new proposed project."[49] These measures will not reduce impacts to a less than significant level because they are too vague. The Applicant must be required to conduct monitoring efforts in accordance with specific criteria to ensure scientifically reliable results. The monitoring plan should account for:
   a. the appropriate timing of the proposed monitoring efforts in relation to project activities (i.e., before, after, or during construction);
   b. the duration of the proposed monitoring efforts (i.e., number of years);
   c. other essential elements of the study plan, including the study area, sampling scheme, and response variable(s) that will be examined;
   d. the statistical techniques that will be used to analyze changes in deer use, including the techniques (e.g., power analysis) that should be employed to determine the amount of sampling necessary to detect changes at a pre-specified probability; and
   e. triggers for remedial actions, and the suite of remedial actions that may be necessary, if impacts to deer are detected.

   In short, the Applicant needs to establish a monitoring plan capable of providing reliable information on changes in deer use of the Project area. To be consistent with the objectives of Mono County's General Plan, the Project application should not be considered until the monitoring plan is approved by Mono County and CDFG.
2. The RDEIR concludes the implementation of the proposed mitigation measures would reduce the cumulative impact from the existing and proposed projects on mule deer and

[47] RDEIR, p. 4-50, Goal 1.
[48] Id, p. 5-11.
[49] Id, p. 5-12.

9A-20 Cont.

other wildlife to a level that would not be cumulatively significant.[50] For the reasons described in these comments, the conclusion that impacts would not be cumulatively significant is unfounded and speculative. Furthermore, because the RDEIR does not identify success standards for the proposed mitigation, or remedial actions that will be taken if significant impacts unfold (e.g., deer movement through the Project site ceases), it lacks a mechanism for ensuring impacts would be less than significant.

Sincerely,

Scott Cashen, M.S.
Senior Biologist

[50] Id.

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BY EMAIL

October 17, 2012

Elizabeth Klebaner
Adams Broadwell Joseph & Cardozo
601 Gateway Boulevard, Suite 1000
South San Francisco, CA 94080

Re: Comments on Final Environmental Impact Report for Mammoth Pacific I Replacement Project

Dear Ms. Klebaner,

Per your request, I have reviewed the Final Environmental Impact Report ("FEIR") for the Mammoth Pacific I Replacement Project ("Project") published by the County of Mono ("County") as the lead agency under the California Environmental Quality Act ("CEQA")[1] and related documents.[2,3,4] My review focuses on the Project's impacts related to air quality and hazardous materials.

I. Background

Mammoth Pacific L.P. ("MPLP" or "Applicant"), a subsidiary of Ormat Nevada, Inc. ("Ormat"), proposes to replace its aging Mammoth Pacific Unit I ("MP-I") geothermal power plant located near Casa Diablo Hot Springs in Mono County, CA,

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[1] County of Mono, Mammoth Pacific I Replacement Project, Final Environmental Impact Report, California Clearinghouse Number 2011022020, September 2012.

[2] County of Mono, Mammoth Pacific I Replacement Project, Second Revised Draft Environmental Impact Report, California Clearinghouse Number 2011022020, July 2012.

[3] County of Mono, Mammoth Pacific I Replacement Project, Revised Draft Environmental Impact Report, California Clearinghouse Number 2011022020, February 2012; hereinafter "RDEIR."

[4] County of Mono, Mammoth Pacific I Replacement Project Draft Environmental Impact Report, California Clearinghouse Number 2011022020, July 2011; hereinafter "DEIR."

with a new, more modern and efficient power plant while maintaining the existing geothermal wellfield, pipeline system and ancillary facilities.[5]

The existing MP-I plant, which is located approximately 1,200 feet northeast of the intersection of U.S. Highway 395 and California State Route 203 on 90 acres of private land owned by Ormat, has a design capacity of approximately 14 megawatts ("MW")[6] and consists of a binary power plant[7], a geothermal wellfield, production and injection fluid pipelines, and ancillary facilities.[8] The existing MP-I plant, permitted by the County in 1982 and in operation since 1984, is one of three existing geothermal power plants (MP-I, MP-II, and PLES-I) located in the Casa Diablo geothermal development complex. The three existing plants are operated out of a single control room located adjacent to the existing MP-I generation facilities[9] and share a common geothermal wellfield.[10] The principal reason for the Project is to replace the aging, leak prone MP-I generation unit, whose condensing capacity has been severely restricted due to the need to plug damaged condenser tubes.[11]

The M-1 replacement plant, proposed to be located on private land about 500 feet northeast of the existing MP-I generation facilities and immediately adjacent to the existing MP-II generation facilities[12], would have a generating capacity of approximately 18.8 MW (net).[13] The Project includes: the construction of the new M-1 plant generation facilities; the demolition and decommissioning of the existing MP-I generation facilities; the construction of new paved access roads; the installation of a fire

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[5] FEIR, at p. 1.

[6] The California Energy Commission's

[7] A binary cycle power plant is a type of geothermal power plant that allows cooler geothermal reservoirs to be used than with dry steam and flash steam plants. With binary cycle geothermal power plants, pumps are used to pump hot water from a geothermal well, through a heat exchanger, and the cooled water is returned to the underground reservoir. A second "working" or "binary" fluid with a low boiling point, typically a butane or pentane hydrocarbon, is pumped at fairly high pressure through a heat exchanger, where it is vaporized and then directed through a turbine. The vapor exiting the turbine is then condensed by cold air radiators or cold water and cycled back through the heat exchanger. (Description excerpted from Wikipedia.)

[8] FEIR, at p. 1.

[9] DEIR, at p. 5-2.

[10] *Id.*, at p. 5-7.

[11] *Id.* at p. 4-131.

[12] FEIR, at p. 1.

[13] FEIR, at p. 4.

water storage tank and motive fluid storage tanks; the construction of an electrical shelter, a machinery room a main electrical room, an electrical substation, interconnection transmission to connect the M-1 plant to the existing Southern California Edison Casa Diablo substation, and two aboveground interconnection pipelines to interconnect the existing geothermal production and injection pipelines to the M-1 plant site.[14] According to the EIR, the Project would not include changes to the existing wellfield or wellfield operations.[15]

Geothermal fluids from the existing production wells would be transported to the proposed M-1 geothermal plant through existing production pipelines. The M-1 plant would utilize Ormat Energy Converter ("OEC") technology, a proprietary modular binary geothermal power generation equipment that uses an organic "working" or "motive" fluid for non-contact heat transfer from the geothermal fluid. Specifically, the Project would use an Integrated Two Level Unit ("ITLU"), which provides two levels of heat extraction from the geothermal fluid in a series with a higher temperature and pressure unit, Level 1, and a lower temperature and pressure unit, Level 2. The geothermal heat vaporizes the motive fluid which then turns a binary turbine, which together would turn a common generator producing electricity that would be delivered to the substation and transferred to the interconnection transmission line. The vaporized motive fluid exits the turbine and is condensed in an air–cooled condenser system that uses large fans to pull a cooling air stream over the tubes carrying the motive fluid. The condensed motive fluid is then pumped back to the heat exchangers for re–heating and vaporization, completing the closed cycle. The cooled geothermal fluid from the heat exchangers is pumped under pressure to the geothermal injection wells.[16]

The existing MP–I plant uses isobutane as the motive fluid in its binary power generation equipment. The new M–1 plant would use normal pentane (n–pentane) as the binary motive fluid.[17] Both working fluids, isobutane and n-pentane, are volatile organic compounds, which are precursors for the formation of ozone, a regulated air

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[14] DEIR, at pp. 2-4–2-17.

[15] *Id.* at p. 1-1.

[16] DEIR, pp. 2-1–2-2.

[17] DEIR, p. 2-2.

pollutant[18] for which short- and long-term state and national ambient air quality standards have been established.[19]

The OEC unit contains approximately 250,000 pounds of motive fluid (in the vaporizers, preheaters, condensers and piping) in a closed–loop system, with no significant, routine release or discharge of motive fluid.[20] Bulk quantities of n–pentane would be stored in pressure vessels and bulk storage containers on the M–1 power plant site.[21] During operations, vaporized n-pentane would be condensed in an air-cooled tube condenser and returned to the preheaters and vaporizers to repeat the cycle. Any non-condensable gases which may leak into the motive fluid system would collect in the OEC condenser and removed through a vapor recovery unit ("VRU"). During purging, the majority of the n-pentane vapors would be condensed into liquid n-pentane and returned to the OEC unit. The noncondensible gases and the remaining, uncontrolled n-pentane vapors would be discharged into the atmosphere.[22] Like the existing MP-I facility, the M-1 plant would release fugitive emissions into the atmosphere. These emissions would be released from leaks of n-pentane through leaking valves, flanges, seals, and other connections.

According to the EIR, the M-1 plant would emit fugitive emissions of n-pentane at a rate of 205 pounds per day ("lbs/day") or 37.4 tons per year ("tons/year").[23] Fugitive emissions of isobutene from the existing MP-I facility are estimated by Ormat to occur at a rate of 500 lbs/day or 91.3 tons/year.[24]

During M-1 plant startup operations, the existing MP-I plant would continue to operate until the new M-1 replacement plant becomes commercial.[25] The period of simultaneous operation authorized in the FEIR is two years. Once the M-1 plant becomes commercial, the MP-I plant will be dismantled and the plant facilities would be removed from the site, the site would be-regraded, covered with gravel and

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[18] DEIR, pp. 2-19 and 4-36.

[19] California Air Resources Board, Ambient Air Quality Standards, June 7, 2012; http://www.arb.ca.gov/research/aaqs/aaqs2.pdf.

[20] DEIR, pp. 2-15–2-16.

[21] *Id.*, at p. 2-2.

[22] *Id.*, at p. 2-18.

[23] *Id.* at p. 4-38.

[24] *Ibid.*

[25] *Id.* at p. 1-1.

converted to a fenced equipment storage yard that would be used periodically for overflow parking.[26]

II. Emission Estimates of Volatile Organic Compounds from Project Operation Are Not Adequately Documented

In response to a comment by James Clark, PhD, on the RDEIR's lack of documentation validating the VOC emission estimates[27] due to fugitive losses of motive fluid from the existing MP-I and the proposed M-1 facilities, the FEIR explains that: a) the inventory loss of 500 lb/day isobutane from MP-I was based on historical plant inventory losses based on proprietary isobutane purchase records; and b) the inventory loss of 205 lb/day n-pentane from M-1 was based on emission estimate methods for VOC leaks from equipment leaks and proprietary engineering estimates developed by the U.S. Environmental Protection Agency ("USEPA") using operational information on Ormat-manufactured equipment in operation at other locations.[28] The FEIR's explanation how the respective emission estimates for fugitive losses of motive fluids from the existing and proposed facilities were derived is unsatisfactory and fails to constitute adequate documentation and, further, is suspect, as detailed below.

Existing MP-I Facility

For the existing MP-I facility, the FEIR fails to document whether the estimated 500 lb/day of VOC emissions were derived as the maximum or average daily inventory losses based on historical plant purchase records. If average daily inventory losses were used as the basis, then the FEIR must indicate the timeframe over which the purchase records were averaged. When relying on purchase records to derive emissions, the Applicant should, at a minimum, provide a table listing either the gallons per purchase record or annualized inventory losses based on the facility's purchase records and demonstrate how the estimate of 500 lb/day of VOC emissions were derived. CEQA

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[26] *Ibid.*

[27] In his letter, Dr. Clark refers to photochemically reactive compounds as "reactive organic gases" or "ROG," rather than "VOCs." The term ROG is used by the California Air Resources Board ("CARB") for chemical compounds with photochemical reactivity and is, for example, used for purposes of the agency's emission inventory for the state. The term "VOCs" is used by the U.S. Environmental Protection Agency ("USEPA") for photochemically reactive chemical compounds. The CARB's and USEPA's definitions of VOCs and ROGs differ somewhat with respect to in/excluded compounds but both agencies include isobutane and n-pentane as photochemically reactive compounds. Therefore, the terms ROG and VOCs are used interchangeably for purposes of this comment letter.

[28] FEIR, Response to Comment 9D-04, at p. 39.

requires that an environmental review document be adequately supported and that persons not involved in preparing the EIR understand the conclusion reached in the EIR. Here, the information provided requires the reviewer to accept this estimate in blind faith.

Project M-1 Facility

The FEIR's approach deriving a total of 205 lb/day of VOC (n-pentane) emissions for the new Project M-1 facility is problematic for a number of reasons:

First, the FEIR's estimates of fugitive emissions of n-pentane from Project equipment including valves, pump seals, turbine seals, flanges, connectors, and the purge system were allegedly based on emission factors reported in USEPA's 1995 *Protocol for Equipment Leak Emission Estimates* (EPA-453/R-95-017). Review of this document shows that the FEIR relied on average emission factors (leak rates) for refinery equipment for estimating emissions from the Project's six valves in gas service, five valves in liquid service, five pump seals, two turbine seals, and 220 flanges and connectors. The FEIR fails to discuss the applicability of the *average emission factors for refineries* from the USEPA's document to the Project's equipment. Further, for the eight components of the purge system (normal operations), the FEIR relies on a VOC emission factor of 0.005 kilograms per hour per source ("kg/hr/source") which is nowhere to be found in the USEPA's document. The FEIR fails to explain how it derived this emission factor, leaving the reviewer once again with no other option than to accept this estimate in blind faith. In addition, the FEIR's equipment list fails to include the facility's pressure relief valves, which the DEIR indicates would be used at the facility.[29] Emissions from these pressure relief valves must be included in the emission estimates. (*See* Comment III below.)

Second, the FEIR's estimates of operational losses of n-pentane from fill, drain, and lube leaks of 92 lb/day[30] were based on "Ormat operating experience."[31] The FEIR provides no documentation whatsoever for this operating experience or information on what basis this estimate was derived, *e.g.*, the number of facilities inventoried; their respective MW-output and number and type of OEC(s) (*e.g.*, single-level or integrated

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[29] DEIR, at p. 2-18: "Safeguards inherent to the design of the power plant would include *relief valves*, manual and automatic shutoffs, interlocks, vents, and check valves." (*Emphasis* added.)

[30] FEIR, table "Fugitive n-Pentane Emission Calculations – Typical 16 MW Air-Cooled OEC (Reference Methodology EPA453/R-95-017 Protocol for Equipment Leak Emissions)", at p. 39.

[31] FEIR, footnote * to table "Fugitive n-Pentane Emission Calculations – Typical 16 MW Air-Cooled OEC (Reference Methodology EPA453/R-95-017 Protocol for Equipment Leak Emissions)", at p. 39.

two-level unit); the type and quantity of motive fluid (isobutane, n-pentane, or other) in the facilities' systems; the number of years the information was collected; etc. Finally, it begs the question, why the FEIR estimates emissions from the existing MP-I plant and losses of n-pentane from "fill drain, and lube leaks" from the new M-1 plant based on "operating experience" and "purchase records" at other Ormat facilities but estimates fugitive equipment leaks from the Project's valves, pump seals, turbine seals, flanges, connectors, and the purge system based on the USEPA methodology. At the very least, the EIR should be revised to a) include a discussion why it considered the approaches it chose to estimate emissions applicable the respective emission sources and b) validate the use of USEPA's emission factors for refineries for estimating fugitive equipment leaks from M-1 with information based on experience and purchase records gathered at other geothermal facilities, preferably ones that also use integrated two-level binary OEC technology.

Third, the VOC (n-pentane) emission calculations presented by the FEIR in Response to Comment 9D-04 were based on a "Typical 16 MW Air-Cooled OEC;" the Project's OEC would generate 18.8 MW. The FEIR fails to specify whether the number of equipment components (valves, pump seals, turbine seals, flanges, connectors, and purge system) used to calculate fugitive equipment leak emissions were based on this "typical" 16-MW OEC or rather based on site-specific information for the Project. Further, the FEIR failed to appropriately scale the "OEC operational losses" from the "typical" 16 MW equipment to the 18.8-MW Project equipment. To address these deficiencies, the EIR should be revised, if necessary, to provide emission estimates specific to the components of the 18.8 MW Project rather than for a generic 16-MW plant.

III. Emissions of Volatile Organic Compounds from Project Operation Are Likely Underestimated, Potentially Significant and Unmitigated

As discussed in the following, information available for similar plants indicates that the FEIR underestimates emissions of VOCs from Project operations.

Emission Estimates for Fugitive Losses of Volatile Organic Compounds from Pressure Relief Valves

As discussed above, the FEIR did not estimate VOC emissions from pressure relief valves and the record does not contain information on how many pressure relief valves would be in service at the facility. However, information available for another geothermal plant that uses OEC technology for one of its four units, the Brady Geothermal Plant in Fallon, NV, indicates that relief valves are located on the n-pentane storage tank and on the OEC vaporizers and condensers. Each pressure relief valve relieves directly to atmosphere. The OEC at the Brady Geothermal Plant is a 5-MW

unit.[32] Here, the 18.8 MW M-1 Project would require three n-pentane storage tanks[33], two vaporizers (one each for level 1 and level 2 of the OEC unit)[34], and air-cooled tube condenser system. Thus, it can be conservatively assumed that the Project would have at least six pressure relief valves, one for each of the above-listed plant components.

Based on a leak rate of 0.16 kg/hr/source for VOC emissions from pressure relief valves from USEPA's 1995 *Protocol for Equipment Leak Emission Estimates*, fugitive losses of n-pentane from six pressure relief valves can be estimated at 50.8 lb/day.[35] Adding this estimate for emissions from six pressure relief valves to the FEIR's estimate of total VOC emissions (205 lb/day) results in a revised total of 256 lb/day. This estimate exceeds the 250 lb/day threshold for VOC emissions from stationary sources established by the Great Basin Unified Air Pollution Control District ("GBUAPCD") for requiring best available control technology ("BACT").

Emission Estimates for Fugitive Losses of Volatile Organic Compounds from Proposed CD-4 Geothermal Project

Comparison with the VOC emission estimate provided by the Applicant for the proposed CD-4 geothermal project further supports the supposition that emissions from the M-1 Project are underestimated: Based on the FEIR's emissions estimate of 512 lb/day VOC emissions for the 33-MW CD-4 project, it can be calculated that the facility generates more than 15 pounds per MW and day ("lb/MW-day") of VOC emissions[36]; in comparison, based on the FEIR's estimate of 205 lb/day of VOC emissions, the 18.8-MW Project would generate less than 11 lb/MW-day of VOC emissions.[37] Based on these calculated pro-rated (MW-based) daily VOC emission factor for the proposed CD-4 project of 15.5 lb/MW-day and the Project's design capacity of 18 MW, VOC emissions from the Project can be estimated at 291.7 lb/day[38], more than

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[32] The Right-to-Know Network, Risk Management Plan (RMP) Database, Brady Geothermal Plant; http://data.rtknet.org/rmp/rmp.php?database=rmp&detail=3&datype=T&facility_id=100000183428.

[33] *See* FEIR, Figures 5, 6, 9, 13, and 26.

[34] *See* FEIR, Figure 4.

[35] (0.16 kg/hr/pressure relief valve) × (6 pressure relief valves) × (24 hours/day) × (2.20462 lb/kg) = 50.79 lb/day.

[36] CD-4 plant pro-rated emissions: (512 lb/day) / (33 MW) = 15.5 lb/MW-day.

[37] Project M-1 plant pro-rated emissions: (205 lb/day) / (18.8 MW) = 10.9 lb/MW-day.

[38] Revised Project M-1 plant emissions based on CD-4 pro-rated emission factor and design capacity: (15.5 lb/MW-day) × (18.8 MW) = 291.7 lb/day.

40 percent higher than the FEIR's estimate of 205 lb/day.[39] This emission estimate considerably exceeds the GBUAPCD's BACT threshold of 250 lbs/day for VOC emissions from stationary sources.

Recommendation for Revision of FEIR to Address Potentially Significant Operational VOC Emission Estimates

I recommend that the County revise the EIR to include emission estimates based on an accurate Project-specific component count, validated by experience at other Ormat facilities using the proposed technology. If revised Project VOC emissions should exceed the GBUAPCD's BACT significance threshold of 250 lbs/day of VOC emissions from stationary sources, a BACT analysis should be prepared for the Project's equipment to minimize fugitive losses from equipment leaks. Technologies that should be evaluated in such a BACT analysis include, *e.g.*, leakless components.

IV. The FEIR Fails to Identify and Mitigate Significant Impacts on Air Quality due to VOC Emissions from Project Operations

The Project would replace the existing MP-I plant which has been operating for 28 years (since 1984) and is nearing the end of its useful life. During the startup of the Project there would be an up to two-year transition period during which both the MP-I and M-1 plant operations would overlap. In comment letters on the RDEIR, your office and James Clark, PhD, discussed the document's failure to disclose the potential increase in VOC emissions during this transition period.[40] In response, the FEIR claims that emissions from contemporaneous operation of the two plants would not increase fugitive (VOC) motive fluid emissions:

> The operating rate of the respective plants during the transition period is limited by the geothermal fluid provided to each plant, and the maximum geothermal fluid available to Casa Diablo is fixed to the existing maximum geothermal fluid pumping capacity of the wellfield (6,900,000 pounds per hour). This physical pumping limit would not change with the MP-I Replacement Project (RDEIR page 2-17), and the geothermal fluid flow rates to the respective facilities would be inversely proportional. As such when geothermal fluid flow to the M-1 plant increases the geothermal fluid flow to MP-I plant must decrease proportionally. Similarly, the combined emissions of isobutane and n-pentane occurring while both plants are operating at reduced capacities would be proportional to the

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[39] (291.7 lb/day) / (205 lb/day) = 1.43.

[40] See FEIR, Comment 9-14 and Comment 9D-06.

> respective fraction that each plant is operating. Motive fluid emissions would range from about 500 pounds per day (when only the MP-I plant is operating) to zero emissions of isobutane and about 205 pounds per day of n-pentane (when only the M-1 plant is operating). In general, when the MP-I plant is operating at a higher capacity then the M-1 plant must be operating at a proportionally lower capacity and vice versa. Thus, at any time the M-1 plant is operating during the transition period there would be a reduction in the total emissions of motive fluid from the MP-I plant.[41]

This explanation fails to acknowledge that the existing MP-I plant has been operating at far less than its design capacity over the past decade and therefore is likely not drawing geothermal fluid at the maximum design capacity rate, but instead only a fraction thereof. As discussed in the DEIR, the condensing capacity of the aging, leak prone MP-I generation unit has been severely restricted due to the need to plug damaged condenser tubes.[42] As a result, both of the 5-MW generation units (U100 and U200) have been operating at substantially reduced capacity, as previously discussed in the March 15, 2012 comment letter on the RDEIR by David Marcus.[43] In the past decade, the annual capacity factor[44] for Unit 1 (U100) ranged from 61% to 21%; the annual capacity factor for Unit 2 (U200) ranged from 60% to 37%. The combined capacity factor for the MP-I plant ranged from 56% to 37%, as shown in the inset figure below.

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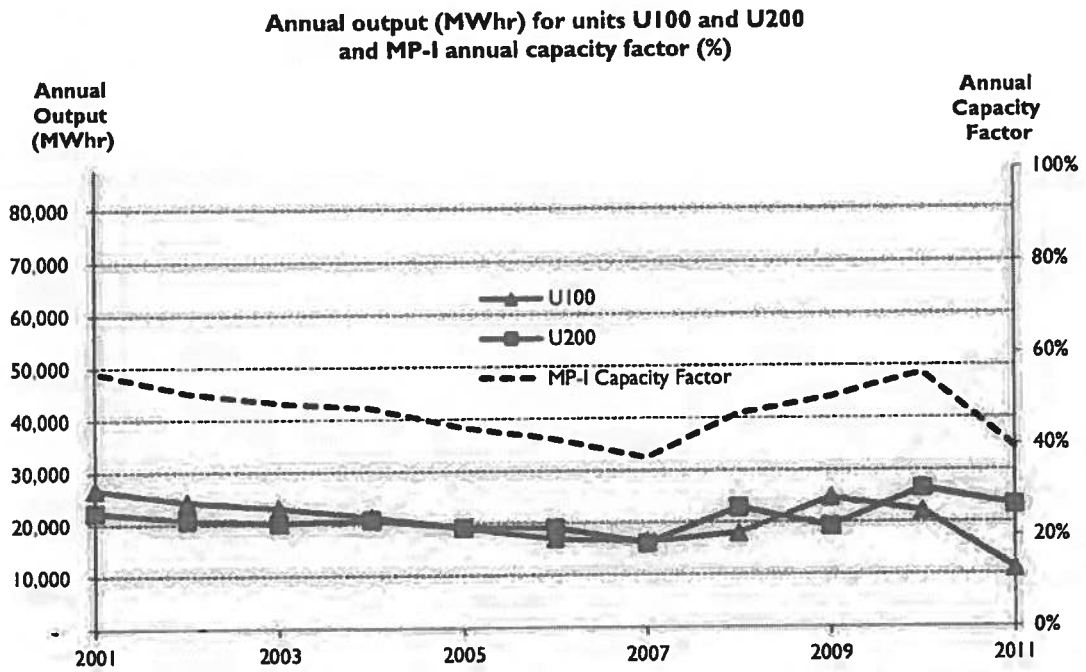
[41] FEIR, Response to Comment 9D-06, p. 40.

[42] *Id.* at p. 4-131.

[43] *See* FEIR, Comment Letter 9B.

[44] The capacity factor is the ratio of actual output to potential output if operated continuously at 100 percent of rated capacity.



Annual output for MP-I generation units U100 (5 MW) and U200 (5 MW) from: California Energy Commission, Energy Almanac at http://energyalmanac.ca.gov/electricity/web_qfer/plant_stats_2.php.

Annual capacity factor for MP-I (10 MW) calculated as: (annual output U100 + annual output U200) / (10 MW × 8,760 hours)

Because VOC emissions from the existing MP-I plant of 500 lbs/day were calculated as inventory losses based on historical plant purchase records (*see* Comment I), these emission estimates most likely reflect these low capacity factors and corresponding reduced pumping of geothermal fluid from the wellfield. Conservatively assuming that the geothermal wellfield and associated piping were sized to supply 100% of the existing MP-I plant's design capacity (to ensure operating reliability, the wellfield capacity was likely sized considerably larger), means that there is unused pumping capacity available for the new M-1 plant without reducing current operations of the existing MP-I plant. Thus, VOC emissions from the new plant must be added to the 500 lbs/day of VOC emissions from the existing plant (or the revised emissions based on Comments II and III).

Consequently, the contemporaneous operation of the existing MP-I plant and the Project would result in increased emissions of VOCs, which as ozone precursors would contribute to the region's non-attainment status of this pollutant. This is a significant impact on air quality (*i.e.*, additional VOC emissions up to the full pumping capacity of the wellfield has been reached) that the FEIR fails to identify and mitigate. I recommend that the County prepare a revised EIR that addresses this issue.

V. The EIR Fails to Provide an Off-Site Consequence Analysis for the Flammable Motive Fluid n-Pentane

As discussed previously, the existing MP-I plant uses isobutane as the motive fluid, whereas the Project M-1 plant would use n-pentane. As the FEIR readily acknowledges, these chemicals have considerably different chemical and physical properties: *e.g.*, isobutane is a flammable gas at standard temperature and pressure; in contrast, n-pentane is a flammable liquid at standard temperature and pressure.[45] Due to their different chemical and physical properties, these chemicals require different handling and equipment during transportation, transfer, and storage.

The record for the FEIR does not include an off-site consequence analysis for the Project's highly flammable motive fluid, n-pentane, as required by the Chemical Accident Prevention Provisions under USEPA's Risk Management Plan ("RMP") rule (Section 112(r) of the federal Clean Air Act).[46] The DEIR acknowledges that the chemical is flammable and recognizes that the Project is subject to the USEPA's RMP rule. Yet, rather than providing an off-site consequence analysis for n-pentane, the DEIR states that MPLP would revise and update its "integrated program" for the existing three plants (which is intended to meet the requirements of the California Accidental Release Prevention program, the USEPA's RMP, and the federal Occupational Safety and Health Administration's Process Safety Management Program) "[p]rior to delivery of n–pentane, to reflect the new M–1 plant"[47] This approach improperly defers an analysis that should be part of the CEQA review process for the Project into the future.

I recommend that the County revise the EIR to provide an off-site consequence analysis for the flammable motive fluid n-pentane using USEPA's RMP*Comp model as required by the USEPA's RMP to satisfy the requirements of CEQA and disclose all potential impacts to the public.

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[45] FEIR, Response to Comment 9D-02, at pp. 38-39.

[46] U.S. Environmental Protection Agency, Risk Management Plan (RMP) Rule; http://epa.gov/emergencies/content/rmp/index.htm.

[47] DEIR, at p. 2-17.

VI. Recommendation

I recommend that the County prepare a revised EIR for review and comment by the public that addresses the above issues.

Please feel free to call me at (415) 492-2131 or e-mail at petra.pless@gmail.com if you have any questions.

With best regards,

Petra Pless, D.Env.

Petra Pless, D.Env.

440 Nova Albion Way, #2
San Rafael, CA 94903
(415) 492-2131 phone
(815) 572-8600 fax
petra.pless@gmail.com

Dr. Pless is a court-recognized expert with over 20 years of experience in environmental consulting conducting and managing interdisciplinary environmental research projects and preparing and reviewing environmental permits and other documents for U.S. and European stakeholder groups. Her broad-based experience includes air quality and air pollution control; water quality, water supply, and water pollution control; biological resources; public health and safety; noise studies; California Environmental Quality Act ("CEQA"), Clean Air Act ("CAA"), and National Environmental Policy Act ("NEPA") review; industrial ecology and risk assessment; and use of a wide range of environmental software.

EDUCATION

Doctorate in Environmental Science and Engineering (D.Env.), University of California Los Angeles, 2001

Master of Science (equivalent) in Biology, Technical University of Munich, Germany, 1991

PROFESSIONAL HISTORY

Pless Environmental, Inc., Principal, 2008–present

Environmental Consultant, Sole Proprietor, 2006–2008

Leson & Associates (previously Leson Environmental Consulting), Kensington, CA, Environmental Scientist/Project Manager, 1997–2005

University of California Los Angeles, Graduate Research Assistant/Teaching Assistant, 1994–1996

ECON Research and Development, Environmental Scientist, Ingelheim, Germany, 1992–1993

Biocontrol, Environmental Projects Manager, Ingelheim, Germany, 1991–1992

REPRESENTATIVE EXPERIENCE

Air Quality and Pollution Control

Projects include CEQA/NEPA review; CAA attainment and non-attainment new source review; prevention of significant deterioration ("PSD") and Title V permitting; control technology analyses (BACT, LAER, RACT, BARCT, BART, MACT); technology evaluations and cost-effectiveness analyses; criteria and toxic pollutant and greenhouse gas emission inventories; emission offsets; ambient and source monitoring; analysis of emissions estimates and ambient air pollutant concentration modeling. Some typical projects include:

— Critically reviewed and prepared technical comments on the air quality, biology, noise, water quality, and public health and safety sections of CEQA/NEPA documents for numerous

commercial, residential, and industrial projects (*e.g.*, power plants, airports, residential developments, retail developments, university expansions, hospitals, refineries, slaughterhouses, asphalt plants, food processing facilities, printing facilities, mines, quarries, and recycling facilities) and provided litigation support in a number of cases filed under CEQA.

- Critically reviewed and prepared technical comments on the air quality and public health sections of the Los Angeles Airport Master Plan (Draft, Supplement, and Final Environmental Impact Statement/Environmental Impact Report) for the City of El Segundo. Provided technical comments on the Draft and Final General Conformity Determination for the preferred alternative submitted to the Federal Aviation Administration.
- Prepared comments on proposed PSD and Title V permit best available control technology ("BACT") analysis for greenhouse gas emissions from a proposed direct reduced iron facility in Louisiana.
- Prepared technical comments on the potential air quality impacts of the California Air Resources Board's *Proposed Actions to Further Reduce Particulate Matter at High Priority California Railyards.*
- For several California refineries, evaluated compliance of fired sources with Bay Area Air Quality Management District Rule 9-10. This required evaluation and review of hundreds of source tests to determine if refinery-wide emission caps and compliance monitoring provisions were being met.
- Critically reviewed and prepared technical comments on draft Title V permits for several refineries and other industrial facilities in California.
- Evaluated the public health impacts of locating big-box retail developments in densely populated areas in California and Hawaii. Monitored and evaluated impacts of diesel exhaust emissions and noise on surrounding residential communities.
- In conjunction with the permitting of several residential and commercial developments, conducted studies to determine baseline concentrations of diesel exhaust particulate matter using an aethalometer.
- For an Indiana steel mill, evaluated technology to control NOx and CO emissions from fired sources, including electric arc furnaces and reheat furnaces, to establish BACT. This required a comprehensive review of U.S. and European operating experience. The lowest emission levels were being achieved by steel mills using selective catalytic reduction ("SCR") and selective non-catalytic reduction ("SNCR") in Sweden and The Netherlands.
- For a California petroleum coke calciner, evaluated technology to control NOx, CO, VOCs, and PM10 emissions from the kiln and pyroscrubbers to establish BACT and LAER. This required a review of state and federal clearinghouses, working with regulatory agencies and pollution control vendors, and obtaining and reviewing permits and emissions data from other similar facilities. The best-controlled facilities were located in the South Coast Air Quality Management District.
- For a Kentucky coal-fired power plant, identified the lowest NOx levels that had been permitted and demonstrated in practice to establish BACT. Reviewed operating experience of European, Japanese, and U.S. facilities and evaluated continuous emission monitoring data. The lowest NOx levels had been permitted and achieved in Denmark and in the U.S. in Texas and New York.

- In support of efforts to lower the CO BACT level for power plant emissions, evaluated the contribution of CO emissions to tropospheric ozone formation and co-authored report on same.
- Critically reviewed and prepared technical comments on applications for certification ("AFCs") for numerous natural-gas fired, solar, biomass, and geothermal power plants in California permitted by the California Energy Commission. The comments addressed construction and operational emissions inventories and dispersion modeling, BACT determinations for combustion turbine generators, fluidized bed combustors, diesel emergency generators, etc.
- Critically reviewed and prepared technical comments on draft PSD permits for several natural gas-fired power plants in California, Indiana, and Oregon. The comments addressed emission inventories, greenhouse gas emissions, BACT, case-by-case MACT, compliance monitoring, cost-effectiveness analyses, and enforceability of permit limits.
- For a California refinery, evaluated technology to control NOx and CO emissions from CO Boilers to establish RACT/BARCT to comply with BAAQMD Rule 9-10. This required a review of BACT/RACT/LAER clearinghouses, working with regulatory agencies across the U.S., and reviewing federal and state regulations and State Implementation Plans ("SIPs"). The lowest levels were required in a South Coast Air Quality Management District rule and in the Texas SIP.
- In support of several federal lawsuits filed under the federal Clean Air Act, prepared cost-effectiveness analyses for SCR and oxidation catalysts for simple cycle gas turbines and evaluated opacity data.
- Provided litigation support for a CEQA lawsuit addressing the adequacy of pollution control equipment at a biomass cogeneration plant.
- Prepared comments and provided litigation support on several proposed regulations including the Mojave Desert Air Quality Management District Rule 1406 (fugitive dust emission reduction credits for road paving); South Coast Air Quality Management District Rule 1316, San Joaquin Valley Air Pollution Control District Rule 2201, Antelope Valley Air Quality Management District Regulation XIII, and Mojave Desert Air Quality Management District Regulation XIII (implementation of December 2002 amendments to the federal Clean Air Act).
- Critically reviewed draft permits for several ethanol plants in California, Indiana, Ohio, and Illinois and prepared technical comments.
- Reviewed state-wide average emissions, state-of-the-art control devices, and emissions standards for construction equipment and developed recommendations for mitigation measures for numerous large construction projects.
- Researched sustainable building concepts and alternative energy and determined their feasibility for residential and commercial developments, *e.g.*, regional shopping malls and hospitals.
- Provided comprehensive environmental and regulatory services for an industrial laundry chain. Facilitated permit process with the South Coast Air Quality Management District. Developed test protocol for VOC emissions, conducted field tests, and used mass balance methods to estimate emissions. Reduced disposal costs for solvent-containing waste streams by identifying alternative disposal options. Performed health risk screening for air toxics

emissions. Provided permitting support. Renegotiated sewer surcharges with wastewater treatment plant. Identified new customers for shop-towel recycling services.

— Designed computer model to predict performance of biological air pollution control (biofilters) as part of a collaborative technology assessment project, co-funded by several major chemical manufacturers.

— Experience using a wide range of environmental software, including air dispersion models, air emission modeling software, database programs, and geographic information systems.

Water Quality and Pollution Control

Experience in water quality and pollution control, including surface water and ground water quality and supply studies, evaluating water and wastewater treatment technologies, and identifying, evaluating and implementing pollution controls. Some typical projects include:

— Evaluated impacts of on-shore oil drilling activities on large-scale coastal erosion in Nigeria.

— For a 500-MW combined-cycle power plant, prepared a study to evaluate the impact of proposed groundwater pumping on local water quality and supply, including a nearby stream, springs, and a spring-fed waterfall. The study was docketed with the California Energy Commission.

— For a 500-MW combined-cycle power plant, identified and evaluated methods to reduce water use and water quality impacts. These included the use of zero-liquid-discharge systems and alternative cooling technologies, including dry and parallel wet-dry cooling. Prepared cost analyses and evaluated impact of options on water resources. This work led to a settlement in which parallel wet dry cooling and a crystallizer were selected, replacing 100 percent groundwater pumping and wastewater disposal to evaporation ponds.

— For a homeowner's association, reviewed a California Coastal Commission staff report on the replacement of 12,000 linear feet of wooden bulkhead with PVC sheet pile armor. Researched and evaluated impact of proposed project on lagoon water quality, including sediment resuspension, potential leaching of additives and sealants, and long-term stability. Summarized results in technical report.

Applied Ecology, Industrial Ecology and Risk Assessment

Experience in applied ecology, industrial ecology and risk assessment, including human and ecological risk assessments, life cycle assessment, evaluation and licensing of new chemicals, and fate and transport studies of contaminants. Experienced in botanical, phytoplankton, and intertidal species identification and water chemistry analyses. Some typical projects include:

— Conducted technical, ecological, and economic assessments of product lines from agricultural fiber crops for European equipment manufacturer; co-authored proprietary client reports.

— Developed life cycle assessment methodology for industrial products, including agricultural fiber crops and mineral fibers; analyzed technical feasibility and markets for thermal insulation materials from natural plant fibers and conducted comparative life cycle assessments.

— For the California Coastal Conservancy, San Francisco Estuary Institute, Invasive Spartina Project, evaluated the potential use of a new aquatic pesticide for eradication of non-native, invasive cordgrass (*Spartina spp.*) species in the San Francisco Estuary with respect to water

quality, biological resources, and human health and safety. Assisted staff in preparing an amendment to the Final EIR.

- Evaluated likelihood that organochlorine pesticide concentrations detected at a U.S. naval air station are residuals from past applications of these pesticides consistent with manufacturers' recommendations. Retained as expert witness in federal court case.
- Prepared human health risk assessments of air pollutant emissions from several industrial and commercial establishments, including power plants, refineries, and commercial laundries.
- Managed and conducted laboratory studies to license pesticides. This work included the evaluation of the adequacy and identification of deficiencies in existing physical/chemical and health effects data sets, initiating and supervising studies to fill data gaps, conducting environmental fate and transport studies, and QA/QC compliance at subcontractor laboratories. Prepared licensing applications and coordinated the registration process with German environmental protection agencies. This work led to regulatory approval of several pesticide applications in less than six months.
- Designed and implemented database on physical/chemical properties, environmental fate, and health impacts of pesticides for a major multi-national pesticide manufacturer.
- Designed and managed experimental toxicological study on potential interference of delta-9-tetrahydrocannabinol in food products with U.S. employee drug testing; co-authored peer-reviewed publication.
- Critically reviewed and prepared technical comments on applications for certification for several natural-gas fired, solar, and geothermal power plants and transmission lines in California permitted by the California Energy Commission. The comments addressed avian collisions and electrocution, construction and operational noise impacts on wildlife, risks from brine ponds, and impacts on endangered species.
- For a 180-MW geothermal power plant, evaluated the impacts of plant construction and operation on the fragile desert ecosystem in the Salton Sea area. This work included baseline noise monitoring and assessing the impact of noise, brine handling and disposal, and air emissions on local biota, public health, and welfare.
- Designed research protocols for a coastal ecological inventory in Southern California; developed sampling methodologies, coordinated field sampling, determined species abundance and distribution in intertidal zone, and conducted statistical data analyses.
- Designed and conducted limnological study on effects of physical/chemical parameters on phytoplankton succession; performed water chemistry analyses and identified phytoplankton species; co-authored two journal articles on results.

PRO BONO ACTIVITIES

Founding member of "SecondAid," a non-profit organization providing tsunami relief for the recovery of small family businesses in Sri Lanka. (www.secondaid.org.)

PUBLICATIONS & RECOMMENDATIONS

Available upon request.

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Scott Cashen, M.S.—Independent Biological Resources and Forestry Consultant

October 18, 2012

Ms. Elizabeth Klebaner
Adams Broadwell Joseph & Cardozo
601 Gateway Boulevard, Suite 1000
South San Francisco, CA 94080

Subject: Comments on the Environmental Impact Report for the Mammoth Pacific I Replacement Project

Dear Ms. Klebaner:

This letter contains my comments on the Final Environmental Impact Report ("FEIR") prepared for Mammoth Pacific Limited Partnership's ("Applicant") proposed Mammoth Pacific I Replacement Project ("Project"). I submitted comment letters in response to the Draft Environmental Impact Report and the Revised Draft Environmental Impact Report ("RDEIR") prepared by Mono County ("County"). These comment letters established my professional qualifications and described the actions I took to evaluate the DEIR, RDEIR, and the underlying analyses, and are incorporated by reference here.

Impacts to Critical Habitat for the Owens Tui Chub

The Owens tui chub (*Gila bicolor snyderi*) is a subspecies of fish that is listed as endangered under the state and federal Endangered Species Acts. It is known to occur at only six sites, one of which is the headwaters of Hot Creek above the Hot Creek Fish Hatchery. The Hot Creek Headsprings (or Headwaters) site consists of two springs, "AB Spring" and "CD Spring," and it is one of two sites that have been designated as critical habitat for the subspecies. In designating critical habitat for the subspecies, the U.S. Fish and Wildlife ("USFWS") identified activities that may adversely affect critical habitat for the Owens tui chub. These include "activities that decrease available water or cause a significant change in the physical or chemical properties (e.g., temperature, pH, or dissolved gases) of the water."[1] Hydrologic monitoring data indicate the thermal water component in the Hot Creek Headsprings has declined by 30% to 40% since 1990.[2] The data also indicate there has been a decline in the volume of thermal water entering the Hot Creek Headsprings since the early 1990s.[3]

Studies conducted by the USGS indicate the decline in the thermal water component and other surficial changes in the vicinity of Casa Diablo are due to geothermal

[1] Department of the Interior, US Fish and Wildlife Service. 1985. Endangered and Threatened Wildlife and Plants; Endangered Status and Critical Habitat Designation for the Owens Tui Chub. Final rule. Federal Register 50(150): 31592-31597.
[2] Sorey ML. 2000. Geothermal Development and Changes in Surficial Features: Examples from the Western United States. Proceedings of the World Geothermal Congress 2000; Kyushu - Tohoku, Japan, May 28 - June 10, 2000. pp. 705-711. *See also* Second Revised DEIR, Appendix M.
[3] Second Revised DEIR, Appendix M.

development.[4] For example, those studies have reported the following:

1. "[t]he hydrologic monitoring program has detected changes in the hydrologic system caused by geothermal development and variations in precipitation and recharge (Howle and Farrar, 1997). For example, we have delineated decreases in thermal-spring discharge at sites within about 5 km to the east of Casa Diablo that are caused by subsurface pressure declines at the geothermal well field. No changes have as yet been detected in the springs in Hot Creek gorge. There has also been an increase in steam discharge at Casa Diablo and sites farther west due to increased boiling in the geothermal reservoir caused by geothermal production;"[5]

2. "[w]ater levels in geothermal well CW-3 (5 km east of Casa Diablo) show the effects of pressure reductions caused by the withdrawal of geothermal fluid at Casa Diablo; water levels declined significantly in 1991 when the production rate was increased to supply two new power plants. A similar water level decline has not yet occurred in geothermal observation well CH-10B, located 9 km east of Casa Diablo;[6]

3. "[a]t the Hot Creek Fish Hatchery, chemical-flux measurements show that the thermal-water component in the springs has declined by some 30-40% since 1990;"[7]

4. "[t]he best-documented cases [of changes in surficial thermal features] are for the Casa Diablo area in Long Valley caldera, California and for Steamboat Springs, Nevada where hydrologic monitoring programs have delineated some combination of declines in thermal-water discharge, increases in fumarolic steam discharge, and subsidence."[8]

The Hot Creek Headsprings are located less than four kilometers east of Casa Diablo (i.e., within the area that has exhibited surficial changes due to geothermal development). However, the EIR states "no substantive impacts on the Hot Creek headsprings supporting the Owens tui chub critical habitat could be attributed to the existing geothermal development."[9] The EIR does not define "substantive impact." The County also has not provided hydrologic and biologic resource monitoring analyses that would enable me to assess whether the impacts attributable to geothermal development would

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[4] Sorey ML. 2000. Geothermal Development and Changes in Surficial Features: Examples from the Western United States. Proceedings of the World Geothermal Congress 2000; Kyushu - Tohoku, Japan, May 28 - June 10, 2000. pp. 705-711. *See also* US Geological Service. n.d. Long Valley Caldera Hydrologic Studies [internet]. Available at: http://pubs.usgs.gov/dds/dds-81/Intro/MonitoringData/Hydrologic/Hydro.html.

[5] USGS. N.d. Long Valley Caldera Hydrologic Studies [internet]. Available at: http://pubs.usgs.gov/dds/dds-81/Intro/MonitoringData/Hydrologic/Hydro.html.

[6] *Ibid.*

[7] Sorey ML. 2000. Geothermal Development and Changes in Surficial Features: Examples from the Western United States. Proceedings of the World Geothermal Congress 2000; Kyushu - Tohoku, Japan, May 28 - June 10, 2000. pp. 705-711.

[8] *Ibid.*

[9] RDEIR, p. 4-71.

be potentially significant to biological resources such as the Owens tui chub. For example, although the Second RDEIR included hydrologic monitoring data, these data were limited to graphs depicting the relationship between a dependent variable (e.g., water temperature) and independent variable (e.g., year). The graphs provide limited value in assessing potential impacts to biological resources without: (a) statistical analysis, and (b) analytical interpretation of the results.

For example, the graphs depict what appears to be a *statistically significant* drop in the thermal water component in the AB Spring and CD Spring beginning in 1993. In 1988, prior to the decrease in thermal water to the springs, the population estimate for Owens tui chub in the AB Spring was 334±105, and it was 523±146 in the CD Spring.[10] In 1999, after the decrease in thermal water, the population estimate for the AB Spring was 180 to 245, and no tui chub were detected in the CD Spring.[11] The EIR fails to analyze whether the apparent decline in the tui chub populations was related to (a) the corresponding drop in the thermal water component; or (b) other factors (e.g., predation). Thermal water entering the Hot Creek Headsprings has a different chemical composition than non-thermal water, and information provided by the USFWS suggests the chemicals present in the thermal water benefit the Owens tui chub.[12] Consequently, one can infer that the apparent decline in the Owens tui chub populations *could* be due to the decline in the thermal water component.

According to the EIR, the maximum physical pumping capacity for the Casa Diablo complex is approximately 6,900,000 pounds per hour.[13] However, the EIR fails to establish whether the Casa Diablo complex is now operating at full capacity. Comments submitted in response to the RDEIR indicate power production at the existing MP-I facility averaged less than 50 percent of its capacity between 2007 and 2010.[14] This suggests that: (a) pumping from the production wells has also been below capacity; and/or (b) pumping has been at capacity, but the existing MP-I facility has been incapable of producing power at its original capacity due to operational inefficiencies (e.g., degraded equipment). Any incremental increase in pumping due to the Project, as compared to existing conditions, has the potential to exacerbate changes to critical habitat for the Owens tui chub by causing further declines in the thermal water component.

Biologic and Hydrologic Monitoring

The County has indicated that the Project will be subject to the same hydrologic and biologic monitoring and remedial action program requirements as those that are required for MP-II and PLES-I. According to the RDEIR, "[t]he adoption of the prescribed hydrologic and biologic monitoring and mitigation measure program by the MP-I Project would reduce the potential adverse effects of the Project on the Owens tui chub critical

[10] US Fish and Wildlife Service. 2009. Owens Tui Chub: 5-Year Review and Evaluation, Table 1.
[11] *Ibid.*
[12] U.S. Fish and Wildlife Service. 1998. Owens Basin Wetland and Aquatic Species Recovery Plan, Inyo and Mono Counties, California. Portland, Oregon, p. 92.
[13] FEIR, Response to Comment 9-12.
[14] RDEIR Comment 9-12 and 9B-1.

habitat [and Hot Creek Fish Hatchery] to below the level of significance."[15] This statement cannot be verified because the FEIR does not describe the current rate of power production, and the impacts that increasing production above current conditions would have on the Owens tui chub. In addition, the conclusion in the FEIR that impacts would be reduced to below the level of significance is contradicted by the fact that (a) the monitoring and mitigation referenced in the RDEIR was ineffective in reversing the decline of thermal water to the Hot Creek Headsprings that began in 1993; and (b) there appears to have been a significant decline in Owens tui chub populations in the Hot Creek Headsprings that may be due to the decline of thermal water.

Furthermore, the hydrologic and biologic monitoring and mitigation program required for MP-II and PLES-I may be inconsistent with USFWS Recovery Plan for the Owen tui chub. In particular, Recovery Task 2.4.2 is:

> Protect spring discharge. Geothermal development and groundwater pumping in Long Valley may alter aquifer dynamics. **Springs supporting Hot Creek should be protected from adverse impacts of decreased discharge, and changes in the thermal and chemical characteristics of water.** Monitoring programs should be [designed to] determine characteristics (temporal, chemical, physical) of natural spring discharge, if spring discharge is being affected, and the location of activities causing adverse effects. Actions should be taken to protect discharge at 1998 levels.[16]

Based on my review, the hydrological and biological monitoring program has not ensured consistency with the Recovery Task (i.e., it has not prevented potential adverse impacts associated with changes in the thermal and chemical characteristics of water in AB Spring and CD Spring), or that actions are, have been or, or will be taken to protect discharge at 1998 levels.

<u>Impacts Due to Increased Pumping and Project Lifespan</u>

The principal reason for the M-1 Replacement Project is to replace the aging, leak-prone MP-I unit, whose condensing capacity has been severely restricted due to the need to plug damaged condenser tubes.[17] According to the RDEIR, "[t]he aging MP–I power plant would be expected to continue to operate as long as repair and restoration of the facility remains economically practical, but the long-term continuing utilization of the MP-I project geothermal resources could be shortened due to eventual equipment failure."[18] The aforementioned information contradicts the statement in the FEIR that the existing MP-I Project would continue to operate *indefinitely* if the MP-I Replacement Project is not approved.[19] It is reasonable to assume that the Project will extend the duration of geothermal resource extraction from the existing wellfield long after the MP-I unit's operational life.

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[15] RDEIR, p. 12.
[16] U.S. Fish and Wildlife Service. 1998. Owens Basin Wetland and Aquatic Species Recovery Plan, Inyo and Mono Counties, California. Portland, Oregon, p. 92. [emphasis added].
[17] RDEIR, p. 4-131.
[18] RDEIR, p. 2-32.
[19] FEIR, p. 33.

Extending the duration of resource extraction could perpetuate tree-kills, as dicussed in my earlier comments, and have an impact on sensitive species that depend on live trees for habitat. Extending the duration of resource extraction could also lead to a further reduction in the thermal water component within critical habitat for the Owens tui chub. Indeed, the RDEIR indicates *extended geothermal resource production and injection activities from the MP-I Project* could result in changes in the temperature, flow rate or quality of the Hot Creek headsprings, and that these changes could be a potentially significant impact under CEQA.[20] The EIR fails to address these potentially significant impacts.

The FEIR does not provide a mitigation and monitoring program for tree-kills that may be influenced by the Project. In addition, it is my professional opinion that the hydrologic and biologic monitoring and remedial action program imposed by the County currently lacks the ability to ensure that the Project would not have a significant impact to critical habitat for the Owens tui chub in the Hot Creek Headsprings.

Sincerely,

Scott Cashen, M.S.
Senior Biologist

[20] RDEIR, p. 4-135.

Scott Cashen, M.S.
Senior Biologist / Forest Ecologist
3264 Hudson Avenue, Walnut Creek, CA 94597. (925) 256-9185. scottcashen@gmail.com

Scott Cashen has 20 years of professional experience in natural resources management. During that time he has worked as a field biologist, forester, environmental consultant, and instructor of Wildlife Management. Mr. Cashen currently operates an independent consulting business that focuses on CEQA/NEPA compliance issues, endangered species, scientific field studies, and other topics that require a high level of scientific expertise.

Mr. Cashen has knowledge and experience with many taxa, biological resource issues, and environmental regulations. This knowledge and experience has made him a highly sought after biological resources expert. To date, he has been retained as a biological resources expert for over 40 projects. Mr. Cashen's role in this capacity has encompassed all stages of the environmental review process, from initial document review through litigation support and expert witness testimony.

Mr. Cashen is a recognized expert on the environmental impacts of renewable energy development. He has been involved in the environmental review process for 28 renewable energy projects, and he has been a biological resources expert for more of California's solar energy projects than any other private consultant. In 2010, Mr. Cashen testified on 5 of the Department of the Interior's "Top 6 Fast-tracked Solar Projects" and his testimony influenced the outcome of each of these projects.

Mr. Cashen is a versatile scientist capable of addressing numerous aspects of natural resource management simultaneously. Because of Mr. Cashen's expertise in both forestry and biology, Calfire had him prepare the biological resource assessments for all of its fuels treatment projects in Riverside and San Diego Counties following the 2003 Cedar Fire. Mr. Cashen has led field studies on several special-status species, including plants, fish, reptiles, amphibians, birds, and mammals. Mr. Cashen has been the technical editor of several resource management documents, and his strong scientific writing skills have enabled him to secure grant funding for several clients.

AREAS OF EXPERTISE

- CEQA, NEPA, and Endangered Species Act compliance issues
- Comprehensive biological resource assessments
- Endangered species management
- Renewable energy
- Forest fuels reduction and timber harvesting
- Scientific field studies, grant writing and technical editing

EDUCATION

M.S. Wildlife and Fisheries Science - The Pennsylvania State University (1998)
B.S. Resource Management - The University of California, Berkeley (1992)

PROFESSIONAL EXPERIENCE

Litigation Support / Expert Witness

As a biological resources expert, Mr. Cashen reviews CEQA/NEPA documents and provides his client(s) with an assessment of biological resource issues. He then prepares written comments on the scientific and legal adequacy of the project's environmental documents (e.g., EIR). For projects requiring California Energy Commission (CEC) approval, Mr. Cashen has submitted written testimony (opening and rebuttal) in conjunction with oral testimony before the CEC.

Mr. Cashen can lead field studies to generate evidence for legal testimony, and he can incorporate testimony from his deep network of species-specific experts. Mr. Cashen's clients have included law firms, non-profit organizations, and citizen groups.

REPRESENTATIVE EXPERIENCE

Solar Energy Facilities

- Abengoa Mojave Solar Project
- Avenal Energy Power Plant
- Beacon Solar Energy Project
- Blythe Solar Power Project
- Calico Solar Project
- Calipatria Solar Farm II
- Carrizo Energy Solar Farm
- Catalina Renewable Energy Project
- Fink Road Solar Farm
- Genesis Solar Energy Project
- Heber Solar Energy Facility
- Imperial Valley Solar Project
- Ivanpah Solar Electric Generating
- Maricopa Sun Solar Complex
- Mt. Signal and Calexico Solar
- San Joaquin Solar I & II
- Solar Gen II Projects
- SR Solis Oro Loma
- Vestal Solar Facilities
- Victorville 2 Power Project

Geothermal Energy Facilities

- East Brawley Geothermal
- Mammoth Pacific 1 Replacement
- Western GeoPower Plant and

Wind Energy Facilities

- Catalina Renewable Energy Project
- Ocotillo Express Wind Energy
- San Diego County Wind Ordinance
- Tres Vaqueros Repowering Project
- Vasco Winds Relicensing Project

Biomass Facilities

- Tracy Green Energy Project

Development Projects

- Alves Ranch
- Aviano
- Chula Vista Bayfront Master Plan
- Columbus Salame
- Concord Naval Weapons Station
- Faria Annexation
- Live Oak Master Plan
- Napa Pipe
- Roddy Ranch
- Rollingwood
- Sprint-Nextel Tower

Project Management

Mr. Cashen has managed several large-scale wildlife, forestry, and natural resource management projects. Many of these projects have required hiring and training field crews, coordinating with other professionals, and communicating with project stakeholders. Mr. Cashen's experience in study design, data collection, and scientific writing make him an effective project manager, and his background in several different natural resource disciplines enable him to address the many facets of contemporary land management in a cost-effective manner.

REPRESENTATIVE EXPERIENCE

Wildlife Studies

- Peninsular Bighorn Sheep Resource Use and Behavior Study: (*CA State Parks*)
- "KV" Spotted Owl and Northern Goshawk Inventory: (*USFS, Plumas NF*)
- Amphibian Inventory Project: (*USFS, Plumas NF*)
- San Mateo Creek Steelhead Restoration Project: (*Trout Unlimited and CA Coastal Conservancy, Orange County*)
- Delta Meadows State Park Special-status Species Inventory: (*CA State Parks, Locke*)

Natural Resources Management

- Mather Lake Resource Management Study and Plan – (*Sacramento County*)
- Placer County Vernal Pool Study – (*Placer County*)
- Weidemann Ranch Mitigation Project – (*Toll Brothers, Inc., San Ramon*)
- Ion Communities Biological Resource Assessments – (*Ion Communities, Riverside and San Bernardino Counties*)
- Del Rio Hills Biological Resource Assessment – (*The Wyro Company, Rio Vista*)

Forestry

- Forest Health Improvement Projects – (*CalFire, SD and Riverside Counties*)
- San Diego Bark Beetle Tree Removal Project – (*SDG&E, San Diego Co.*)
- San Diego Bark Beetle Tree Removal Project – (*San Diego County/NRCS*)
- Hillslope Monitoring Project – (*CalFire, throughout California*)

Biological Resources

Mr. Cashen has a diverse background with biological resources. He has conducted comprehensive biological resource assessments, habitat evaluations, species inventories, and scientific peer review. Mr. Cashen has led investigations on several special-status species, including ones focusing on the foothill yellow-legged frog, mountain yellow-legged frog, desert tortoise, steelhead, burrowing owl, California spotted owl, northern goshawk, willow flycatcher, Peninsular bighorn sheep, red panda, and forest carnivores.

REPRESENTATIVE EXPERIENCE

Avian

- Study design and Lead Investigator - Delta Meadows State Park Special-Status Species Inventory *(CA State Parks: Locke)*
- Study design and lead bird surveyor - Placer County Vernal Pool Study *(Placer County: throughout Placer County)*
- Surveyor - Willow flycatcher habitat mapping *(USFS: Plumas NF)*
- Independent surveyor - Tolay Creek, Cullinan Ranch, and Guadacanal Village restoration projects *(Ducks Unlimited/USGS: San Pablo Bay)*
- Study design and Lead Investigator - Bird use of restored wetlands research *(Pennsylvania Game Commission: throughout Pennsylvania)*
- Study design and surveyor - Baseline inventory of bird species at a 400-acre site in Napa County *(HCV Associates: Napa)*
- Surveyor - Baseline inventory of bird abundance following diesel spill *(LFR Levine-Fricke: Suisun Bay)*
- Study design and lead bird surveyor - Green Valley Creek Riparian Restoration Site *(City of Fairfield: Fairfield, CA)*
- Surveyor - Burrowing owl relocation and monitoring *(US Navy: Dixon, CA)*
- Surveyor - Pre-construction raptor and burrowing owl surveys *(various clients and locations)*
- Surveyor - Backcountry bird inventory *(National Park Service: Eagle, Alaska)*
- Lead surveyor - Tidal salt marsh bird surveys (*Point Reyes Bird Observatory: throughout Bay Area*)
- Surveyor – Pre-construction surveys for nesting birds (*various clients and locations)*

Amphibian

- Crew Leader - Red-legged frog, foothill yellow-legged frog, and mountain yellow-legged frog surveys *(USFS: Plumas NF)*

- Surveyor - Foothill yellow-legged frog surveys *(PG&E: North Fork Feather River)*
- Surveyor - Mountain yellow-legged frog surveys *(El Dorado Irrigation District: Desolation Wilderness)*
- Crew Leader - Bullfrog eradication *(Trout Unlimited: Cleveland NF)*

Fish and Aquatic Resources

- Surveyor - Hardhead minnow and other fish surveys *(USFS: Plumas NF)*
- Surveyor - Weber Creek aquatic habitat mapping (*El Dorado Irrigation District: Placerville, CA*)
- Surveyor - Green Valley Creek aquatic habitat mapping *(City of Fairfield: Fairfield, CA)*
- GPS Specialist - Salmonid spawning habitat mapping *(CDFG: Sacramento River)*
- Surveyor - Fish composition and abundance study (*PG&E: Upper North Fork Feather River and Lake Almanor*)
- Crew Leader - Surveys of steelhead abundance and habitat use *(CA Coastal Conservancy: Gualala River estuary)*
- Crew Leader - Exotic species identification and eradication *(Trout Unlimited: Cleveland NF)*

Mammals

- Principal Investigator – Peninsular bighorn sheep resource use and behavior study (*California State Parks: Freeman Properties*)
- Scientific Advisor –Study on red panda occupancy and abundance in eastern Nepal *(The Red Panda Network: CA and Nepal)*
- Surveyor - Forest carnivore surveys *(University of CA: Tahoe NF)*
- Surveyor - Relocation and monitoring of salt marsh harvest mice and other small mammals *(US Navy: Skagg's Island, CA)*
- Surveyor – Surveys for Monterey dusky-footed woodrat. Relocation of woodrat houses (*Touré Associates: Prunedale*)

Natural Resource Investigations / Multiple Species Studies

- Scientific Review Team Member – Member of the science review team assessing the effectiveness of the US Forest Service's implementation of the Herger-Feinstein Quincy Library Group Act.
- Lead Consultant - Baseline biological resource assessments and habitat mapping for CDF management units *(CDF: San Diego, San Bernardino, and Riverside Counties)*

- Biological Resources Expert – Peer review of CEQA/NEPA documents (*Adams Broadwell Joseph & Cardoza: California)*
- Lead Consultant - Pre- and post-harvest biological resource assessments of tree removal sites *(SDG&E: San Diego County)*
- Crew Leader - T&E species habitat evaluations for Biological Assessment in support of a steelhead restoration plan *(Trout Unlimited: Cleveland NF)*
- Lead Investigator - Resource Management Study and Plan for Mather Lake Regional Park *(County of Sacramento: Sacramento, CA)*
- Lead Investigator - Biological Resources Assessment for 1,070-acre Alfaro Ranch property *(Yuba County, CA)*
- Lead Investigator - Wildlife Strike Hazard Management Plan *(HCV Associates: Napa)*
- Lead Investigator - Del Rio Hills Biological Resource Assessment *(The Wyro Company: Rio Vista, CA)*
- Lead Investigator – Ion Communities project sites (*Ion Communities: Riverside and San Bernardino Counties*)
- Surveyor – Tahoe Pilot Project: Validation of California's Wildlife Habitat Relationships (CWHR) Model *(University of California: Tahoe NF)*

Forestry

Mr. Cashen has five years of experience working as a consulting forester on projects throughout California. Mr. Cashen has consulted with landowners and timber operators on forest management practices; and he has worked on a variety of forestry tasks including selective tree marking, forest inventory, harvest layout, erosion control, and supervision of logging operations. Mr. Cashen's experience with many different natural resources enable him to provide a holistic approach to forest management, rather than just management of timber resources.

REPRESENTATIVE EXPERIENCE

- Lead Consultant - CalFire fuels treatment projects *(SD and Riverside Counties)*
- Lead Consultant and supervisor of harvest activities – San Diego Gas and Electric Bark Beetle Tree Removal Project *(San Diego)*
- Crew Leader - Hillslope Monitoring Program *(CalFire: throughout California)*
- Consulting Forester – Forest inventories and timber harvest projects *(various clients throughout California)*

Grant Writing and Technical Editing

Mr. Cashen has prepared and submitted over 50 proposals and grant applications. Many of the projects listed herein were acquired through proposals he wrote. Mr. Cashen's clients and colleagues have recognized his strong scientific writing skills and ability to generate technically superior proposal packages. Consequently, he routinely prepares funding applications and conducts technical editing for various clients.

PERMITS

U.S. Fish and Wildlife Service Section 10(a)(1)(A) Recovery Permit for the Peninsular bighorn sheep

CA Department of Fish and Game Scientific Collecting Permit

PROFESSIONAL ORGANIZATIONS / ASSOCIATIONS

The Wildlife Society (Conservation Affairs Committee member)

Cal Alumni Foresters

Mt. Diablo Audubon Society

OTHER AFFILIATIONS

Scientific Advisor and Grant Writer – *The Red Panda Network*

Scientific Advisor – *Mt. Diablo Audubon Society*

Grant Writer – *American Conservation Experience*

Scientific Advisor and Land Committee Member – *Save Mt. Diablo*

TEACHING EXPERIENCE

Instructor: Wildlife Management - The Pennsylvania State University, 1998

Teaching Assistant: Ornithology - The Pennsylvania State University, 1996-1997

EXHIBIT G

Executive Summary

Natural gas plays a key role in our nation's clean energy future. The United States has vast reserves of natural gas that are commercially viable as a result of advances in horizontal drilling and hydraulic fracturing technologies, which enable greater access to gas in rock formations deep underground. These advances have spurred a significant increase in the production of both natural gas and oil across the country.

Responsible development of America's oil and gas resources offers important economic, energy security, and environmental benefits. However, as the use of hydraulic fracturing has increased, so have concerns about its potential human health and environmental impacts, especially for drinking water. In response to public concern, the US House of Representatives requested that the US Environmental Protection Agency (EPA) conduct scientific research to examine the relationship between hydraulic fracturing and drinking water resources (USHR, 2009).

In 2011, the EPA began research under its *Plan to Study the Potential Impacts of Hydraulic Fracturing on Drinking Water Resources.* The purpose of the study is to assess the potential impacts of hydraulic fracturing on drinking water resources, if any, and to identify the driving factors that may affect the severity and frequency of such impacts. Scientists are focusing primarily on hydraulic fracturing of shale formations to extract natural gas, with some study of other oil- and gas-producing formations, including tight sands, and coalbeds. The EPA has designed the scope of the research around five stages of the hydraulic fracturing water cycle. Each stage of the cycle is associated with a primary research question:

- Water acquisition: What are the possible impacts of large volume water withdrawals from ground and surface waters on drinking water resources?
- Chemical mixing: What are the possible impacts of hydraulic fracturing fluid surface spills on or near well pads on drinking water resources?
- Well injection: What are the possible impacts of the injection and fracturing process on drinking water resources?
- Flowback and produced water: What are the possible impacts of flowback and produced water (collectively referred to as "hydraulic fracturing wastewater") surface spills on or near well pads on drinking water resources?
- Wastewater treatment and waste disposal: What are the possible impacts of inadequate treatment of hydraulic fracturing wastewater on drinking water resources?

This report describes 18 research projects underway to answer these research questions and presents the progress made as of September 2012 for each of the projects. Information presented as part of this report cannot be used to draw conclusions about potential impacts to drinking water resources from hydraulic fracturing. The research projects are organized according to five different types of research activities: analysis of existing data, scenario evaluations, laboratory studies, toxicity assessments, and case studies.

Analysis of Existing Data

Data from multiple sources have been obtained for review and analysis. Many of the data come directly from the oil and gas industry and states with high levels of oil and gas activity. Information on the chemicals and practices used in hydraulic fracturing has been collected from nine companies that hydraulically fractured a total of 24,925 wells between September 2009 and October 2010. Additional data on chemicals and water use for hydraulic fracturing are being pulled from over 12,000 well-specific chemical disclosures in FracFocus, a national hydraulic fracturing chemical registry operated by the Ground Water Protection Council and the Interstate Oil and Gas Compact Commission. Well construction and hydraulic fracturing records provided by well operators are being reviewed for 333 oil and gas wells across the United States; data within these records are being scrutinized to assess the effectiveness of current well construction practices at containing gases and liquids before, during, and after hydraulic fracturing.

Data on causes and volumes of spills of hydraulic fracturing fluids and wastewater are being collected and reviewed from state spill databases in Colorado, New Mexico, and Pennsylvania. Similar information is being collected from the National Response Center national database of oil and chemical spills.

In addition, the EPA is reviewing scientific literature relevant to the research questions posed in this study. A *Federal Register* notice was published on November 9, 2012, requesting relevant, peer-reviewed data and published reports, including information on advances in industry practices and technologies. This body of literature will be synthesized with results from the other research projects to create a report of results.

Scenario Evaluations

Computer models are being used to identify conditions that may lead to impacts on drinking water resources from hydraulic fracturing. The EPA has identified hypothetical, but realistic, scenarios pertaining to the water acquisition, well injection, and wastewater treatment and waste disposal stages of the water cycle. Potential impacts to drinking water sources from withdrawing large volumes of water in semi-arid and humid river basins—the Upper Colorado River Basin in the west and the Susquehanna River Basin in the east—are being compared and assessed.

Additionally, complex computer models are being used to explore the possibility of subsurface gas and fluid migration from deep shale formations to overlying aquifers in six different scenarios. These scenarios include poor well construction and hydraulic communication via fractures (natural and created) and nearby existing wells. As a first step, the subsurface migration simulations will examine realistic scenarios to assess the conditions necessary for hydraulic communication rather than the probability of migration occurring.

In a separate research project, concentrations of bromide and radium at public water supply intakes located downstream from wastewater treatment facilities discharging treated hydraulic fracturing wastewater are being estimated using surface water transport models.

Laboratory Studies

Laboratory studies are largely focused on identifying potential impacts of inadequately treating hydraulic fracturing wastewater and discharging it to rivers. Experiments are being designed to test how well common wastewater treatment processes remove selected contaminants from hydraulic fracturing wastewater, including radium and other metals. Other experiments are assessing whether or not hydraulic fracturing wastewater may contribute to the formation of disinfection byproducts during common drinking water treatment processes, with particular focus on the formation of brominated disinfection byproducts, which have significant health concerns at high exposure levels.

Samples of raw hydraulic fracturing wastewater, treated wastewater, and water from rivers receiving treated hydraulic fracturing wastewater have been collected for source apportionment studies. Results from laboratory analyses of these samples are being used to develop a method for determining if treated hydraulic fracturing wastewater is contributing to high chloride and bromide levels at downstream public water supplies.

Finally, existing analytical methods for selected chemicals are being tested, modified, and verified for use in this study and by others, as needed. Methods are being modified in cases where standard methods do not exist for the low-level detection of chemicals of interest or for use in the complex matrices associated with hydraulic fracturing wastewater. Analytical methods are currently being tested and modified for several classes of chemicals, including glycols, acrylamides, ethoxylated alcohols, disinfection byproducts, radionuclides, and inorganic chemicals.

Toxicity Assessments

The EPA has identified chemicals reportedly used in hydraulic fracturing fluids from 2005 to 2011 and chemicals found in flowback and produced water. Appendix A contains tables with over 1,000 of these chemicals identified. Chemical, physical, and toxicological properties are being compiled for chemicals with known chemical structures. Existing models are being used to estimate properties in cases where information is lacking. At this time, the EPA has not made any judgment about the extent of exposure to these chemicals when used in hydraulic fracturing fluids or found in hydraulic fracturing wastewater, or their potential impacts on drinking water resources.

Case Studies

Two rounds of sampling at five case study locations in Colorado, North Dakota, Pennsylvania, and Texas have been completed. In total, water samples have been collected from over 70 domestic water wells, 15 monitoring wells, and 13 surface water sources, among others. This research will help to identify the source of any contamination that may have occurred.

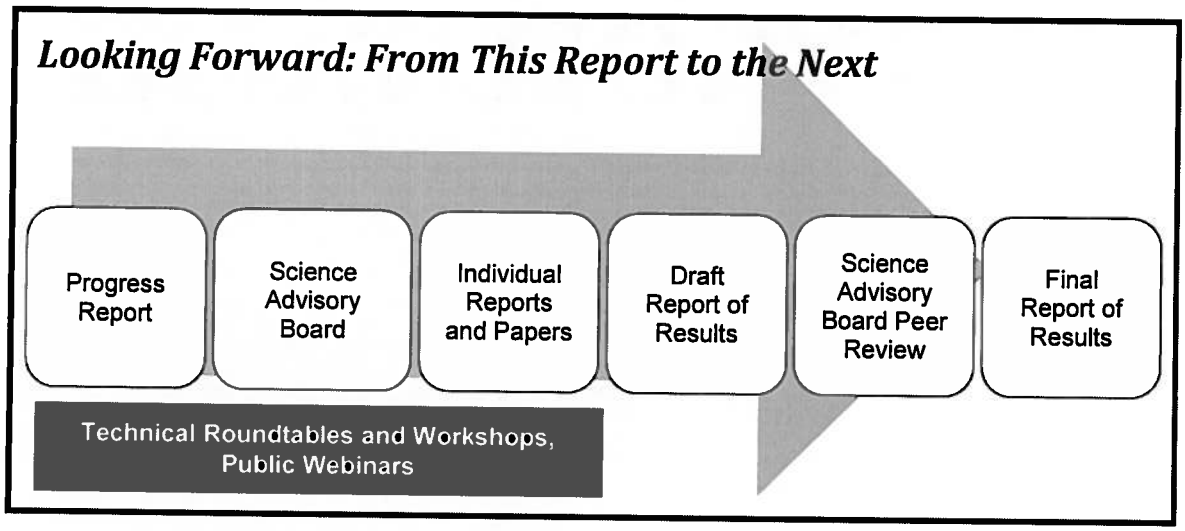
The EPA continues to work with industry partners to begin research activities at potential prospective case study locations, which involve sites where the research will begin before well construction. This will allow the EPA to collect baseline water quality data in the area. Water quality will be monitored for any changes throughout drilling, injection of fracturing fluids, flowback, and production. Samples of flowback and produced water will be used for other parts of the study, such as assessing the efficacy of wastewater treatment processes at removing contaminants in hydraulic fracturing wastewater.

Invigorating the Research Study Through Consultation and Peer Review

The EPA is committed to conducting a study that uses the best available science, independent sources of information, and a transparent, peer-reviewed process that will ensure the validity and accuracy of the results. The agency is working in consultation with other federal agencies, state and interstate regulatory agencies, industry, non-governmental organizations, and others in the private and public sector. In addition to workshops held in 2011, stakeholders and technical experts are being engaged through technical roundtables and workshops, with the first set of roundtables held November 14–16, 2012. These activities will provide the EPA with ongoing access to a broad range of expertise and data, timely and constructive technical feedback, and updates on changes in industry practices and technologies relevant to the study. Technical roundtables and workshops will be followed by webinars for the general public and posting of summaries on the study's website. Increased stakeholder engagement will also allow the EPA to educate and inform the public of the study's goals, design, and progress.

To ensure scientifically defensible results, each research project is subjected to quality assurance and peer review activities. Specific quality assurance activities performed by the EPA make sure that the agency's environmental data are of sufficient quantity and quality to support the data's intended use. Research products, such as papers or reports, will be subjected to both internal and external peer review before publication, which make certain that the data are used appropriately. Published results from the research projects will be synthesized in a report of results that will inform the research questions associated with each stage of the hydraulic fracturing water cycle. The EPA has designated the report of results as a "Highly Influential Scientific Assessment," which will undergo peer review by the EPA's Science Advisory Board, an independent and external federal advisory committee that conducts peer reviews of significant EPA research products and activities. The EPA will seek input from individual members of an *ad hoc* expert panel convened under the auspices of the EPA Science Advisory Board. The EPA will consider feedback from the individual experts in the development of the report of results.

Ultimately, the results of this study are expected to inform the public and provide decision-makers at all levels with high-quality scientific knowledge that can be used in decision-making processes.



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TESTIMONY OF
CYNTHIA C. DOUGHERTY
DIRECTOR,
OFFICE OF GROUND WATER AND DRINKING WATER
OFFICE OF WATER
U.S. ENVIRONMENTAL PROTECTION AGENCY
BEFORE THE
SUBCOMMITTEE ON WATER AND POWER
COMMITTEE ON ENERGY AND NATURAL RESOURCES
UNITED STATES SENATE

October 20, 2011

Good afternoon, Madame Chairman, Ranking Member Lee, and Members of the Subcommittee. I am pleased to be here today to discuss the EPA's role in ensuring that public health and water quality are protected during natural gas extraction and production activities.

Natural gas can enhance our domestic energy options, reduce our dependence on foreign supplies, and serve as a bridge fuel to renewable energy sources. If produced responsibly, natural gas has the potential to improve air quality, stabilize energy prices, and provide greater certainty about future energy reserves.

While natural gas holds promise for an increased role in our energy future, the EPA believes it is imperative that we access this resource in a way that protects drinking water sources and surface waters.

As we listened to citizens at public meetings across the country last year, we heard the concerns many have for their families, their communities, and their water resources. We also heard from citizens who expressed how much their communities sorely need the income that could be gained from natural gas production.

We believe that this important resource can be – and must be – extracted responsibly, in a way that secures its promise for the benefit of all. If improperly managed, natural gas extraction and production, including hydraulic fracturing, may potentially result in impacts to public health or our water resources. If we look at water across the entire shale gas extraction process, from water acquisition to wastewater treatment and disposal, some of the impacts on our water resources may include:

- stress on surface water and its uses and groundwater supplies from the withdrawal of large volumes of water used in drilling and hydraulic fracturing;
- potential contamination of drinking water aquifers resulting from faulty well construction and completion;
- compromised water quality due to challenges with managing and disposing of contaminated wastewaters, known as flowback and produced water, where contaminants could include organic chemicals, metals, salts and radionuclides

The EPA has an important role to play in protecting water resources and in working with federal and state government partners to manage the benefits and risks of shale gas production. We must effectively address the potential consequences of shale gas development on water resources using the best science and technology. To this end, we are working in the following areas and under the following authorities, among others, with stakeholders, including other federal and state agencies, the oil and gas industry, and the public health community, to evaluate and address the potential public health and water quality issues related to shale gas extraction. These actions are important pieces of the Administration's broader effort to ensure that natural gas production occurs in a safe and responsible manner, as laid out in the President's Blueprint for a Secure Energy Future. They are also consistent with the Secretary of Energy Advisory Board's recently released recommendations on steps to support the safe development of natural gas resources.

Research

At the direction of Congress, the EPA launched a study last year to better understand the potential impacts of hydraulic fracturing on drinking water resources. As part of this study, the EPA has engaged thousands of Americans across the country who currently live in areas where hydraulic fracturing is taking place. When complete, this peer-reviewed research study will help us better understand potential impacts of hydraulic fracturing on drinking water resources and factors that may lead to human exposure and risks, while reducing scientific uncertainties about environmental impacts from those processes.

As part of this effort, the EPA has used information gathered from oil and gas companies conducting hydraulic fracturing and from the many stakeholder outreach meetings the EPA held during development of the study plan. The draft study plan was recently reviewed by the EPA's Science Advisory Board, is in the last stages of being finalized, and is expected to be released soon. The EPA plans to release two reports, one in 2012 that will summarize existing data, intermediate progress regarding retrospective case studies, scenario modeling and laboratory studies; and one in 2014 that will provide additional scientific results on these topics and report on prospective case studies and toxicological analyses.

Examples of Authority to Protect Water Resources

While Congress specifically exempted selected oil and gas production activities from several environmental laws, a number of environmental protections continue to apply. The Safe Drinking Water Act (SDWA)'s Underground Injection Control (UIC) program and Sections 301(b) and 402(a) of the Clean Water Act (CWA) are two examples of laws the states and EPA use to regulate certain oil and gas

production activities to protect public health and water quality. For example, the Energy Policy Act of 2005 contains an exclusion from the SDWA UIC program's permitting requirements for hydraulic fracturing for oil and gas, but this exclusion does not extend to oil and gas production activities when diesel fuels are used in fracturing fluids. The SDWA also regulates underground injection of flowback and produced water. The EPA and authorized states have the authority to regulate waste waters from oil and gas wells under Sections 301(b) and 402(a) of the CWA when they are discharged into publicly owned treatment works (POTWs) and surface waters. Under these two examples of authorities, the EPA has a number of activities underway, which I would like to outline for you.

Examples of Activities to Protect Water Resources

Under the CWA and SDWA, the EPA works with states to ensure that gas extraction is carried out consistent with CWA and SDWA regulations to protect surface water and drinking water. This year, the EPA produced a frequently asked questions (FAQ) document to assist state and federal permitting authorities within the Marcellus Shale region in addressing treatment and disposal of wastewater from shale gas extraction.[1] The document covers oil and gas extraction, centralized waste treatment, acceptance and notification requirements for publicly owned treatment works, pretreatment, and storm water. The FAQs have assisted the EPA and state personnel as we have worked with the regulated community to address shale gas extraction wastewater. In addition, the EPA is developing guidance to help states address water quality issues related to Centralized Waste Treatment Facilities or POTWs that accept oil and gas wastewater. As part of its effluent guidelines planning process under CWA section 304(m), the EPA is considering whether to initiate a rulemaking to revise these regulations to address natural gas extraction flowback waters.

[1] This document is available at http://cfpub.epa.gov/npdes/hydrofracturing.cfm

Under SDWA's UIC program, the EPA is working expeditiously to ensure the SDWA programmatic requirements related to hydraulic fracturing when using diesel fuels are implemented appropriately. The EPA is developing guidance to provide information to the states and regulated community on permitting wells that inject diesel fuels during hydraulic fracturing. With regard to flowback and produced water, we are coordinating with our state and tribal co-regulators to ensure proper management of flowback and produced water disposed of via underground injection.

Conclusion

In conclusion, the EPA is committed to using its authorities, consistent with the law and best available science, to protect communities across the nation from impacts to water quality and public health associated with natural gas production activities. Where we know problems exist, the EPA will not hesitate to protect Americans whose health may be at risk.

We remain committed to working with state officials, who are on the front lines of protecting water resources and regulating natural gas production activities. By helping manage environmental impacts and addressing public concerns, natural gas production can proceed in a responsible manner, which protects public health and enhances our domestic energy options. We believe that as a Nation, we can provide for the safe and responsible development of this significant domestic energy resource whose use brings a range of other important national security, environmental and climate benefits.

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THE HILL

E² Wire
THE HILL'S Energy & Environment Blog

Pollutants linked to 'fracking' found in Wyoming groundwater

By Zack Colman - 09/27/12 03:10 PM ET

Chemicals linked to hydraulic fracturing, or "fracking," have been found again in the groundwater of a town in Wyoming that has become a flashpoint in the debate over the drilling practice.

A U.S. Geological Survey (USGS) report found traces of methane, ethane and phenol in a monitoring well in rural Pavillion, Wyo., where residents say fracking has contaminated their drinking water.

Pavillion was thrust to the forefront of the fracking debate in December of 2011, when the Environmental Protection Agency (EPA) **reported** finding groundwater contaminants in two wells there. That report, which drew **harsh criticism** from the natural-gas industry, represented the first time the U.S. government had made a connection between fracking and groundwater pollution.

Alisha Johnson, a spokeswoman with the EPA, told The Hill that the USGS findings are "generally consistent" with EPA's earlier tests.

But a natural-gas industry group questioned the assertion that the USGS study matched the EPA's earlier tests, noting USGS did not test one of the two monitoring wells because the water levels were too low. In March, the Bureau of Land Management issued a report warning that a small sample size, such as the one used by EPA, could create statistical bias in the groundwater samples.

Fracking is a process that injects a high-pressure mixture of water, sand and chemicals into tight rock formations to unlock natural gas. The practice has been credited with reenergizing the domestic gas industry by unlocking hard-to-reach gas deposits.

The natural-gas industry has said fracking is safe, and says studies linking it to groundwater contamination

Comment Letter I14

and seismic activity are false.

But environmentalists have opposed the practice and say it will have a devastating impact on water supplies. The test results in Wyoming are likely to reignite calls to halt fracking.

Steve Everley, a spokesman for natural-gas industry group Energy in Depth, said the USGS decision to disqualify one of the EPA's two Pavillion monitoring wells showed EPA's original analysis was faulty.

Everley said the new findings are better paired with those of the Bureau of Land Management, which told EPA its monitoring wells were insufficient for testing groundwater. It suggested adding more monitoring wells to remove possible bias from the sampling.

"Perhaps the EPA should also listen to the Bureau of Land Management, which warned months ago that the results from one of EPA's wells couldn't be trusted, and advised the EPA to start over," Everley told The Hill on Thursday. "But I suppose that, like so many other facts about Pavillion, wouldn't generate the same sorts of headlines."

Congressional Democrats have warned about risks from fracking, and pressure on the Obama administration from Republicans and some Democrats to expedite natural-gas exports has added another element to the debate.

In a letter sent to Energy Secretary Steven Chu on Wednesday, **20 House Democrats urged the administration** to conduct an environmental impact statement for the effects of fracking before approving natural-gas export agreements or facilities.

The letter signatories expressed concern over U.S. Energy Information Administration (EIA) estimates that 63 percent of export demand would be met by increased production. Of that production, 85 percent of it would come from unconventional drilling, such as fracking.

Source:
http://thehill.com/blogs/e2-wire/e2-wire/259047-study-finds-groundwater-pollution-previously-linked-to-fracking

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EXHIBIT H

Comment Letter I14

Induced Seismicity

EGS: Interactive, Real-Time Map of Earthquakes at The Geysers

- Click on map icons (see legend) for more detailed earthquake information.
- Map data is being pulled successfully. This page is set to refresh data automatically every 10 minutes. The data currently being plotted was last updated on January 30, 2013 16:21:0

Filter Earthquake Data

Last 24 hours > 1.0 View 3D Seismic Distribution Plot Injection Wells

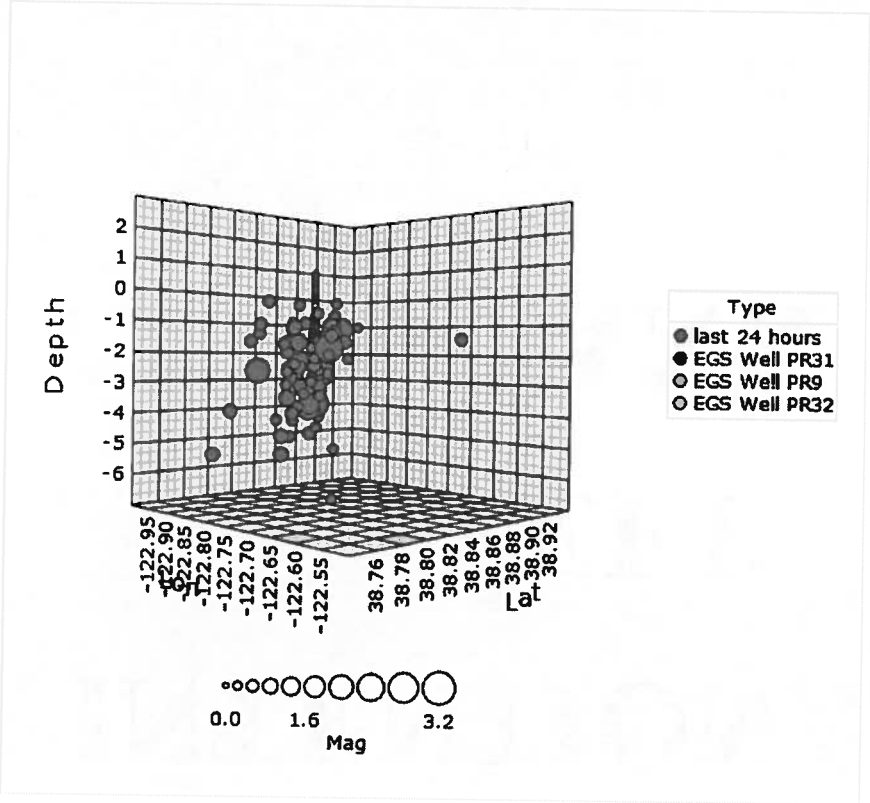
110 events greater than magnitude 1 during the last 24 hours.

Comment Letter I14

3D Seismic Distribution

The 3D scatterplot below shows the selection of earthquakes satisfying the filter criteria above. You can use your mouse to click on the map and rotate it and zoom in or out. Clicking on the bottom right corner of the plot will allow you to resize the window. The units of depth are kilometers and 0.0km is sea level.

Please note: The 3D visualization provided below is implemented using the canvasXpress library, which employs the html5 canvas element in order to simulate 3D without any special download or plugin. It will only work on the latest, most current browsers. If you are having problems viewing the plot and have an older browser, we highly recommend either upgrading your browser, or installing the latest version of a different browser (e.g., Mozilla Firefox or Google Chrome).



About the Geysers

The Geysers Geothermal Field in Northern California is the largest single geothermal field in the world (over 800 MW in 2009 and increasing as EGS activities carry forward). Seismicity related to production and injection has been observed since the 1970s and has been used as a general indicator of fluid paths and reservoir response. An increase in injection rates using wastewater from the areas of Santa Rosa and Lake County, CA, has recently raised concerns regarding the impact of injection-related seismicity on nearby communities.

- Why is water injection necessary at The Geysers?
- What is the history of seismicity at The Geysers?
- What is the risk of a large, damaging earthquake at The Geysers?

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The New York Times

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THE EAST
COMING SOON
WATCH TRAILER

December 12, 2009

Geothermal Project in California Is Shut Down

By JAMES GLANZ

The company in charge of a California project to extract vast amounts of renewable energy from deep, hot bedrock has removed its drill rig and informed federal officials that the government project will be abandoned.

The project by the company, AltaRock Energy, was the Obama administration's first major test of geothermal energy as a significant alternative to fossil fuels and the project was being financed with federal Department of Energy money at a site about 100 miles north of San Francisco called the Geysers.

But on Friday, the Energy Department said that AltaRock had given notice this week that "it will not be continuing work at the Geysers" as part of the agency's geothermal development program.

The project's apparent collapse comes a day after Swiss government officials permanently shut down a similar project in Basel, because of the damaging earthquakes it produced in 2006 and 2007. Taken together, the two setbacks could change the direction of the Obama administration's geothermal program, which had raised hopes that the earth's bedrock could be quickly tapped as a clean and almost limitless energy source.

The Energy Department referred other questions about the project's shutdown to AltaRock, a startup company based in Seattle. Reached by telephone, the company's chief operations officer, James T. Turner, confirmed that the rig had been removed but said he had not been informed of the notice that the company had given the government. Two other senior company officials did not respond to requests for comment, and it was unclear whether AltaRock might try to restart the project with private money.

In addition to a $6 million grant from the Energy Department, AltaRock had attracted some $30 million in venture capital from high-profile investors like Google, Khosla Ventures and Kleiner Perkins Caufield & Byers.

"Some of these startup companies got out in front and convinced some venture capitalists that they were very close to commercial deployment," said Daniel P. Schrag, a professor of geology and director of the Center for the Environment at Harvard University.

Geothermal enthusiasts asserted that drilling miles into hard rock, as required by the technique, could be done quickly and economically with small improvements in existing methods, Professor Schrag said. "What we've discovered is that it's harder to make those improvements than some people believed," he added.

In fact, AltaRock immediately ran into snags with its drilling, repeatedly snapping off bits in shallow formations called caprock. The project's safety was also under review at the Energy Department after

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federal officials said the company had not been entirely forthcoming about the earthquakes produced in Basel in making the case for the Geysers project.

The results of that review have not yet been announced, but the type of geothermal energy explored in Basel and at the Geysers requires fracturing the bedrock then circulating water through the cracks to produce steam. By its nature, fracturing creates earthquakes, though most of them are small.

On Friday, the Energy Department, which has put some $440 million into its geothermal program this year alone, said that despite the latest developments, it remained confident of the technology's long-term prospects. Many geothermal methods do not require drilling so deep or fracturing bedrock.

"The Department of Energy believes that geothermal energy holds enormous potential to heat our homes and power our economy while decreasing our carbon pollution," said Stephanie Mueller, a spokeswoman.

AltaRock has also received some $25 million in federal money for a project in Oregon, and some scientists speculated on Friday that after the spate of problems at the Geysers, the company wanted to focus on a new site.

But the company, whose project at the Geysers was located on land leased from the federal government by the Northern California Power Agency, has held information about its project tightly. Not even the power agency has been informed of AltaRock's ultimate intentions at the site, said Murray Grande, who is in charge of geothermal facilities for the agency.

"They just probably gave up, but we don't know," Mr. Grande said. "We have nothing official from them at all."

But a resident of the nearby town of Anderson Springs, which is already shaken by quakes generated by less ambitious geothermal projects, reacted with jubilation when told it appeared the new project was ending.

"How I feel is beyond anything that words can express," said the resident, Jacque Felber, who added that an unnerving quake had rattled her property the night before. "I'm just so relieved, because with this going on, I'm afraid one of these days it's going to knock my house off the hill."

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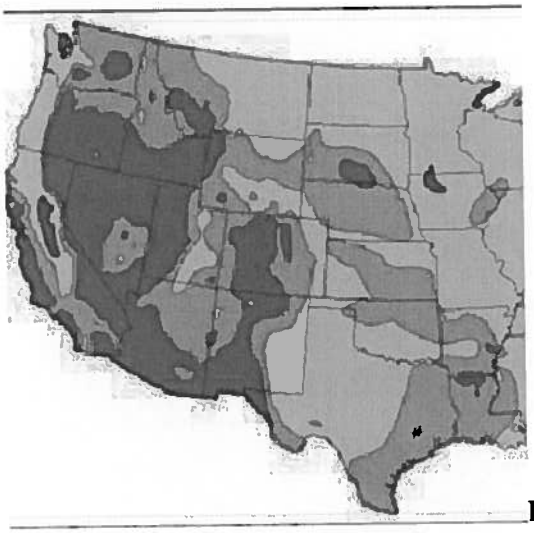
How Does Geothermal Drilling Trigger Earthquakes?

People living near a geothermal drilling project in fault-riddled northern California are worried about more earthquakes after a similar project triggered a major jolt in Switzerland. A seismologist explains the forces at work

By Katherine Harmon



DRILLING HOT SPOTS: This map shows the estimated temperature of the ground 3.7 miles (6 kilometers) under the surface. Red is 392 degrees Fahrenheit (200 Celsius). Image: WIKIMEDIA COMMONS/US DEPARTMENT OF ENERGY

Despite the promise of cheap, clean power, geothermal energy development may be on shaky ground. There have been rumblings from residents and scientists alike that drilling deep to tap naturally occurring heat could cause bigger earthquakes.

Already on edge about temblors, northern California locals are eying an expansive new geothermal project proposed by a company called AltaRock that's going to be boring down more than two miles (3.2 kilometers). The area near the town of Anderson Springs—about 90 miles (150 kilometers) north of San Francisco—is home to natural geothermal vents (nicknamed The Geysers by early visitors who saw the steam vents there) and has been exploited for its natural energy-generating capacity for the better part of the last century. Starting in the 1970s, as technology improved, engineers started to crank up the production levels. Small earthquakes began shortly thereafter.

Just a few years ago, a now-infamous geothermal project in Basel, Switzerland, which drilled three miles (4.8 kilometers) into Earth's crust, set off a magnitude 3.4 earthquake, rocking the town and shutting the operation down entirely, *The New York Times* recalled recently.

Drilling has even been fingered as the cause of a massive 2006 mud volcano in Java, which displaced more than 30,000 people after a gas exploration project went awry. "We are more certain than ever that the Lusi mud volcano is an unnatural disaster," Richard Davies of the Center for Research into Earth Energy Systems at Durham University in England said in a statement after investigating the incident.

The U.S. Department of Energy has already chipped in $36 million for AltaRock's project, and in an effort to drive down the price of renewable energy Google has anted up $6.25 million, the *Times* reported.

But will these deep holes—and deep-pocketed investors—trigger the next big one? To find out, we spoke with U.S. Geological Survey Earthquake Hazards Team seismologist David Oppenheimer, who is based in Menlo Park, Calif., just a couple hours south of the area.

How does geothermal drilling work?
The traditional geothermal drilling process has been to drill into the sandstone that has water in its pore spaces. When they drill into the rock, there's a surge of steam—just like popping a lid off a soda bottle—then the steam rises and spins a turbine.

At The Geysers, they have been condensing 25 percent of the steam and introducing it back into the reservoir to keep the water levels up.

About a million years ago, there was a magmatic intrusion (protovolcano) that didn't make it to the surface. Under the surface is a rock called felsite—you can think of it like granite; it's the heat source for the sandstone.

The new project is going to exploit the felsite directly. But there's no water in the felsite, so they drill, then they pipe water under strong pressure and flow rate, to fracture the rock. They'll be using earthquake-monitoring equipment and will send cameras down the hole to see which direction the fractures were occurring. Then they drill a second hole to intersect the new fracture.

So the potential is to extract much more heat, but you have to create your own fractures and you have to introduce water.

If the new fractures are triggering earthquakes, how do they control them?
What they need to do, from an engineering perspective, is keep the size of the fractures small. So they will control the [water] flow rates and pressures to make sure it doesn't become a runaway earthquake.

We've been monitoring [The Geysers] since 1975. All the earthquakes we see there are [human]

induced. When they move production into a new area, earthquakes start there, and when they stop production, the earthquakes stop.

They've been inducing earthquakes since the 1960s, and the largest has been less than a [magnitude] 4.5. Earthquakes are occurring in many, many fractures. So that's very different than if you go south to the Bay Area with the San Andreas Fault. For earthquakes larger than 6.0 to happen, you need a big fault. Therefore, it's unlikely they'll intersect a large fault and trigger a larger earthquake.

The threshold goal for the earthquakes is 2.0 or lower. They don't want a repeat of Basel, Switzerland.

How is geothermal drilling different from other energy projects like natural gas or oil?
There are some similarities to oil fields. In oil fields for secondary recovery, they inject water into the ground to try to force more oil out. Frequently, though, oil fields aren't located in tectonically active areas.

So why don't they do geothermal drilling somewhere that isn't prone to earthquakes?
In Texas, you don't have the heat source. If you drill all the way to the outer core, there will be molten rock. But nobody knows how to do that. In tectonically active areas, you have more heat sources (from failed volcanoes and the like).

There is some geothermal potential all over the country if we're talking about geothermal for heating—but not necessarily for spinning large turbines.

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Action 1.1: All policies and actions applicable to geothermal development generally that do not conflict with policies specifically applicable to deer migration zones shall be enforced by appropriate permit conditions.

Action 1.2: Development may be prevented in any part of a deer migration zone upon a finding that it will interfere with adopted regulations of the California Department of Fish and Game and the goals of the CDFG deer herd management plans.

Action 1.3: The County shall cooperate with the CDFG in devising conditions meant to carry out this policy.

Objective F
Geothermal exploration and development projects shall be carried out with the fewest visual intrusions reasonably possible.

Policy 1: Permit conditions shall require compliance with all applicable policies and actions of the Conservation/Open Space Element.

Objective G
The permit holder shall establish procedures that ensure that neither geothermal exploration nor development will cause violations of state or federal ambient air quality standards or the rules and regulations of the Great Basin Unified Air Pollution Control District (GBUAPCD).

Policy 1: Permit conditions shall require compliance with all requirements of the regional air pollution control district, and with all other applicable provisions of the Conservation/Open Space Element.

Action 1.1: Air quality shall be monitored by a representative of the MCEDD, or the regional air pollution control district with jurisdiction. The costs of such monitoring shall be funded by the permit holder or project operator.

Objective H
Mono County shall establish procedures that assure that neither geothermal exploration nor development creates unacceptable noise.

Policy 1: Project conditions shall require compliance with all applicable provisions of the Noise Element and the County Noise Ordinance.

GOAL 2: Permit the productive and beneficial development of alternative energy sources, including geothermal resources, consistent with the objectives of Goal I and national and local interests.

Objective A
Provided that the environment is protected in the manner required by the policies and actions of Goal I of this section of the Conservation/Open Space Element, County policy shall ensure the orderly and sound economic development of geothermal resources under the appropriate circumstances.