1. EXECUTIVE SUMMARY

1.1. INTRODUCTION

The Health Assessment Document for Diesel Exhaust (DE) represents the Agency's first comprehensive review of the potential health effects from ambient exposure to exhaust from diesel engines. This assessment identifies and characterizes the potential human health hazards of DE (i.e, hazard assessment) and characterizes the related dose-response associated with the key health effects (i.e., dose-response assessment). This is part of the information needed for a complete risk assessment of DE in support of EPA's Clean Air Act regulatory programs. 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 (including this chapter) and four appendices. Chapter 2 provides a characterization of diesel emissions, atmospheric transformation, and human exposures to DE 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), other noncancer health effects (Chapter 5), and carcinogenicity (Chapter 7). Chapters 6 and 8 contain dose-response analyses to provide insight about the significance of the potential noncancer and cancer hazards, respectively. Chapter 9 characterizes the overall nature of the potential health hazard and risk from environmental exposure to DE and discusses the overall confidence and uncertainties of the assessment. Major conclusions of the health assessment for DE are provided below.

1.2. COMPOSITION OF DIESEL EXHAUST

DE is a complex mixture of hundreds of constituents in either a gas or particle phase. Gaseous components of DE include carbon dioxide, oxygen, nitrogen, water vapor, carbon monoxide, nitrogen compounds, sulfur compounds, and low-molecular-weight hydrocarbons. Among the gaseous components of DE that are 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 or DPM) are composed of elemental carbon, adsorbed organic compounds, and small amounts of sulfate, nitrate, metals, and other trace elements. DPM consists of fine and ultrafine particles. These particles are highly respirable and have a very large surface area, which make them an excellent carrier for adsorbed inorganic and organic compounds. The most toxicologically relevant organic compounds that are adsorbed onto the particles include PAHs, nitro-PAHs, and oxidized PAH derivatives. PAHs and

their derivatives comprise about 1% or less of the DPM mass. Many of the organic compounds present on the particle and in the gases are known to have mutagenic and carcinogenic properties.

1.3. DIESEL EMISSIONS

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 indicate 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 microns or less) and about 23% of the inventory excluding natural and miscellaneous sources. Estimates of the DPM percentage of the total inventory in urban centers can be higher. For example, estimates range from 10% to 36% in some areas in California, Colorado, and Arizona. Available data indicate that over the years, there have been significant reductions in DPM emissions from the exhaust of on-road diesel engines, whereas very limited data suggest that exhaust emissions from nonroad engines have increased.

DE emissions vary significantly in chemical composition and particle sizes with different engine types (heavy-duty, light-duty), engine operating conditions (idle, accelerate, decelerate), and fuel formulations. The mass of particles emitted and the organics on the particles from on-road diesel engines have been reduced over the years. Available data indicate that toxicologically relevant organic components of DE (e.g., PAHs, nitro-PAHs) were present in DPM and DE emitted from older vehicle engines and are still present in emissions from newer engines. There is insufficient information, however, to characterize the changes in the composition of DPM from nonroad diesel engines over time.

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 either directly emitted from diesel-powered engines (primary particulate matter) or is 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 consequence of DE aging is, because some compounds in the DE mixture are altered during aging to more toxic forms while others are made less toxic.

1.5. EXPOSURE TO DIESEL EXHAUST

DPM mass (expressed as $\mu g/m^3$ of DPM) has historically been measured as a surrogate for whole DE. Although considerable uncertainty exists as to whether DPM is the most appropriate dosimeter for human health effects, it is considered a reasonable choice until more definitive information about the mechanisms or mode(s) of action of DE becomes available. In the ambient environment, exposure to DE comes from both on-road and nonroad engine exhaust. A large percentage of the U.S. population is exposed to ambient $PM_{2.5}$, of which DE is a part. Estimates suggest that nonroad sources of DE contribute as much to the nationwide PM inventory as do on-road DE sources. With limited information from actual measurements of DE, various types of models and assumptions are used to estimate human exposure to on-road generated DE as measured by DPM. Exposure information is useful to provide a context for the health effects information, and estimates for the early to mid-1990s suggest that annual average DE exposure from on-road engines alone was in the range of about 0.5 to close to 1.0 µg DPM/m^3 of inhaled air in many rural and urban areas, respectively. For urban areas where people spend a large portion of their time outdoors, the exposures may range up to 4.0 µg DPM/m^3 of inhaled air. Exposure estimates are adjusted to account for time spent outdoors. Exposures could be higher still, if there is a nonroad DE source that adds to the on-road- generated exposure.

1.6. HEALTH EFFECTS

Available evidence indicates that adverse human health effects may result from current-day environmental inhalation exposure to DE. DE exposure may cause acute and chronic noncancer respiratory effects and has the potential to cause lung cancer in humans.

1.6.1. Acute Effects

Available information for characterizing potential health effects associated with acute or short-term exposure is limited. On the basis of available human and animal evidence, it is concluded that DE can cause acute irritation (e.g., eye, throat, bronchial irritation), neurophysiological symptoms (e.g., lightheadedness, nausea), and respiratory symptoms (cough and phlegm). There is also evidence for possible immunologic effects and/or exacerbation of allergenic responses to known allergens. The lack of exposure-response information precludes the development of recommendations about levels of exposure that would be protective for these effects.

1.6.2. Chronic Noncancer Respiratory Effects

The information in 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 may pose a chronic respiratory hazard to humans. Chronic animal inhalation studies show a spectrum of dose-dependent chronic inflammation and histopathological changes in the lung in several animal species including rats, mice, hamsters, and monkeys.

This assessment provides an estimate of an air-level exposure of DE (as measured by DPM) to which humans may be exposed throughout their lifetime without experiencing any untoward or adverse noncancer health effects. This exposure level, known as the reference concentration (RfC), for DE of 14 $\mu g/m^3$ of DPM was derived on the basis of dose-response data from four chronic rat inhalation studies. This value is almost the same as the long-term $PM_{2.5}$ NAAQS (National Ambient Air Quality Standard) of 15 $\mu g/m^3$.

1.6.3. Carcinogenic Effects

This assessment concludes that DE is likely to be carcinogenic to humans by inhalation at any exposure condition. This characterization 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 different occupations. The human evidence is considered strong but less than sufficient to definitively conclude that DE exposure is causally associated with lung cancer, because of the possible confounding effects of smoking and the lack of actual DE exposure data for the workers. In addition to the human evidence, there is extensive evidence for the induction of lung cancer in the rat from chronic inhalation exposure to high concentrations of DE, and supporting evidence of carcinogenicity of DPM and associated organic compounds 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. There is also suggestive evidence for the bioavailability of the organics from DE in humans and animals. The precise role of DPM with its organic component in DE-induced carcinogenicity is unclear, although in high-exposure animal test systems, DPM and its elemental carbon core are shown to be the most important fraction of DE.

Although the available human evidence shows the hazard to be present at exposures generally higher than ambient levels, it is reasonable to presume that the hazard extends to ambient environmental exposure levels. Because of an incomplete understanding of the mode of action for DE-induced lung cancer in humans, and some evidence for a mutagenic mode of action, it is a prudent public health policy to presume a cancer hazard for DE at any exposure condition. This presumption pertains only to the carcinogenic hazard and does not inform about the

magnitude of the risk at ambient levels. Overall, the evidence for a potential cancer hazard to humans resulting from chronic inhalation exposure to DE is persuasive, even though assumptions and thus uncertainties are involved.

Given a carcinogenicity hazard, EPA typically performs a dose-response assessment of 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. For DE, the exposure-response data in rat studies are not deemed appropriate for the estimation of human risk. Exposure-response data in available human studies are considered too uncertain to derive a confident quantitative estimate of cancer unit risk. Therefore, EPA has chosen not to derive a quantitative estimate of cancer unit risk.

In the absence of a unit risk to assess environmental cancer risk, simple analyses are performed to provide a perspective of the range of the possible lung cancer risk from environmental exposure to DE. The analyses make use of epidemiologic findings of lung cancer risks from occupational exposures to DE, and consider the exposure margins between occupational and environmental exposures to DE. The magnitude of the possible lifetime cancer risk, based on the simple analyses, indicates the significance of the potential lung cancer hazard from ambient exposure to DE. These analyses, however, are subject to considerable uncertainties, and should not be viewed as a definitive quantitative characterization of risk.

1.7. SOURCES OF UNCERTAINTIES

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 underlying mechanisms by which DE causes observed toxicities in humans and animals. A major uncertainty of this assessment is how the physical and chemical nature of the past exposures to DE compares with present-day exposures, and how representative the DE exposure-response data are from occupational and toxicological studies for the characterization of possible hazard and risk from present-day environmental exposures. Available data are not sufficient to provide definitive answers to these questions, as changes in DE composition over time cannot be confidently quantified and the modes of action for DE toxicity and carcinogenicity are unknown in humans. Despite these uncertainties, this assessment assumes that prior-year toxicologic and epidemiologic findings can be applied to more current exposures, both of which use $\mu g/m^3$ of DPM mass as the dosimeter.

Other uncertainties include the assumptions that health effects observed at high dose may be applicable to low dose, and that toxicologic findings in laboratory animals are predictive of human responses. In the absence of more complete understanding of how DE may cause adverse health effects in humans and laboratory animals, the assumptions used in this assessment (i.e., a

biological threshold for chronic respiratory effects) and absence of a threshold for lung cancer are considered prudent and reasonable.

The assessment addresses the potential DE health hazards for average healthy adults. There is no DE-specific information that provides direct insight to the question of variable susceptibility within the general human population and vulnerable subgroups, including infants and children, and people with preexisting health conditions, particularly respiratory conditions. Despite these uncertainties, the default approach of using an uncertainty factor of 10 to account for possible interindividual variation to DE in the derivation of the RfC is appropriate and reasonable given the lack of DE-specific data.

In providing a perspective on the significance of the environmental cancer hazard of DE, this assessment considers the differences in the magnitude of DE exposures between the occupational and environmental settings. Variation in DE exposure is a source of uncertainty. Because of variation in activity patterns, different population subgroups could potentially receive higher or lower exposure to DE depending on their proximity to DE sources. Accordingly, DE exposure estimates used in this assessment have included possible high-end exposures.

Lastly, this assessment considers only potential heath effects from exposures to DE alone. DE exposure could be additive or synergistic to 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 at this time. Further research is needed to improve the knowledge and database on DE exposures and potential human health effects, and thereby reduce uncertainties of future risk assessments of DE.