

Health Assessment Document for Diesel Emissions

NOTICE

THIS DOCUMENT IS A PRELIMINARY DRAFT. It has not been formally released by the Environmental Protection Agency and should not at this stage be construed to represent Agency policy. It is being circulated for comment on its technical accuracy and policy implications.

National Center for Environmental Assessment-Washington Office
Office of Research and Development
U.S. Environmental Protection Agency
Washington, DC

DISCLAIMER

This document is a draft for review purposes only and does not constitute U.S. Environmental Protection Agency policy. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

CONTENTS

1. EXECUTIVE SUMMARY	1-1
2. DIESEL EMISSIONS CHARACTERIZATION, ATMOSPHERIC TRANSFORMATION, AND EXPOSURES	2-1
2.1. INTRODUCTION	2-1
2.2. PRIMARY DIESEL EMISSIONS	2-3
2.2.1. Diesel Combustion and Formation of Primary Emissions	2-3
2.2.2. Diesel Emission Standards and Emission Trends Inventory	2-5
2.2.3. Engine Technology Description and Chronology	2-8
2.2.3.1. Injection Rate	2-9
2.2.3.2. Turbocharging, Charge-Air Cooling, and Electronic Controls	2-10
2.2.3.3. Indirect and Direct Injection High-Speed Diesel Engines	2-13
2.2.3.4. Two-Stroke and 4-Stroke High-Speed Diesel Engines	2-14
2.2.3.5. Near-Term Diesel Emission Reduction Technologies	2-16
2.2.3.6. Future (2004+) Diesel Emission Reduction Technologies	2-18
2.2.4. History of Dieselization	2-24
2.2.4.1. Dieselization of the On-Road Fleet	2-24
2.2.4.2. Dieselization of Railroad Locomotive Engines	2-30
2.2.4.3. Historical Trends in Diesel Fuel Use and Impact of Fuel Properties on Emissions	2-31
2.2.5. Chronological Assessment of Emission Factors	2-35
2.2.5.1. On-Road Vehicles	2-35
2.2.5.2. Locomotives	2-44
2.2.6. Physical and Chemical Composition of Particles	2-44
2.2.6.1. SOF and Elemental Carbon Content of Particles	2-47
2.2.6.2. PAHs and Nitro-PAH Emissions	2-51
2.2.6.3. Aldehyde Emissions	2-56
2.2.6.4. Dioxin and Furan Emissions	2-56
2.2.6.5. Particle Size	2-56
2.3. ATMOSPHERIC TRANSFORMATION OF DIESEL EXHAUST	2-60
2.3.1. Gas-Phase Diesel Exhaust	2-61
2.3.1.1. Organic Compounds	2-62
2.3.1.2. Inorganic Compounds	2-64
2.3.1.3. Atmospheric Transport of Gas-Phase Diesel Exhaust	2-65
2.3.2. Particle-Phase Diesel Exhaust	2-65
2.3.2.1. Particle-Associated PAH Photooxidation	2-67
2.3.2.2. Particle-Associated PAH Nitration	2-67
2.3.2.3. Particle-Associated PAH Ozonolysis	2-68
2.3.2.4. Atmospheric Transport of Diesel Exhaust Particle Matter	2-69
2.3.3. Diesel Exhaust Aging	2-69
2.4. AMBIENT DIESEL EXHAUST CONCENTRATIONS AND EXPOSURES	2-70
2.4.1. Diesel Exhaust Gases in the Ambient Atmosphere	2-70

CONTENTS (continued)

2.4.2.	Ambient Concentrations of Diesel PM	2-71
2.4.2.1.	Receptor Modeling Estimates of Diesel PM	2-71
2.4.2.2.	Elemental Carbon Surrogate for Diesel PM	2-74
2.4.2.3.	Dispersion Modeling Results	2-77
2.4.3.	Exposures to Diesel PM	2-78
2.4.3.1.	Exposure Measurements	2-79
2.4.3.2.	Modeling Exposures to Diesel PM	2-80
2.4.4.	Ambient Diesel PM Summary	2-84
2.5.	SUMMARY	2-86
2.6.	REFERENCES	2-88
3.	DOSIMETRY OF DIESEL EXHAUST PARTICLES IN THE RESPIRATORY TRACT	3-1
3.1.	INTRODUCTION	3-1
3.2.	CHARACTERISTICS OF INHALED DPM AND RELATIONSHIP TO PM _{2.5}	3-1
3.3.	REGIONAL DEPOSITION OF INHALED DPM	3-2
3.3.1.	Deposition Mechanisms	3-3
3.3.1.1.	Biological Factors Modifying Deposition	3-4
3.3.2.	Particle Clearance and Translocation Mechanisms	3-7
3.3.2.1.	ET Region	3-8
3.3.2.2.	TB Region	3-8
3.3.2.3.	A Region	3-12
3.3.3.	Translocations of Particles to Extra-alveolar Macrophage Compartment Sites	3-19
3.3.3.1.	Clearance Kinetics	3-20
3.3.3.2.	Interspecies Patterns of Clearance	3-20
3.3.3.3.	Biological Factors Modifying Clearance	3-21
3.3.3.4.	Respiratory Tract Disease	3-21
3.4.	PARTICLE OVERLOAD	3-22
3.4.1.	Introduction	3-22
3.4.2.	Relevance to Humans	3-24
3.4.3.	Potential Mechanisms for an AM Sequestration Compartment for Particles During Particle Overload	3-26
3.5.	MODELING THE DISPOSITION OF PARTICLES IN THE RESPIRATORY TRACT	3-27
3.5.1.	Introduction	3-27
3.5.2.	Dosimetry Models for DPM	3-27
3.5.2.1.	Introduction	3-27
3.5.2.2.	Deposition Models	3-28
3.5.2.3.	Physiologically Based Models for Clearance	3-29
3.5.2.4.	Model Assumptions and Extrapolation to Humans	3-32
3.5.3.	Deposition of Organics	3-34
3.6.	BIOAVAILABILITY OF ORGANIC CONSTITUENTS PRESENT ON	

CONTENTS (continued)

DIESEL EXHAUST PARTICLES	3-34
3.6.1. In Vivo Studies	3-35
3.6.1.1. Laboratory Investigations	3-35
3.6.1.2. Studies in Occupationally Exposed Humans	3-36
3.6.2. In Vitro Studies	3-36
3.6.2.1. Extraction of Diesel Particle-Associated Organics By Biological Fluids	3-36
3.6.2.2. Extraction of Diesel Particle-Associated Organics by Lung Cells and Cellular Components	3-37
3.6.3. Modeling Studies	3-38
3.7. SUMMARY	3-39
3.8. REFERENCES	3-41
4. MUTAGENICITY OF DIESEL EXHAUST	4-1
4.1. GENE MUTATIONS	4-1
4.2. CHROMOSOME EFFECTS	4-4
4.3. OTHER GENOTOXIC EFFECTS	4-6
4.4. SUMMARY	4-6
4.5. REFERENCES	4-7
5. NONCANCER HEALTH EFFECTS OF DIESEL EXHAUST	5-1
5.1. HEALTH EFFECTS OF WHOLE DIESEL EXHAUST	5-1
5.1.1. Human Studies	5-1
5.1.1.1. Short-Term Exposures	5-1
5.1.1.2. Long-Term Exposures	5-11
5.1.2. Laboratory Animal Studies	5-15
5.1.2.1. Acute Exposures	5-15
5.1.2.2. Short-Term and Subchronic Exposures	5-21
5.1.2.3. Chronic Exposures	5-26
5.2. COMPARISON OF HEALTH EFFECTS OF FILTERED AND UNFILTERED DIESEL EXHAUST	5-78
5.3. INTERACTIVE EFFECTS OF DIESEL EXHAUST	5-82
5.4. COMPARATIVE RESPONSIVENESS AMONG SPECIES TO THE PULMONARY EFFECTS OF DIESEL EXHAUST	5-84
5.5. DOSE-RATE AND PARTICULATE CAUSATIVE ISSUES	5-85
5.6. SUMMARY AND DISCUSSION	5-89
5.6.1. Effects of Diesel Exhaust on Humans	5-89
5.6.2. Effects of Diesel Exhaust on Laboratory Animals	5-91
5.6.2.1. Effects on Survival and Growth	5-91
5.6.2.2. Effects on Pulmonary Function	5-92
5.6.2.3. Histopathological and Histochemical Effects	5-92
5.6.2.4. Effects on Airway Clearance	5-93
5.6.2.5. Neurological and Behavioral Effects	5-94

CONTENTS (continued)

5.6.2.6. Effects on Immunity and Allergenicity	5-94
5.6.2.7. Other Noncancerous Effects	5-94
5.6.3. Comparison of Filtered and Unfiltered Diesel Exhaust	5-94
5.6.4. Interactive Effects of Diesel Exhaust	5-95
5.6.5. Conclusions	5-95
5.7. REFERENCES	5-96
6. NONCANCER DOSE-RESPONSE EVALUATION: RfC DERIVATION	6-1
6.1. INTRODUCTION—BACKGROUND OF THE INHALATION RfC AND ORAL RfD	6-1
6.1.1. The Acceptable Daily Intake	6-1
6.1.2. Oral RfD and Inhalation RfC—Dose-Response Assessments Inclusive of Uncertainty Factors	6-1
6.1.3. UFs—Designation and Application	6-2
6.1.4. Animal-to-Human Extrapolation Factor in the RfC—A Human Equivalent Concentration	6-3
6.1.5. Basic Procedures for Derivation of an RfC—Identification of the Critical Effect, the Principal Study, Application of UF, and Assignment of Confidence Level	6-4
6.2. ISSUES IN DERIVATION OF THE DIESEL RfC	6-5
6.2.1. Chronic Noncancer Effects in Humans—Relevancy of Rodent Data	6-5
6.2.2. Pulmonary Pathology and Immunologic Effects as Critical Effects	6-5
6.2.3. Application of UFs	6-5
6.2.4. Relationship of DPM to Ambient Levels of PM _{2.5}	6-6
6.3. APPROACH FOR DERIVATION OF THE RfC FOR DIESEL ENGINE EMISSIONS	6-6
6.3.1. Consideration of Long-Term Inhalation Studies	6-6
6.3.2. Derivation of a HEC—Application of a Pharmacokinetic Model	6-6
6.4. CHOICE OF THE CRITICAL EFFECT—RATIONALE AND JUSTIFICATION	6-8
6.4.1. Mode-of-Action and Candidate Effects	6-8
6.4.2. Rationale and Justification	6-9
6.5. PRINCIPAL STUDIES FOR INHALATION RfC DERIVATION	6-10
6.6. SUPPORTING STUDIES FOR INHALATION RfC DERIVATION	6-13
6.6.1. Respiratory Tract Effects in Species Other Than the Rat	6-17
6.6.2. Application of the Benchmark Dose Approach to Derivation of the RfC	6-19
6.7. DERIVATION OF THE INHALATION RfC	6-20
6.7.1. The Effect Level—A NOAEL From a Chronic Inhalation Study	6-20
6.7.2. Application of UFs—Animal-to-Human and Sensitive Subgroups	6-21
6.7.3. Designation of Confidence Level	6-22
6.8. SUMMARY	6-22
6.9. REFERENCES	6-23

CONTENTS (continued)

7.	CARCINOGENICITY OF DIESEL EXHAUST	7-1
7.1.	INTRODUCTION	7-1
7.2	EPIDEMIOLOGIC STUDIES OF THE CARCINOGENICITY OF EXPOSURE TO DIESEL EXHAUST	7-2
7.2.1.	Cohort Studies	7-2
7.2.1.1.	Waller (1981): Trends in Lung Cancer in London in Relation to Exposure to Diesel Fumes	7-2
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	7-4
7.2.1.3.	Rushton et al. (1983): Epidemiological Survey of Maintenance Workers in the London Transport Executive Bus Garages and Chiswick Works	7-5
7.2.1.4.	Wong et al. (1985): Mortality Among Members of a Heavy Construction Equipment Operators Union With Potential Exposure to Diesel Exhaust Emissions	7-7
7.2.1.5.	Edling et al. (1987): Mortality Among Personnel Exposed to Diesel Exhaust	7-10
7.2.1.6.	Boffetta and Stellman (1988): Diesel Exhaust Exposure and Mortality Among Males in the American Cancer Society Prospective Study	7-11
7.2.1.7.	Garshick et al. (1988): A Retrospective Cohort Study of Lung Cancer and Diesel Exhaust Exposure in Railroad Workers	7-13
7.2.1.8.	Gustavsson et al. (1990): Lung Cancer and Exposure to Diesel Exhaust Among Bus Garage Workers	7-16
7.2.1.9.	Hansen (1993): A Followup Study on the Mortality of Truck Drivers	7-18
7.2.2.	Case-Control Studies of Lung Cancer	7-19
7.2.2.1.	Williams et al. (1977): Associations of Cancer Site and Type With Occupation and Industry From the Third National Cancer Survey Interview	7-19
7.2.2.2.	Hall and Wynder (1984): A Case-Control Study of Diesel Exhaust Exposure and Lung Cancer	7-26
7.2.2.3.	Damber and Larsson (1987): Occupation and Male Lung Cancer, a Case-Control Study in Northern Sweden	7-27
7.2.2.4.	Lerchen et al. (1987): Lung Cancer and Occupation in New Mexico	7-29
7.2.2.5.	Garshick et al. (1987): A Case-Control Study of Lung Cancer and Diesel Exhaust Exposure in Railroad Workers	7-30
7.2.2.6.	Benhamou et al. (1988): Occupational Risk Factors of Lung Cancer in a French Case-Control Study	7-33

CONTENTS (continued)

7.2.2.7.	Hayes et al. (1989): Lung Cancer in Motor Exhaust-Related Occupations	7-35
7.2.2.8.	Steenland et al. (1990): A Case-Control Study of Lung Cancer and Truck Driving in the Teamsters Union	7-36
7.2.2.9.	Steenland et al. (1998): Diesel Exhaust and Lung Cancer in the Trucking Industry: Exposure-Response Analyses and Risk Assessment	7-38
7.2.2.10.	Boffetta et al. (1990): Case-Control Study on Occupational Exposure to Diesel Exhaust and Lung Cancer Risk	7-40
7.2.2.11.	Emmelin et al. (1993): Diesel Exhaust Exposure and Smoking: A Case-Referent Study of Lung Cancer Among Swedish Dock Workers	7-41
7.2.3.	Case-Control Study of Prostate Cancer	7-43
7.2.3.1.	Aronsen et al. (1996): Occupational Risk Factors for Prostate Cancer: Results from a Case-Control Study in Montreal, Quebec, Canada	7-43
7.2.4.	Summaries of Studies and Meta-Analyses of Lung Cancer	7-48
7.2.4.1.	Cohen and Higgins (1995): Health Effects of Diesel Exhaust: Epidemiology	7-48
7.2.4.2.	Bhatia et al. (1998): Diesel Exhaust Exposure and Lung Cancer	7-49
7.2.4.3.	Lipsett and Campleman (1999): Occupational Exposure to Diesel Exhaust and Lung Cancer: A Meta-Analysis	7-52
7.2.5.	Case-Control Studies of Bladder Cancer	7-54
7.2.5.1.	Howe et al. (1980): Tobacco Use, Occupation, Coffee, Various Nutrients, and Bladder Cancer	7-54
7.2.5.2.	Wynder et al. (1985): A Case-Control Study of Diesel Exhaust Exposure and Bladder Cancer	7-56
7.2.5.3.	Hoar and Hoover (1985): Truck Driving and Bladder Cancer Mortality in Rural New England	7-58
7.2.5.4.	Steenland et al. (1987): A Case-Control Study of Bladder Cancer Using City Directories as a Source of Occupational Data	7-59
7.2.5.5.	Iscovich et al. (1987): Tobacco Smoking, Occupational Exposure, and Bladder Cancer in Argentina	7-61
7.2.5.6.	Iyer et al. (1990): Diesel Exhaust Exposure and Bladder Cancer Risk	7-63
7.2.5.7.	Steineck et al. (1990): Increased Risk of Urothelial Cancer in Stockholm From 1985 to 1987, After Exposure to Benzene and Exhausts	7-65
7.2.6.	Discussion and Summary	7-66
7.2.6.1.	The Cohort Mortality Studies	7-72

CONTENTS (continued)

7.2.6.2.	Case-Control Studies of Lung Cancer	7-75
7.2.6.3.	Reviews and Meta-analyses of Lung Cancer	7-77
7.2.6.4.	Case-Control Studies of Bladder Cancer	7-78
7.2.6.5.	Relevant Methodologic Issues	7-79
7.2.6.6.	Criteria of Causal Inference	7-81
7.3.	CARCINOGENICITY OF DIESEL EMISSIONS IN LABORATORY ANIMALS	7-85
7.3.1.	Inhalation Studies (Whole Diesel Exhaust)	7-86
7.3.1.1.	Rat Studies	7-86
7.3.1.2.	Mouse Studies	7-102
7.3.1.3.	Hamster Studies	7-105
7.3.1.4.	Monkey Studies	7-106
7.3.2.	Inhalation Studies (Filtered Diesel Exhaust)	7-106
7.3.3.	Inhalation Studies (Diesel Exhaust Plus Co-Carcinogens)	7-107
7.3.4.	Lung Implantation or Intratracheal Instillation Studies	7-108
7.3.4.1.	Rat Studies	7-108
7.3.4.2.	Syrian Hamster Studies	7-112
7.3.4.3.	Mouse Studies	7-114
7.3.5.	Subcutaneous and Intraperitoneal Injection Studies	7-114
7.3.5.1.	Mouse Studies	7-114
7.3.6.	Dermal Studies	7-116
7.3.6.1.	Mouse Studies	7-116
7.3.7.	Summary and Conclusions of Laboratory Animal Carcinogenicity Studies	7-121
7.4.	MODE OF ACTION OF DIESEL EMISSION-INDUCED CARCINOGENESIS	7-126
7.4.1.	Potential Role of Organic Exhaust Components in Lung Cancer Induction	7-127
7.4.2.	Role of Inflammatory Cytokines and Proteolytic Enzymes in the Induction of Lung Cancer by Diesel Exhaust	7-131
7.4.3.	Role of Reactive Oxygen Species in Lung Cancer Induction by Diesel Exhaust	7-132
7.4.4.	Relationship of Physical Characteristics of Particles to Cancer Induction	7-135
7.4.5.	Integrative Hypothesis For Diesel-induced Lung Cancer	7-136
7.4.6.	Summary	7-138
7.5.	CANCER WEIGHT-OF-EVIDENCE: HAZARD EVALUATION	7-139
7.5.1.	Cancer Hazard Summary	7-139
7.5.2.	Supporting Information	7-140
7.5.2.1.	Human Data	7-140
7.5.2.2.	Animal Data	7-141
7.5.2.3.	Other Key Data	7-142
7.5.2.4.	Mode of Action	7-142
7.6.	DISCUSSION OF THE ROLE OF DIESEL EXHAUST IN THE OVERALL PICTURE OF PM ₁₀	7-142

CONTENTS (continued)

7.7. REFERENCES	7-143
8. CANCER DOSE-RESPONSE EVALUATION	8-1
8.1. INTRODUCTION	8-1
8.2. REVIEW OF PREVIOUS QUANTITATIVE RISK ESTIMATES	8-1
8.2.1. Comparative Potency Method	8-2
8.2.2. Suitability of Comparative Potency Approach	8-5
8.2.3. Animal Bioassay-Based Cancer Potency Estimates	8-6
8.2.4. Suitability of Laboratory Animal Bioassay Approach	8-7
8.2.5. Epidemiology-Based Estimation of Cancer Potency	8-8
8.2.6. Suitability of Using Epidemiologic Data	8-10
8.2.6.1. Railroad Worker Data	8-12
8.2.6.2. Teamster Truck Driver Data	8-12
8.3. OBSERVATIONS ABOUT RISK	8-13
8.3.1. Perspectives	8-13
8.4. SUMMARY OF CANCER DOSE-RESPONSE CONSIDERATIONS	8-15
8.5. REFERENCES	8-16
9. CHARACTERIZATION OF HEALTH HAZARD AND DOSE-RESPONSE FOR DIESEL ENGINE EXHAUST	9-1
9.1. INTRODUCTION	9-1
9.2. WHAT IS DIESEL EXHAUST IN A HEALTH HAZARD ASSESSMENT CONTEXT?	9-2
9.3. NONOCCUPATIONAL AND OCCUPATIONAL EXPOSURE	9-5
9.4. HAZARD CHARACTERIZATION	9-6
9.4.1. Health Effects Other Than Cancer: Acute Exposures	9-6
9.4.2. Effects Other Than Cancer: Chronic Exposure	9-7
9.4.3. Health Effects Other Than Cancer: Derivation of Inhalation Reference Concentration	9-8
9.5. CARCINOGENICITY HAZARD CHARACTERIZATION	9-10
9.5.1. Cancer Hazard	9-11
9.6. CANCER DOSE-RESPONSE ASSESSMENT	9-14
9.7. SUSCEPTIBLE SUBGROUPS	9-15
9.8. REFERENCES	9-16

LIST OF TABLES

2-1.	Emission standards: HD highway diesel engines	2-6
2-2.	Emission standards: locomotives (g/bhp/hr)	2-7
2-3.	Vehicle classification and weights for on-road trucks	2-25
2-4.	Truck fleet results for 1992 from Census of Transportation (1995), results in thousands	2-27
2-5.	Emissions results from tunnel tests (adapted from Yanowitz et al., 1999b)	2-41
2-6.	Remote sensing results for hd vehicles (Yanowitz et al., 1999b)	2-42
2-7.	Concentrations of nitro-polycyclic aromatic hydrocarbons identified in a LD diesel particulate extract	2-52
2-8.	Comparison of PAH and nitro-PAH emissions for IDI naturally aspirated engines and two DI turbocharged engines	2-54
2-9.	Classes of compounds in diesel exhaust	2-61
2-10.	Calculated atmospheric lifetimes for gas-phase reactions of selected compounds present in automotive emissions with important reactive species	2-63
2-11.	Major components of gas-phase diesel engine emissions and their known atmospheric transformation products	2-64
2-12.	Major components of particle-phase diesel engine emissions and their known atmospheric transformation products	2-66
2-13.	Ambient diesel PM concentrations reported from chemical mass balance modeling	2-72
2-14.	Diesel PM 2.5 concentrations in urban and rural locations using EC surrogate for NESCAUM (1995) and IMPROVE (1992-1995) network sites	2-75
2-15.	Modeled diesel PM2.1 for South Coast Air Basin in 1982	2-78
2-16.	Diesel PM1.0 exposures reported by Zaebst et al. (1991) and calculated using the EC ratiometric approach	2-80
2-17.	Annual average diesel PM exposures for 1990 in the general population and among the highest exposed demographic groups in nine urban areas (on-road sources only)	2-82
2-18.	Projected annual average diesel PM exposures from all on-road vehicles	2-83
2-19.	Modeled and estimated concentrations of diesel PM in microenvironments (California EPA, 1998a)	2-84
2-20.	Estimated indoor air and total air exposures to diesel PM in California in 1990	2-85
3-1.	Predicted doses of inhaled diesel exhaust particles per minute based on total lung volume (M), total airway surface area (M_1), or surface area in alveolar region (M_2)	3-7
3-2.	Alveolar clearance in laboratory animals exposed to DPM	3-14
5-1.	Human studies of exposure to diesel exhaust	5-16
5-2.	Short-term effects of diesel exhaust on laboratory animals	5-22
5-3.	Effects of chronic exposures to diesel exhaust on survival and growth of laboratory animals	5-27

LIST OF TABLES (continued)

5-4.	Effects of chronic exposures to diesel exhaust on organ weights and organ-to-body-weight ratios	5-29
5-5.	Effects of diesel exhaust on pulmonary function of laboratory animals	5-33
5-6.	Histopathological effects of diesel exhaust in the lungs of laboratory animals	5-37
5-7.	Effects of exposure to diesel exhaust on the pulmonary defense mechanisms of laboratory animals	5-48
5-8.	Effects of inhalation of diesel exhaust on the immune system of laboratory animals	5-57
5-9.	Effects of diesel particulate matter on the immune response of laboratory animals	5-61
5-10.	Effects of exposure to diesel exhaust on the liver of laboratory animals	5-66
5-11.	Effects of exposure to diesel exhaust on the hematological and cardiovascular systems of laboratory animals	5-68
5-12.	Effects of chronic exposures to diesel exhaust on serum chemistry of laboratory animals	5-70
5-13.	Effects of chronic exposures to diesel exhaust on microsomal enzymes of laboratory animals	5-72
5-14.	Effects of chronic exposures to diesel exhaust on behavior and neurophysiology	5-75
5-15.	Effects of chronic exposures to diesel exhaust on reproduction and development in laboratory animals	5-77
5-16.	Composition of exposure atmospheres in studies comparing unfiltered and filtered diesel exhaust	5-79
6-1.	UFs and their default values used in EPA's noncancer RfD and RfC methodology	6-3
6-2.	Human equivalent continuous concentrations from the principal studies	6-14
6-3.	Decision summary for the derivation of the RfC for diesel engine emissions	6-23
7-1.	Epidemiologic studies of the health effects of exposure to diesel exhaust: cohort mortality studies	7-20
7-2.	Epidemiologic studies of the health effects of exposure to diesel exhaust: case-control studies of lung cancer	7-44
7-3.	Epidemiologic studies of the health effects of exposure to diesel exhaust: case-control studies of bladder cancer	7-67
7-4.	Summary of animal inhalation carcinogenicity studies	7-87
7-5.	Tumor incidence and survival time of rats treated by surgical lung implantation with fractions from diesel exhaust condensate (35 rats/group)	7-110
7-6.	Tumor incidences in rats following intratracheal instillation of diesel exhaust particles (DPM), extracted DPM, carbon black (CB), benzo[<i>a</i>]pyrene (BaP), or particles plus BaP	7-113
7-7.	Tumorigenic effects of dermal application of acetone extracts of diesel particulate matter (DPM)	7-117
7-8.	Dermal tumorigenic and carcinogenic effects of various emission extracts	7-120

LIST OF TABLES (continued)

7-9. Cumulative (concentration × time) exposure data for rats exposed to whole diesel exhaust 7-122

8-1. Estimated 95% upper confidence limits of the lifetime risk of cancer from inhalation of 1 µg/m³ diesel particulate matter (DPM) 8-3

LIST OF FIGURES

2-1.	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	2-4
2-2.	Effect of turbocharging and aftercooling on NO _x and PM (Mori, 1997)	2-11
2-3.	An example of uniflow scavenging of a 2-stroke diesel engine with a positive displacement blower (Adapted from Taylor, 1990)	2-14
2-4.	NO _x -storage catalyst operation under oxidizing and reducing conditions	2-19
2-5.	A comparison of the NO _x reduction efficiency over a range of temperature conditions for the sulfur-intolerant NO _x storage catalyst system and the more sulfur-tolerant, active Pt-zeolite catalyst system	2-20
2-6.	Schematic showing the operating principles of the continuously regenerating trap (CRT)	2-22
2-7.	Efficiency of NO to NO ₂ conversion over the oxidation catalyst component of the CRT at different exhaust temperatures and at differing diesel fuel sulfur levels	2-23
2-8.	Estimated sulfate (primarily H ₂ SO ₄) PM emissions from a LD truck equipped with a low-temperature Pt-zeolite lean-NO _x catalyst system (Wall, 1998)	2-24
2-9a.	Number of HD diesel trucks sold in years 1957-1998 based on industry sales data	2-26
2-9b.	Diesel truck sales (domestic) for the years 1939-1997	2-27
2-10a.	Diesel truck sales as a percentage of total truck sales for the years 1957-1998	2-28
2-10b.	Diesel truck sales as a percentage of total truck sales for the years 1939-1997	2-29
2-11.	Model year distribution of in-use truck fleet in 1992	2-29
2-12.	Diesel fuel use since 1949	2-33
2-13.	On-highway diesel fuel consumption since 1949, values in thousands of gallons	2-34
2-14.	Model year trends in NO _x emissions (g/mile)	2-37
2-15.	Model year trends in PM emissions (g/mile)	2-38
2-16.	Model year trends in HC emissions (g/mile)	2-39
2-17.	Comparison of 2-stroke and 4-stroke engines PM emissions on a g/mi and g/gal basis (low altitude data only)	2-43
2-18.	Line-haul and switch emissions data	2-45
2-19.	Comparison of SOF emissions for 2- and 4-stroke engines in g/mi and as a percentage of total PM	2-48
2-20.	Trends in PM solids emissions with model year, a reasonable surrogate for elemental carbon content	2-49
2-21.	Parity plot showing approximate agreement between PM elemental carbon and PM solids measurements in g/mi	2-50
2-22.	1-Nitropyrene emission rates from several HD diesel vehicles	2-55
2-23.	Chassis dynamometer measurements of total aldehyde emissions from HD diesel vehicles	2-57
2-24.	Particle size distribution in diesel exhaust, taken from Kittelson (1998)	2-58
3-1.	Modeled deposition distribution patterns of inhaled diesel exhaust particles in the airways of different species	3-6

LIST OF FIGURES (continued)

3-2.	Modeled clearance of insoluble 4- μ m particles deposited in tracheobronchial and alveolar regions in humans	3-9
3-3.	Short-term thoracic clearance of inhaled particles as determined by model prediction and experimental measurement	3-11
3-4.	Clearance from lungs of rats of ^{134}Cs -FAP fused aluminosilicate tracer particles inhaled after 24 months of diesel exhaust exposure at concentrations of 0 (control), 0.35 (low), 3.5 (medium), and 7.0 (high)	3-22
3-5.	Lung burdens of DPM within rats exposed to 0.35 (low), 3.5 (medium), and 7.0 (high)	3-23
7-1.	Pooled relative risk estimates and heterogeneity-adjusted 95% confidence intervals for all studies and subgroups of studies included in the meta-analysis	7-51
7-2.	Pooled estimates of relative risk of lung cancer in epidemiological studies involving occupational exposure to diesel exhaust (random-effects models)	7-53
7-3.	Lung cancer and exposure to diesel exhaust in railroad workers	7-82
7-4.	Lung cancer and exposure to diesel exhaust in truck drivers	7-83
7-5.	Pathogenesis of lung disease in rats with chronic, high-level exposure to particles	7-137

PREFACE

This draft health risk assessment document was prepared by the National Center for Environmental Assessment (NCEA), which is the health risk assessment program in EPA's Office of Research and Development. The assessment has been prepared for EPA's Office of Mobile Sources which requested advice regarding the potential health hazards associated with diesel engine use. As diesel exhaust emissions also affect air toxics and ambient particulate matter, other EPA air programs also have an interest in this assessment. The previous draft of this assessment was released for public comment in February 1998, and the Agency's Clean Air Scientific Advisory Committee (CASAC) met in public session in May 1998 to review the draft. This November 1999 draft is a revision of that 1998 draft, but also builds on the 1990-1999 history of the development of this diesel health risk assessment.

The scientific literature search for this assessment is generally current through January 1999, though a few more recent publications on key topics also have been included.

This November 1999 draft assessment will be reviewed by CASAC in December 1999, and concurrently, public comments will be accepted for a limited time. Following the receipt of comments from CASAC and the public, NCEA plans to finalize the assessment.

AUTHORS AND CONTRIBUTORS

The National Center for Environmental Assessment (NCEA), within EPA's Office of Research and Development (ORD), was responsible for the preparation of this document. Authors and chapter managers for this draft health assessment document are listed below.

CHAPTER 1. EXECUTIVE SUMMARY

Authors

NCEA Diesel Team

CHAPTER 2. DIESEL EMISSIONS CHARACTERIZATION, ATMOSPHERIC TRANSFORMATION, AND EXPOSURES

Chapter Manager/Author

Marion Hoyer, Office of Mobile Sources, U.S. Environmental Protection Agency, Ann Arbor, MI.

Contributors

Chad Bailey, Office of Mobile Sources, U.S. Environmental Protection Agency, Ann Arbor, MI.

Tom Baines, Office of Mobile Sources, U.S. Environmental Protection Agency, Ann Arbor, MI.

David Cleverly, National Center for Environmental Assessment, U.S. Environmental Protection Agency, Washington, DC.

William Ewald, National Center for Environmental Assessment, U.S. Environmental Protection Agency, Research Triangle Park, NC.

Robert McCormick, Colorado School of Mines, Golden, CO

Joseph McDonald, Office of Mobile Sources, U.S. Environmental Protection Agency, Ann Arbor, MI.

Joseph Somers, Office of Mobile Sources, U.S. Environmental Protection Agency, Ann Arbor, MI.

Janet Yanowitz, Colorado School of Mines, Golden, CO.

Barbara Zielinska, Desert Research Institute, Reno NV.

CHAPTER 3. DOSIMETRY OF DIESEL EXHAUST PARTICLES IN THE RESPIRATORY TRACT

Authors

James McGrath, National Center for Environmental Assessment, U.S. Environmental Protection Agency, Research Triangle Park, NC.

William Pepelko, National Center for Environmental Assessment, U.S. Environmental Protection Agency, Washington, DC.

Contributor

Gary Foureman, National Center for Environmental Assessment, U.S. Environmental Protection Agency, Research Triangle Park, NC.

CHAPTER 4. MUTAGENICITY OF DIESEL EXHAUST

Author

Lawrence Valcovic, National Center for Environmental Assessment, U.S. Environmental Protection Agency, Washington, DC.

CHAPTER 5. NONCANCER HEALTH EFFECTS OF DIESEL EXHAUST

Authors

James McGrath, National Center for Environmental Assessment, U.S. Environmental Protection Agency, Research Triangle Park, NC.

Contributor

Gary Foureman, National Center for Environmental Assessment, U.S. Environmental Protection Agency, Research Triangle Park, NC.

**CHAPTER 6. NONCANCER DOSE-RESPONSE
EVALUATION: RfC DERIVATION****Authors**

Gary Foureman, National Center for Environmental Assessment, U.S. Environmental Protection Agency, Research Triangle Park, NC.

Contributor

James McGrath, National Center for Environmental Assessment, U.S. Environmental Protection Agency, Research Triangle Park, NC.

CHAPTER 7. CARCINOGENICITY OF DIESEL EXHAUST**Authors**

Aparna Koppikar, National Center for Environmental Assessment, U.S. Environmental Protection Agency, Washington, DC.

William Pepelko, National Center for Environmental Assessment, U.S. Environmental Protection Agency, Washington, DC.

Contributors

Drew Levy, University of Washington, Seattle, WA

Robert Young, Oak Ridge National Laboratory, Oak Ridge, TN

CHAPTER 8. CANCER DOSE-RESPONSE EVALUATION

Authors

Chao Chen, National Center for Environmental Assessment, U.S. Environmental Protection Agency, Washington, DC.

William Pepelko, National Center for Environmental Assessment, U.S. Environmental Protection Agency, Washington, DC.

Contributor

Charles Ris, National Center for Environmental Assessment, U.S. Environmental Protection Agency, Washington, DC.

CHAPTER 9. CHARACTERIZATION OF HEALTH HAZARD AND DOSE-RESPONSE FOR DIESEL ENGINE EXHAUST

Author

Charles Ris, National Center for Environmental Assessment, U.S. Environmental Protection Agency, Washington, DC.

Contributors

NCEA Diesel Team

This document was preceded by three earlier drafts: a Workshop Review Draft (EPA/600/8-90/057A, July 1990), an External Review Draft (EPA/600/8-90/057B, December 1994), and an SAB Review Draft (EPA/600/8-90/057C, February 1998). The Science Advisory Board's Clean Air Scientific Advisory Committee (CASAC) reviewed the 1994 draft in public sessions in May 1995 and the 1998 draft in May 1998. 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.

ACKNOWLEDGMENTS

Document Production

Terri Konoza
National Center for Environmental Assessment
U.S. Environmental Protection Agency
Washington, DC

Kay Marshall
Clara Laucho
Eric Sorensen
The CDM Group, Inc.
Chevy Chase, MD

Printing and Distribution

Linda Bailey-Becht
Judy Theisen
National Center for Environmental Assessment
U.S. Environmental Protection Agency
Washington, DC

1. EXECUTIVE SUMMARY

The Health Assessment Document for Diesel Emissions represents the Agency's first comprehensive review of health effects from exposure to exhaust from diesel engines. In-depth research on diesel exhaust (DE) started in the 1970s, and EPA began regulating emission levels for certain types of diesel engines during the same period. EPA wanted to be aware of the current health issues as it continues with Clean Air Act regulatory programs, hence the need for this assessment. In nine chapters, this health assessment addresses key themes or questions such as (1) the health effects of concern for humans, (2) the best insight as to the mode of action and measure of dose/exposure for the toxic response(s), (3) what dose-response analysis suggests about the possible impact/risk to a human population, and (4) the overall nature of the hazard and the related confidence or uncertainties.

Diesel exhaust is a complex mixture of particles and gases with hundreds of chemical compounds, including many organic compounds, present on the particles and in the gases. The particles have an elemental carbon core, with individual particles being very small (a mean aerodynamic diameter of about 0.2 μm) and thus highly respirable. The small particles have a large surface area upon which many organic compounds are adsorbed. The particle organics generally contribute 10%-30% of particle weight and, for example, contain various types of polyaromatic hydrocarbons (PAHs). The gases have both inorganic and organic constituents (e.g., sulfur dioxide, nitrogen oxides, benzene, ethylene, toluene, aldehydes, olefins, and low-molecular-mass PAHs). Both the particles and the numerous organic compounds of DE have toxicological properties that are capable of influencing a toxic response in humans, though the role of either or both in producing a toxic effect in humans is unknown.

DE particles contribute to ambient particulate matter, e.g., $\text{PM}_{2.5}$. Compared to other sources of ambient PM, the elemental carbon core is nearly unique to DE, as are a few of the adsorbed organic compounds. The DE gases are more ubiquitous in an urban environment.

Diesel engines may be on-road (vehicle engines) or off-road (many types of engines powering equipment, machinery, railroad locomotives, and ships). Quantitatively, amounts of specific emission constituents vary by type of engine and even within the same engine type. Qualitatively, the basic composition is fairly consistent, for example, an elemental carbon core particle with PAHs adsorbed to the particle and also present in the gases. Over the years, the mass of particles emitted in engine exhaust has been reduced, as have the accompanying organics.

For years researchers have measured DE concentrations using particle mass per unit volume, i.e., $\mu\text{g}/\text{m}^3$ of diesel particulate matter. This assessment adopts $\mu\text{g}/\text{m}^3$ as a dosimeter and further assumes that the important toxicologic agents in DE will be proportional to $\mu\text{g}/\text{m}^3$. This leads to some uncertainty, but the best dosimeter will not be known until the mode of action for DE toxicity is better understood. Questions have been raised as to whether toxicological findings generated from exposure to older engine exhaust can appropriately be applied to current-day engine exhaust exposures. This question is not resolvable with present information, except to note that available evidence does not point to significant shifts in DE composition relative to the total organics over the years, and that organics are believed to be in relative proportion to the mass of particles.

The primary chronic health concerns include nonmalignant respiratory effects and lung carcinogenicity. The DE particulates can be a component of ambient $\text{PM}_{2.5}$. Compared to ambient $\text{PM}_{2.5}$ with no DE component, DE is likely to have a higher proportion of fine and ultrafine particulates and is likely to have a higher or at least a varied content of toxicologically active organic compounds. Although some similarities exist between DE and ambient PM, the differences are potentially significant. A comparison of the DE RfC and the $\text{PM}_{2.5}$ standard has considerable complexity. For ambient PM we see increased mortality and morbidity in human studies from various forms of chronic respiratory disease. For DE we expect adverse respiratory effects but have not clearly observed them in human studies, possibly because few such studies have focused on respiratory effects. Animal studies conducted at higher than ambient exposure levels, the most prominent being in the rat, provide the basis for the expectation of human respiratory disease. A recommended human chronic exposure level without appreciable hazard (i.e., inhalation Reference Concentration, RfC, $5 \mu\text{g}/\text{m}^3$) from adverse noncancer respiratory effects is provided in the assessment. From an acute exposure standpoint, DE is an irritant to the respiratory system given sufficient episodic exposure and may cause a variety of inflammation-related symptoms (e.g., headache, eye discomfort, asthma-like reactions, nausea, etc.) depending on individual susceptibility to the DE constituents. Data also suggest that DE is a factor in exacerbating or initiating allergic hypersensitivity; this is an emerging area of concern.

The carcinogenicity of DE also has been of research and public health interest. Diesel engine exhaust is “highly likely” to be carcinogenic by the inhalation route of exposure, according to EPA’s 1996 Proposed Guidelines for Carcinogen Risk Assessment. This hazard is viewed as being applicable to ambient (i.e., environmental) exposures. Many of the organics present on the DE particles and in the gases, though in small quantities, are mutagenic and/or carcinogenic in their own right. DE shows a pattern of statistically increased lung cancer in more than 20, but not

all, human occupational studies where DE exposure is prominent. Lung cancer increases are, on average, about 33-47% above background levels, though specific studies suggest some modestly higher increases. There are some uncertainties about the magnitude of the increase, because questions about exposure are almost always present in the human studies in which the increases are seen, and with lung cancer, the question of confounding by cigarette smoke is present. Nevertheless, analysis of the occupational studies shows that the pattern of increased lung cancer remains after consideration of these issues. Bladder cancer also has been elevated in some epidemiologic studies, though the totality of the evidence is too weak to form a clear conclusion. Although rat inhalation cancer bioassays were once thought to be useful for inferring a human cancer hazard or supporting human evidence, in recent years, the rat lung cancer responses seen with DE exposure are thought to be less clear for human hazard prediction and unsuitable for environmental exposure risk estimation. None of the available studies show that the lung cancer hazard is present at environmental levels of exposure, although the margin may be relatively small between some higher environmental exposures and occupational exposures where lung cancer risks are thought to be present.

The plausibility of an environmental lung cancer hazard from DE by inhalation exposure is supported by findings contained in this assessment. Overall, the evidence for a likely human lung cancer hazard by inhalation is persuasive, even though, in the absence of complete data, inferences and thus uncertainties are involved. Some of the key uncertainties include: (1) methodologic limitations inherent in epidemiologic studies, as well as a lack of reliable historical exposure data for occupationally exposed cohorts, (2) uncertainties regarding the extent of bioavailability of organic compounds present on diesel particles and their impact on the carcinogenic process, and (3) other uncertainties regarding the mode of action of DE on lung cancer in humans.

A decision has been made in this assessment that, despite the finding that DE is best characterized as highly likely to be a lung cancer hazard, the available data are currently unsuitable to make a confident quantitative statement about the magnitude of the lung cancer risk attributable to DE at ambient exposure levels. Therefore, this assessment does not adopt or recommend a specific cancer unit risk estimate for DE. However, information is provided to put DE cancer hazard in perspective and to assist decisionmakers and the public to make prudent public health judgments in the absence of a definitive estimate of the upper bound on cancer risk. Efforts to derive cancer risk estimates for environmental purposes continue, with the focus being on epidemiologic studies because the epidemiology-based estimates are always the ideal starting

point, while also recognizing that the rat inhalation studies are no longer favored and other approaches identified to date have limitations.

There is no DE-specific information that provides direct insight to the question of variable susceptibility within the population. Default approaches to account for uncertainty in inter-individual susceptibility have been included in the derivation of the RfC. Individuals with preexisting lung burdens of particulates may have less of a margin of safety from DE particulate-driven hazards than might be inferred from incremental DE exposure analysis, although this cannot be quantified. DE exposure could be additive to many other daily or lifetime exposures to organics and PM. For example, adults who predispose their lungs to increased particle retention (e.g., smoking or high particulate burdens from nondiesel sources), have existing respiratory or lung inflammation or repeated respiratory infections, or have chronic bronchitis, asthma, or fibrosis could be more susceptible to adverse impacts from DE exposure. Although there is no information from studies of DE, infants and children could have a greater susceptibility to the acute/chronic toxicity of DE because they have greater ventilatory frequency, resulting in greater respiratory tract particle deposition. The issue of DE impacts on allergenicity and potential onset and exacerbation of childhood asthma is being actively investigated, but firm conclusions await peer review and publication of ongoing work.

Another aspect of differential susceptibility involves subgroups that may receive additional exposure to DE because of their proximity to DE sources. Those having outside time in their daily routine and being near a diesel emission source would likely receive more exposure than others in the population. The highest exposed are most likely the occupational subgroups whose job brings them very close to diesel emission sources (e.g., trucking industry, machinery operations, engine mechanics, some types of transit operations, railroads, etc.).

Ongoing analyses by EPA, other Federal agencies, and worldwide researchers are expected to improve the existing epidemiology and related exposure databases. These will provide new opportunities to evaluate the potential health effects of DE on the general population and susceptible subgroups.