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IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Diesel and Gasoline Engine Exhausts and Some Nitroarenes. Lyon (FR): International Agency for Research on Cancer; 1989. (IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, No. 46.)

Diesel and Gasoline Engine Exhausts

1. Composition of Engine Exhausts

1.1. Introduction

Diesel and gasoline engines are the major power train sources used in vehicles. They are both internal, intermittent combustion engines. In diesel engines, the fuel is self-ignited as it is injected into air that has been heated by compression. In gasoline engines, the fuel is ignited by sparking-plugs. The fuels used in diesel and gasoline engines also differ, with diesel fuel consisting of higher boiling range petroleum fractions (see IARC, 1989). Primarily because of its higher density, a litre of diesel fuel contains approximately 13% more energy than a litre of gasoline.

There are two categories of diesel engine: open-chamber or direct-injection engines are preferred for heavy-duty applications because they offer the best fuel economy; divided-chamber or indirect-injection engines have been preferred for light-duty applications because they are less sensitive to differences in fuels, have a wider range of speeds (and therefore greater power:weight ratio), run more quietly and emit fewer pollutants (National Research Council, 1982).

The major products of the complete combustion of petroleum-based fuels in an internal combustion engine are carbon dioxide (13%) and water (13%), with nitrogen from air comprising most (73%) of the remaining exhaust. A very small portion of the nitrogen is converted to nitrogen oxides and some nitrated hydrocarbons. Some excess oxygen may be emitted, depending on the operating conditions of the engine. Gasoline engines are designed to operate at a nearly stoichiometric ratio (air:fuel ratio, ≃14.6:1); diesel engines operate with excess air (air:fuel ratio, ≃25–30:1; Lassiter & Milby, 1978).

Incomplete combustion results in the emission of carbon monoxide, unburnt fuel and lubricating oil (Yamaki *et al.*, 1986) and of oxidation and nitration products of the fuel and lubricating oil. These incomplete combustion products comprise thousands of chemical components present in the gas and particulate phases (Zaebst *et al.*, 1988); some specific chemical species and classes found in engine exhausts are listed in Table 1. The concentration of a chemical species in vehicle exhaust is a function of several factors, including engine type, engine operating conditions, fuel and lubricating oil composition and emission control system (Johnson, 1988).

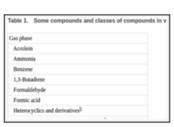
Table 1. Some compounds and classes of compounds in v
Gas phase
Acrolein
Ammonia
Benzene
1,3-Butadiene
Formaldehyde
Formic acid
Heterocyclics and derivatives

Table 1.

Some compounds and classes of compounds in vehicle engine exhaust.

Reports of measurements of polycyclic aromatic hydrocarbons (PAHs) emitted from spark-ignition gasoline engines first appeared in the literature in the 1950s (Kotin *et al.*, 1954) and early 1960s (Begeman & Colucci, 1962; Hoffmann & Wynder, 1962a). More recently, nitrated PAHs (nitroarenes) were detected in vehicle engine emissions. Some nitroarenes that have been identified in exhaust are listed in Table 2. Research has also been undertaken to determine if these compounds are formed as a result of the combustion process or subsequently in the exhaust. It has been shown in many studies that PAHs may undergo further reaction during sampling, but that these reactions can be minimized by using proper sampling apparatus and procedures (see section

2.3; Schuetzle, 1983; Schuetzle & Perez, 1983; Lies *et al.*, 1986).

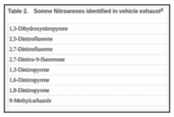

Table 2.

Somne Nitroarenes identified in vehicle exhaust.

Considerable effort has been made to identify mutagenic and carcinogenic chemicals in vehicle exhausts, primarily from diesel engines. Most effective has been the use of protocols combining short-term bioassays for genetic and related effects or for tumorigenicity with chemical analysis (Brune *et al.*, 1978; Schuetzle *et al.*, 1982; Grimmer *et al.*, 1983a, 1984, 1987).

The use of the *Salmonella typhimurium* mutagenesis assay to study factors which may alter the emission of mutagens from diesel and gasoline engines has been reviewed (Claxton, 1983). Effects of engine design, fuel composition and operation on mutagenicity in *S. typhimurium* have been reported (Huisingh *et al.*, 1978; Clark *et al.*, 1981; Huisingh *et. al.*, 1981; Clark *et al.*, 1982a,b,c; Ohnishi *et al.*, 1982; Zweidinger, 1982; Clark *et al.*, 1984; Schuetzle & Frazier, 1986). The effect of sampling methodology, environment (laboratory, tunnels and ambient urban air) and atmospheric transformation in the *S. typhimurium* mutagenesis assay have also been reported (Ohnishi *et al.*, 1980; Claxton & Barnes, 1981; Pierson *et al.*, 1983; Brooks *et al.*, 1984). Typical factors that affect emissions are shown in Tables 3 and 4. The data on mutagenicity are included for comparative purposes to indicate the quantity of total genotoxic components. The reader is referred to section 3.2 (p. 119) for summaries of studies of the genetic effects of diesel and gasoline engine exhausts.

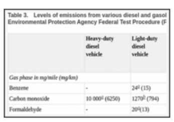

Table 3.

Levels of emissions from various diesel and gasoline engines (1980–85; US Environmental Protection Agency Federal Test Procedure (FTP) cycle only) and their mutagenicity.

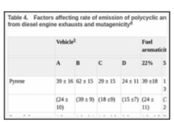

Table 4.

Factors affecting rate of emission of polycyclic aromatic hydrocarbons in μg/mile (μg/km) from diesel engine exhausts and mutagenicity.

In the descriptions below of the chemical and physical characteristics of emissions from diesel and spark-ignition (gasoline) engines, primary emphasis is placed on the identification of PAHs in different engines, with different fuels and under various operating conditions.

1.2. Diesel engine exhaust

In reviewing the data, the reader should recognize that detailed chemical characterization of engine emissions, especially for nitroarenes, was performed mostly in the late 1970s and 1980s. During that period, substantial changes occurred in engine and emission control technologies, and additional changes are to be expected in the future. It is also reasonable to expect that the emissions characterized recently may not represent fully emissions in earlier times. The available data refer mainly to light-duty vehicles; quantitative data on emissions from heavy-duty diesel engines are relatively sparse. Because of these limitations, the data presented here should be considered only as illustrative of the emissions of internal combustion engines; they should not be interpreted as representative of either current emissions from the wide range of engines used at present or of those that may have occurred in the past.

Compounds emitted from diesel engines include all of the compounds and compound classes listed in Table 1. Diesel engines produce two to ten times more particulate emissions than gasoline engines (without catalytic converter) of comparable power output and two to 40 times more particulate emissions than gasoline engines equipped with a catalytic converter (Table 3). The particles consist primarily of elemental carbon (Ball, 1987; 60–80%, Zaebst *et al.*, 1988), sulfuric acid (2–7%; Pierson & Brachaczek, 1983) and some metallic species, e.g., iron from the engine and exhaust system (Lang *et al.*, 1981), barium from fuel (Hampton *et al.*, 1983) and zinc from lubricating oil (Hare & Baines, 1979), and adsorbed organic compounds (National Research Council, 1982).

(a) Distribution in particulate and gas phases

The distribution of emissions between the gas and particulate phases is determined by the vapour pressure, temperature and concentration of the individual species. The partitioning of constituents between the particulate and gas phases has been measured by several investigators (Hampton *et al.*, 1983; Schuetzle, 1983). On the basis of these data, an empirical relationship between the molecular weight and the particulate- to gas-phase partition coefficient (P:G) for several of these compounds was derived, as shown for the PAHs in Table 5 (Schuetzle & Frazier, 1986).

Table 5. Particulate- to gas-phase partition coefficients for hydrocarbons in diesel exhaust[a]

Compound	Molecular weight
Phenanthrene	178
Anthracene	178
Pyrene	202
Fluoranthene	202
Benz[*a*]anthracene	228
Benzo[*a*]pyrene[b]	252

Table 5.

Particulate- to gas-phase partition coefficients for some polycyclic aromatic hydrocarbons in diesel exhaust.

(b) Gas-phase emissions

Gas-phase emissions from diesel engines comprise C_1–C_{18} hydrocarbons, two- to four-ring PAHs and nitrated and oxygenated derivatives of C_1–C_{12} hydrocarbons and two- to three-ring PAHs. The C_1–C_{10} hydrocarbons result almost entirely from the combustion process, which involves cracking of higher molecular weight materials (National Research Council, 1982). The quantities of some of these gas-phase species in diesel exhaust are given in Table 3.

(c) Particulate-phase emissions

Diesel particles are aggregates of spherical primary particles of 0.1–0.5 μm (National Research Council, 1982). Those generated under laboratory conditions in dilution tunnels have mass or volume median diameters ranging from 0.15 to 0.50 μm, depending on the operating conditions (Cheng *et al.*, 1984). Smaller primary spheres, formed within the combustion cylinder, grow by agglomeration and by acting as nuclei for the condensation of organic compounds (Duleep & Dulla, 1980).

The elemental carbon core of the particles has a large surface area which greatly enhances adsorption of organic compounds. Larger particles (>0.2 μm) tend to be flaky in nature (Moore *et al.*, 1978). If an engine is running under low load, there may be incomplete combustion, leading to a relatively low particle concentration and a higher proportion of organic compounds associated with the core particles (Dutcher *et al.*, 1984).

A variety of solvents has been used to extract organic compounds from diesel particles (Bjørseth, 1983; see p. 80). The soluble organic fraction of diesel particles usually accounts for 15–45% of the total particulate mass. Figure 1 shows the distribution of mass for the various subfractions of a standard heavy-duty diesel particulate extract (Schuetzle *et al.*, 1985).

Fig. 1.

Analytical scheme for fractionation of heavy-duty diesel partic
Bureau of Standards Standard Reference Material (NBS SRM)

The nonpolar fractions contain hydrocarbons derived from unburnt fuel and lubricating oil. In addition, many PAHs in the molecular weight range of 178–320 have been identified. Some PAHs and thioarenes identified in diesel engine exhausts are listed in Table 6 (Tong & Karasek, 1984). The alkyl substituted derivatives of at least some PAHs are more abundant than the parent hydrocarbons. If the amount of dimethylanthracenes or dimethyl-phenanthrenes is taken as 1.00, the relative abundance of anthracene or phenanthrene is 0.27, that of the methyl derivatives, 0.54, and that of the trimethyl derivatives, 0.37 (Schuetzle *et al.*, 1981). Since moderately polar fractions have been found to contribute a significant proportion of the mutagenicity of the total soluble organic fraction, much effort has been expended to characterize them. The distribution of PAH derivatives in one light-duty diesel particulate extract is given in Table 7 (Schuetzle, 1983).

Table 6. Polycyclic aromatic comounds identified or tentati
particulate extracts[a]

Compound	Molecular weight
Acenaphthylene	152
Fluorene	166
Trimethylnaphthalene	170
Anthracene	178
Phenanthrene	178
Dimethylbiphenyl	182

Table 6.

Polycyclic aromatic comounds identified or tentatively identified in three light-duty diesel particulate extracts.

Table 7. Distribution of polycyclic aromatic hydrocarbon (F
fraction[a] of a light-duty diesel particulate extract[b]

PAH derivative	Fraction (
PAH ketones	24.7
PAH carboxyaldehydes	20.6
PAH acid anhydrides	9.1
Hydroxy-PAH	19.0
PAH quinones	12.0
Nitro-PAH	0.5
Other oxygenated PAH	14.1

Table 7.

Distribution of polycyclic aromatic hydrocarbon (PAH) derivatives in the moderately polar fraction of a light-duty diesel particulate extract.

The types of nitroarenes identified in diesel vehicle particles are listed in Figure 2. More than 50 nitrated derivatives of PAHs have been identified tentatively and 23 have been identified positively. These compounds occur in very low concentrations in comparison with the other PAH derivatives (Schuetzle & Jensen, 1985). The concentrations of nitroarenes measured in a light-duty diesel particulate extract by a method with a 0.3-ppm (μg/g) limit of detection are given in Table 8. Overall, about 40% of the direct mutagenicity of diesel particulate extracts can be accounted for by 1-nitro-3-acetoxypyrenes, dinitro-pyrenes and 1-nitropyrene (Manabe *et al.*, 1985). Studies in which biological and other methods were used to estimate the contribution of nitro-PAH to the genetic effects of diesel emissions are discussed in section 3.2.

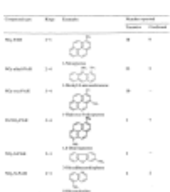

Fig. 2.

Types of nitro-polycyclic aromatic hydrocarbons (PAHs) and nitroheterocyclic compounds identified in diesel emission particulates[a].

Table 8. Concentrations of some nitroarenes (μ g/g) in dies

Compound	Concentration
1-Nitronaphthalene[a,b]	0.95[c]
2-Nitronaphthalene[a,b]	0.35[c]
2-Nitrofluorene[b]	1.2[c]
1-Nitropyrene[b]	75
3-Nitrofluoranthene	3.5[c]
8-Nitrofluoranthene	1.3[c]
6-Nitrobenzo[*a*]pyrene[b]	4.2[c]

Table 8.

Concentrations of some nitroarenes (μ g/g) in diesel particulate extracts.

Examples of compounds in the polar soluble organic fraction of diesel vehicle particulate extracts include phenols (1-naphthol, 2-naphthol, cresol), acids (benzoic, naphthoic, phthalic and phenathroic acid), bases (benzacridines, dibenzacridines, pyridine, aniline) and some polar nitroarenes (National Research Council, 1982).

(d) Effect of engine source, fuel and operating conditions on emissions

In this section, the influence of several factors on the emission of four compounds — pyrene, benzo[*a*]pyrene, benzo[*e*]pyrene and 1-nitropyrene — is summarized (Schuetzle & Frazier, 1986). Particulate samples were collected from four diesel vehicles produced by four major manufacturers, which run on a variety of diesel fuels under various operating conditions (see Table 4). Overall, the emission rates of these compounds varied by no more than a factor of three.

The emission of PAHs was increased by a factor of three to four when the aromaticity of the fuel (content of aromatic hydrocarbons) increased from 22 to 55%, resulting in 2–24 and 2–60 mg/l pyrene, respectively. Exhaust pipe emissions of pyrene were not related to the pyrene content of the fuel, indicating that the primary source of PAHs is their formation during the combustion process and not their presence in unburnt fuel in the exhaust. In contrast, fuel aromaticity had no effect on the emission of 1-nitropyrene, suggesting that nitrogen oxides, and not pyrene, are the limiting factor in the chemical formation of 1-nitropyrene (Schuetzle & Frazier, 1986).

Table 4 also presents data that demonstrate the effect of engine operating conditions on diesel emissions. Changes in engine timing have little effect on PAH emissions, but the 1-nitropyrene content increased by several fold, correlating with the increase in emissions of nitrogen oxides. Engine speed and load significantly affect the emission of nitroarenes in engine exhaust, as shown in Table 9. High load and high speed raise engine and exhaust temperatures, enhancing the partial oxidation of nitroarenes. Thus, the emission of nitroarenes, and possibly of other oxygenated PAH species, is highly dependent on source conditions (Schuetzle & Perez, 1983).

Table 9.

Effects of engine operating conditions on concentration of nitro-polycyclic aromatic hydrocarbons in heavy-duty diesel particles.

1.3. Gasoline engine exhaust

All research to date indicates that emissions from spark-ignition engines run on unleaded gasoline are qualitatively similar to the emissions from diesel engines (Alsberg *et al.*, 1984; see Tables 3, 6 and 10). However, there are significant quantitative differences (see section 1.4). The data reported below relate to four-stroke engines, unless otherwise specified, although the emissions from two-stroke engines are qualitatively similar. Since several PAHs have been shown to be carcinogenic (IARC, 1983, 1987a), much research has been directed to the identification of individual compounds in these emissions (Table 10; Grimmer *et al.*, 1977). As for diesel fuel, the emission of PAHs (measured as benzo[*a*]-pyrene) varies with the aromatic content of the gasoline (Schuetzle & Frazier, 1986).

Table 10.

Polycyclic aromatic hydrocarbons identified in gasoline engine fuel and exhaust (μg/l of original or combusted fuel)[a].

Little detailed information is available on the occurrence of PAH derivatives (e.g., nitroarenes) in gasoline exhaust. Some acridines, including benz[*c*]acridine, dibenz[*a,h*]-acridine and dibenz[*a,j*]acridine, have been identified in gasoline engine exhaust (Sawicki *et al.*, 1965). 1,2-Dichloroethane (38–2900 μg/m^3) and 1,2-dibromoethane (22–1360 μg/m^3) have been measured in exhausts from engines run on leaded gasoline (Tsani-Bazaca *et al.*, 1981). Methyl bromide has been found in the exhaust of cars using leaded (71–217 μg/m^3) and unleaded (<4–5 μg/m^3)

gasoline (Harsch & Rasmussen, 1977).

The particles emitted from gasoline engines run on leaded fuel are physically different from particles emitted from diesel engines. Particles from gasoline engines are discrete, compact and dense. The mass median equivalent diameter of the particles, as measured along roads at steady speed (≃80 km/h) is 0.03–0.04 μm but increases to 0.2–0.4 μm when the vehicle is operated under cyclic conditions. Particulate mass comprises ammonium and lead sulfates, lead bromochloride and lead oxide, which are soluble in water. The proportion of organic solvent-extractable material is much smaller than that typically found in diesel particles (see Table 3). The remaining elemental carbon core of the particle has fewer sites available for adsorption of organic material, but quantitative comparisons with diesel particles are not available (Chamberlain *et al.*, 1978).

1.4. Comparison of emissions from different engines

A number of studies have recently been undertaken to determine emissions from a wide variety of engines. Levels of selected gas and particulate species and of total particulate matter from light-duty diesel, heavy-duty diesel and gasoline engines (with and without catalytic converters) in 1980–85 are summarized in Table 3.

The levels of carbon monoxide and nitrogen oxides emitted are similar for light-duty diesel and for gasoline engines with catalytic converters. The particulate emission levels from light-duty and heavy-duty diesels are two to ten and eight to 40 times greater, respectively, than the emission levels from catalyst equipped light-duty gasoline engines (Table 3).

Fuel evaporation (e.g., from fuel lines and carburettors) has become relatively more important as a source of hydrocarbons since emissions from exhaust pipes have been reduced. Currently, fuel evaporation accounts for 30–60% of the total hydrocarbon emissions from passenger gasoline vehicles with catalytic converters. The vapour pressure of most current diesel fuels under ambient conditions is so low that emissions due to evaporation of diesel fuels are not significant (National Research Council, 1982).

The levels of PAHs in emissions from light-duty diesel engines and from gasoline engines without catalytic converters are comparable, although the diesel engines emit at least ten times more nitroarenes than the gasoline engines. Catalytic converters reduce the level of total PAHs by more than ten times (Table 3).

Nitric acid, which can react with PAHs to form nitroarenes, has been measured in diesel exhaust (Harris *et al.*, 1987), and Paputa-Peck *et al.* (1983) measured low-molecular-weight nitroarenes in diesel particles (Table 8). In view of the vapour pressure relationships, these nitroarenes would also be present in the gas phase (Hampton *et al.*, 1983). A value for 2-nitrofluorene is given in Table 3 (Schuetzle & Frazier, 1986). Liberti *et al.* (1984) found several gas-phase nitro-PAHs in diesel exhaust (Table 11).

Table 11. Gas-phase nitro-polycyclic aromatic hydrocarbo

Species	Relative conce
x-Nitrofluorene[b]	1.00
1-Nitronaphthalene	0.10
x-Methyl-1-nitronaphthalene[b]	0.20
2-Nitronaphthalene	0.30
2-Nitrofluorene	0.75
9-Nitroanthracene	0.50
Dinitronaphthalene	0.20

Table 11.

Gas-phase nitro-polycyclic aromatic hydrocarbons identified in diesel exhaust.

Aliphatic amines are present at very low concentrations in exhausts from cars equipped with catalytic converters. Total emissions were less than 2.2 mg/mile (1.4 mg/km), and average emission rates of monomethylamine and dimethylamine were no more than 0.3 and 0.1 mg/mile (0.2 and 0.06 mg/km), respectively (Cadle & Mulawa, 1980). Levels of 0.1–1.4 μg/m^3

N-nitrosomorpholine and 0.5–17.2 $\mu g/m^3$ *N*-nitrosodimethylamine were measured in crankcase gases of heavy-duty diesel engines (Goff *et al.*, 1980). In one study in a vehicle tunnel, no *N*-nitrosodimethylamine was detected (detection limit, 0.1 $\mu g/m^3$) in the air (Hampton *et al.*, 1983).

2. Occurrence and Analysis

2.1. Occupational exposure

The occupational exposures to components of diesel engine exhaust of several groups of workers, including railroad workers, workers in mines with diesel-powered equipment, bus garage workers, truck drivers, fork-lift truck operators and fire-fighters, have been studied. The exposures of toll-booth attendants, border-station inspectors, traffic-control officers, professional drivers (truck, bus, taxi), car mechanics, car ferry workers, parking garage attendants and lumberjacks to components of gasoline engine exhaust have also been studied. Many workers are exposed to both diesel and gasoline engine exhausts. The extent of exposure to these specific exhausts in different occupational groups depends on many factors, such as country and time period considered; in addition, environmental exposure to exhausts (see section 2.2) influences the total exposure of workers.

A primary focus of this monograph is on human exposure to respirable particles emitted by diesel and gasoline engines. It is important in studying such exposures that the relative contributions from various types of engine exhaust be distinguished from each other and from those of other particulate sources. In source apportionment studies, chemical tracers are used which are unique to the combustion source, representative of the total particulate emissions, chemically stable, present in abundance, and easy to collect and analyse. Many compounds that may appear to be good tracers are not representative of the total sample, varying significantly with the fuel source, temperature of combustion and other factors.

Methods have been developed and used for apportioning the contribution of vehicle emissions from various sources. These are based upon the use of barium (a diesel fuel additive) and of lead for diesel and gasoline vehicles, respectively (Hampton *et al.*, 1983; Johnson, 1988). The method may not be suitable for characterizing certain occupational exposures (e.g., mining, train and heavy-equipment operations) because barium is not typically used as a fuel additive in these applications.

Several new methods have been developed to apportion sources of occupational exposure to engine exhaust. For example, Currie and Klouda (1982) used measurements of $^{14}C/^{12}C$ to distinguish between carbon compounds in particles derived from combustion of old carbon sources (e.g., petroleum) and of contemporary carbon sources (e.g., wood, tobacco). Johnson *et al.* (1981) developed a thermal-optical analytical technique which has been used to apportion samples containing cigarette smoke and diesel exhaust particles (Zaebst *et al.*, 1988). Cantrell *et al.* (1986) indicated that size selective sampling is a suitable method for distinguishing diesel particles from other particles in coal mines.

Unfortunately, for the studies of exposure reviewed in this section, the source apportionment techniques described above were not available. The data on components of engine exhausts, such as carbon monoxide, nitrogen oxides and sulfur dioxide, can be used to indicate the presence of engine exhaust but cannot be used to apportion exposures. Thus, information on single components reported in these studies cannot be used to rank relative exposures to total engine exhaust reliably, due to the variable relationships among the components resulting from factors such as engine speed, engine load and control techniques.

It should also be noted that occupational exposures to PAHs can be measured, but samples are typically not large enough to allow quantitative measurements to be made.

(a) Workers whose predominant exhaust exposure is that from diesel engines

(i) Railroad workers

Diesel locomotives were introduced on railroads in Canada and the USA in 1928 and in Germany in 1932. In the USA, the change-over to diesel engines was 95% complete by 1959 (Garshick *et al.*, 1988).

Hobbs *et al.* (1977) reviewed the earlier literature on air contaminants in the environment of train crews. In addition, measurements of air contaminants in locomotives and cabooses were made during their passage through tunnels and during freighting and switch-yard operations. These authors estimated 8-h time-weighted averages (TWAs) for combined tunnel and freight operations, and Heino *et al.* (1978) evaluated levels of diesel exhaust components in locomotive cabs and round-houses in Finland (Table 12).

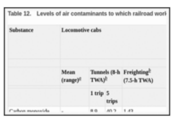

Table 12.

Levels of air contaminants to which railroad workers are exposed.

As part of a large epidemiological study on railroad workers, Hammond *et al.* (1984) presented data on components of diesel exhaust. The respirable particles collected had a dichloromethane extractable fraction of 46% (liquid chromatography fractionation), which was found to be composed of 45% aliphatic hydrocarbons, 33% olefinic and aromatic hydrocarbons and 23% polar compounds. The aromatic fraction included phenanthrene and alkylated phenanthrenes.

Woskie *et al.* (1988a) conducted an industrial hygiene survey of the US railroad industry as a part of epidemiological studies reported by Garshick *et al.* (1987, 1988). Personal exposure to respirable particles was measured and then corrected for the estimated contribution of cigarette smoke particulates. These data are presented in Table 13. Corrections for cigarette smoke were made by analysing composited respirable particulate samples for nicotine content; an adjusted respirable particulate concentration was then calculated for each job group, and the applicable average fraction of cigarette smoke was subtracted from the average respirable particulate concentration.

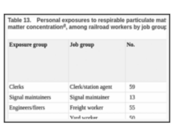

Table 13.

Personal exposures to respirable particulate matter, and adjusted respirable particulate matter concentration, among railroad workers by job group.

(ii) Mine workers

The first diesel engine-powered vehicles in underground mines were used in Germany in 1927 (Kaplan, 1959), and they are now used widely throughout the world (Daniel, 1984). Other sources of exposure in mines include activities that produce large quantities of airborne particles, and blasting, which produces particles and gases such as methane and sulfur dioxide. In addition, these gases may be released spontaneously from the ore bed or from surrounding geological formations. Some exposures that may occur in mines, depending on the ores present, were evaluated by previous IARC working groups; these include radon (IARC, 1988), silica (IARC, 1987b), nickel (IARC, 1987a), chromium (IARC, 1987a) and asbestos (IARC, 1987a).

Lassiter and Milby (1978) gave examples of the levels of carbon monoxide and nitrogen dioxide that can be found at the diesel operator's position in an underground mine. On the basis of 2977 samples taken in 1963–72, the average concentration of carbon monoxide was 8.5 ppm (9.7 mg/m^3), 5% of the samples containing >50 ppm (>57 mg/m^3); 1504 samples contained an average concentration of 0.2 ppm (0.4 mg/m^3) nitrogen dioxide, with 0.75% above 3 ppm (>6 mg/m^3) and one sample >5 ppm p(>10 mg/m^3).

A study conducted for the US Bureau of Mines on levels of diesel exhaust components in 24 mines included two coal mines (Holland, 1978); the results are shown in Table 14. Anthracene and phenanthrene were found at measurable levels, but five other PAHs (benz[*a*]anthracene, benzo[*a*]pyrene, benzo[*e*]pyrene, chrysene and pyrene) were not.

Table 14. Levels of diesel exhaust components (mg/m^3) in

Contaminant	Diesel exhaust source		
	No. of samples	Mean	Range
Carbon monoxide	6	140	11.5–344
Nitric oxide	3	6.3	<0.1–16.5
Nitrogen dioxide	5	16.8	1–40
Sulfur dioxide	5	0.3	0–<1
Sulfuric acid	4	12.8	<0.2–46
Formaldehyde	10	7	0–42

Table 14.

Levels of diesel exhaust components (mg/m^3) in 24 US mines.

Levels of air contaminants due to diesel emissions in other coal mines are summarized in Table 15.

Table 15. Levels of air contaminants (mg/m^3, unless otherw

Contaminant	Concentration	Samplin
Carbon monoxide	8 (mean)	Personal
	0–2.3	Personal
	3.9–26.7	Average samples
Nitrogen oxides	0–5.2 ppm	Average samples
Nitrogen dioxide	0.7 (mean)	Personal
	0.06–0.5	Personal

Table 15.

Levels of air contaminants (mg/m^3, unless otherwise specified) in coal mines.

The environment of six potash mines in New Mexico, USA, was investigated in 1976 (Attfield *et al.*, 1982). The use of diesel equipment in these mines had begun between 1950 and 1966, and seven to 57 diesel-powered units were used. Environmental concentrations in production jobs and other areas in the six mines (based on 25–34 samples) were 6–10 mg/m^3 carbon monoxide, 0.2–6.6 mg/m^3 nitrogen dioxide and 0.1–4.0 ppm aldehydes.

Cornwell (1982) evaluated employee exposure to diesel emissions at a molybdenum mine in Colorado, USA. Diesel-powered equipment used in the mine included drills, five-yard load haul-dumps and two-yard load haul-dumps. Personal and area sampling was conducted for oxides of carbon, nitrogen and sulfur, formaldehyde, respirable particulate matter, PAHs and cyclohexane-soluble material (sum of particulate and gaseous samples). The results are shown in Table 16.

Table 16. Air contaminant levels in a molybdenum mine[a]

Contaminant	Concentration
Carbon monoxide	<1.1–6.1 mg/m^3
Nitric oxide	ND–9.0mg/m^3
Nitrogen dioxide	ND–6.4
	0.08–0.78 mg/m^3
	0.06–4.32 mg/m^3
Sulfur dioxide	ND–0.05 mg/m^3
Formaldehyde	ND

Table 16.

Air contaminant levels in a molybdenum mine.

Daniel (1984) reported 0.2–1.3 ppm (0.4–2.6 mg/m^3) nitrogen dioxide, 3.1–8.7 ppm (3.8–10.7 mg/m^3) nitric oxide and 0.5–2.1 ppm (0.6–2.4 mg/m^3) carbon monoxide in a South Dakota, USA, gold mine when samples were taken during the operation of a diesel mine vehicle. He found 0.3–0.6 ppm (0.8–1.6 mg/m^3) sulfur dioxide, 0.1–0.3 mg/m^3 sulfate, 0.4–1.7 mg/m^3 respirable combustible dust and 1.1–4.4 mg/m^3 total respirable dust.

(iii) Bus garage and other bus workers

Exposures of bus garage and other bus workers to diesel exhaust emissions are listed in Table 17. Few studies addressed other exposures that may occur in bus garages, such as to metal fumes from welding and similar operations and to asbestos during brake servicing.

Table 17. Levels of air contaminants in bus garages (mg/m

Contaminant	Concentration	Sampling
Carbon monoxide	2–18	Diesel areas
	7–11	Terminal (background)
	22–46	Terminal (bus arrival/departure)
	6–8	Package receiving area

Table 17.

Levels of air contaminants in bus garages (mg/m^3, unless otherwise specified).

The table includes the results of analyses of air during operations in two diesel bus garages in Egypt (El Batawi & Noweir, 1966) and measurements of airborne concentrations of diesel exhaust components in three bus repair facilities in Denver, CO, USA (Apol, 1983). In the latter study, sampling took place in March 1982 at several locations within each facility during peak dispatch and return times. A carbon monoxide level of 195 mg/m^3 was recorded in one garage early in the morning near buses with gasoline engines that were starting up. The author stated that exposure of drivers to this and higher levels for 10–15 min is possible. Pryor (1983) also conducted an industrial hygiene survey of diesel exhaust at the garage of a bus company in Denver, CO, in 1982, where buses with gasoline engines parked nearby. Area samples were taken to measure carbon monoxide, sulfur dioxide, nitrogen dioxide, total particulate matter and formaldehyde in the terminal and in package-receiving areas (Table 17). The high concentrations of carbon monoxide in the terminal dropped to the background concentration within a few minutes of bus arrival or departure. The higher levels of carbon monoxide in the reservation room and at the inlet corresponded to peak car traffic in the parking area, and dropped to a background level within 10–15 min of the end of the peak traffic.

Waller *et al.* (1985) measured pollutant levels in two diesel bus garages in London, UK, in 1979. Sampling took place close to the buses in an area of only limited worker exposure, so the data are said by the authors to present extreme upper limits only. Table 17 gives data on levels of PAHs near the door of one garage during two different periods. del Piano *et al.* (1986), reporting in an abstract, found concentrations of several air contaminants in Italian bus garages surveyed over two years, as shown in the table. Gamble *et al.* (1987a) studied 232 workers in four diesel bus garages in the USA. Mean TWA concentrations of respirable particles and nitrogen dioxide in personal samples, combined over three shifts and for all four garages, were reported (Table 17). Ulfvarson *et al.* (1987) measured personal exposures of workers in a bus garage with both large and small diesel-powered vehicles as well as gasoline-powered ones. Storage, engine warm-up, refuelling, washing and repairs were all performed at the garage. Elevated concentrations, especially of diesel exhaust, accumulated in garage bays in the morning, afternoon and evening when most of the buses were coming or going. Specific exposures in the garage as measured by personal sampling during these periods of high activity are detailed in Table 17.

(iv) Truck drivers

Ziskind *et al.* (1978) measured the concentrations of several gases in the cabins of heavy-duty diesel trucks under a variety of conditions. Concentrations of carbon monoxide, nitric oxide and nitrogen dioxide in the air and in the cabins were measured continuously. The maximal total concentrations in cabins measured during idling and road testing were as follows: carbon monoxide, 30 ppm (34 mg/m^3); nitric oxide, 2 ppm (2.5 mg/m^3); nitrogen dioxide, 3 ppm (6 mg/m^3). The maximal self-contamination concentrations (total cabin concentration minus ambient concentration) were: carbon monoxide, 10.5 ppm (12 mg/m^3); nitric oxide, 1.55 ppm (1.9 mg/m^3); nitrogen dioxide, 0.7 ppm (1.4 mg/m^3). The authors found a correlation between vehicle-induced concentrations of specific gases in cabins and several testing parameters, including condition of windows, type of cabin configuration and the presence of exhaust leaks and underside cabin openings.

The results of a study of truck drivers on roll-on roll-off ships by personal sampling over an entire work shift (Ulfvarson *et al.*, 1987) are given in Table 18.

Table 18.

Levels of airborne contaminants measured for truck drivers on Swedish roll-on roll-off ships (mg/m^3).

(v) Fork-lift truck operators

Breathing zone exposures were measured in an army ammunition depot in the USA in the winter of 1983 during the use of diesel-powered fork-lift trucks. PAHs, sulfur dioxide and carbon monoxide levels were below the detection limits [not given], while the concentration of particulate matter ranged from <0.01 to 1.3 mg/m^3, that of nitrogen dioxide from 0.1 to 3.2 ppm (<0.2–6.4 mg/m^3) and that of total sulfates from <10 to 32 $\mu g/m^3$. Area samples taken during the same test provided the following mean values: 1.1–2.6 ppm nitrogen oxides, 1.2–3.3 ppm (1.4–3.8 mg/m^3) carbon monoxide, 0.2–0.4 ppm (0.4–0.7 mg/m^3) sulfur dioxide and 7.4–8.5 ppm total hydrocarbons (Ungers, 1984). In a follow-up study in the summer of 1984 (Ungers, 1985), the level of PAHs was below the detection limit (3 ng/m^3), while breathing zone values during warehouse operations were in the following ranges: particles, 0.5–5.0 mg/m^3; sulfate, 0.02–0.6 mg/m^3; sulfite, <0.02–0.09 mg/m^3; nitric oxide, 1.6–13.6 mg/m^3; and nitrogen dioxide, 0.7–2.5 mg/m^3.

(vi) Fire-fighters

Fire-fighters are frequently and repeatedly exposed to diesel engine exhaust and other combustion products (Froines *et al.*, 1987). Exposure to diesel exhaust occurs during response to an incident and in the fire station. When personal sampling was used to determine the exposures of fire-fighters in fire stations in three US cities — Boston, New York and Los Angeles — in 1985, total airborne particle levels (TWA) ranged from <0.1 to 0.48 mg/m^3. The authors predicted an average total particulate exposure of roughly 0.3 mg/m^3 on a typical day in Boston or New York. With an estimated 0.075 mg/m^3 contributed by background and smoking, exposure would be to approximately 0.225 mg/m^3 diesel exhaust particles and 0.054 mg/m^3 of dichloromethane extractable material. Sampling during simulated ‘worst case’ exposures in Los Angeles fire stations gave an upper bound concentration of 0.748 mg/m^3 particles.

(b) Workers whose predominant exhaust exposure is that from gasoline engines

(i) Toll-booth workers

Ayres *et al.* (1973) evaluated exposure to engine exhaust for perions who worked in both a tunnel and in an adjacent toll plaza in New York City, USA (Table 19). The authors reported a close correlation among the concentrations of various pollutants, such that the level of carbon monoxide could be considered to be indicative of total automotive pollution levels. Following the installation of ventilation systems in toll booths, carbon monoxide levels dropped to 16–18 mg/m^3.

Table 19.

Levels of air contaminants (mg/m^3, unless otherwise specified) to which toll-booth operators are exposed.

A study of exposure to carbon monoxide of toll collectors on an interstate highway near Louisville, KY, USA, was reported by Johnson *et al.* (1974). Testing was conducted over a 12-day period in April 1973, and ambient concentrations of carbon monoxide, lead and manganese at three booths were determined as an overall mean 8-h TWA (Table 19). Carboxyhaemoglobin (COHb) levels in the workers were measured before and after shifts; typical pre-shift levels were 0.8–1.5%; the post-shift mean was 3.9%, with a range of 1.6–11.7%.

Burgess *et al.* (1977) evaluated the exposure of toll-booth collectors in the Boston area, at a tunnel and at two interchanges during 1972–74 (Table 19). Airborne lead levels in the work environment were roughly four times ambient urban levels; correlated increases were found in the hair and blood of the workers.

(ii) Border-station inspectors

Cohen *et al.*(1971) studied a group of such workers at the San Ysidro, CA, USA, station in 1969. Ambient and expired carbon monoxide levels were measured over roughly a 24-h period encompassing three shifts. Average hourly carbon monoxide levels were 15 mg/m^3 (8.00 to 16.00 h), 75 mg/m^3 (16.00 to 0.00 h) and 131 mg/m^3 (0.00 to 8.00 h); hourly levels ranged from 6 to 195 mg/m^3. Taking data from all shifts combined, nonsmoking individuals had significantly higher expired carbon monoxide levels at the end of the shift than before the shift, corresponding to COHb levels of 3.6% after the shift and 1.5% before the shift. For smokers, the estimated pre- and post-shift COHb levels, estimated from carbon monoxide in expired air, were 4.8% and 6.4%, respectively.

Environmental sampling was conducted by the National Institute for Occupational Safety and Health at a number of US border crossing facilities in 1973–74, to investigate the exposure of Federal border inspectors (Kronoveter, 1976). Inspectors are rotated between different work locations through a shift, and the facilities are operated three shifts per day, seven days per week. Mean 8-h average carbon monoxide levels ranged from 2 to 54 ppm (2.3–62 mg/m^3) with maximal 8-h average levels of 3–73 ppm (3.4–83.6 mg/m^3). Sampling for total particulate matter revealed concentrations from <1.0 to 4.3 mg/m^3. Ozone levels ranged from <0.01–0.08 ppm(<0.02–0.16 mg/m^3), and concentrations of lead ranged from <10 to 20) μg/m^3.

deBruin (1967) measured COHb levels in 13 nonsmoking Dutch customs officers stationed at four remote sites in 1965. The mean concentrations at the four locations studied ranged from 0.8 to 1.5% before work and 1.1 to 3.0% after work.

(iii) Traffic-control officers

deBruin (1967) measured COHb levels in nonsmoking and smoking traffic policemen in Rotterdam and Amsterdam, the Netherlands. Results are shown in Table 20. Ambient carbon monoxide levels in Rotterdam at the time of that study averaged 5–15 ppm (6–17 mg/m^3) at crossings and crowded streets, ranging up to 50 ppm (60 mg/m^3).

Table 20. Carboxyhaemoglobin (COHb) levels in traffic con

Group	No. of subjects	% COH
		Before w
Rotterdam		
Exposed nonsmokers (1-4-h average)	36	0.92 ± 0.
Control nonsmokers (office)	16	0.85 ±0.1
Amsterdam		

Table 20.

Carboxyhaemoglobin (COHb) levels in traffic control officers.

Göthe *et al.* (1969) measured COHb levels in 76 traffic policemen in three Swedish towns. Ambient carbon monoxide levels were not given, but in Stockholm nonsmoking officers who had controlled traffic in either the morning or afternoon rush hours had an average COHb of 1.2% ± 0.39; smokers had a level of 3.5% ± 1.17. In Malmö and Örebro, the levels were 0.8% ± 0.14 and

0.6% ± 0.38 for nonsmokers and 5.0% ± 2.44 and 2.4% ± 1.10 for smokers. The authors noted that unexposed persons in Sweden have an average COHb of 0.5%.

(iv) Professional drivers

deBruin (1967) determined COHb levels before and after work in nonsmoking taxi, delivery van and motor hearse drivers in Amsterdam, the Netherlands, in 1965. The mean COHb levels before and after work were 2.0 and 2.15 for 13 taxi drivers exposed for 7 h; 1.5 and 1.65 for six delivery men exposed for 8 h; and 2.0 and 2.45 for four drivers of motor hearses exposed for 6.5 h. The average difference was 0.25%, which was significant ($p > 0.01$).

Maruna and Maruna (1975) investigated δ-aminolaevulinic acid elimination in the urine of 200 taxi drivers in Vienna, Austria, as a means of measuring lead burden. The authors found that 26.5% of the taxi drivers had normal levels (<5.0 mg/1 urine), 27% had borderline levels (5.1–7.0 mg/l) and 46.5% had elevated levels (>7.1 mg/1). The authors concluded that the source of the lead was the atmosphere polluted by automobile engine emissions.

del Piano *et al.* (1986), reporting in an abstract, measured hydrocarbons in the breathing zone of the drivers of an Italian bus company. The concentration of aliphatic hydrocarbons ranged from below 0.01 to 51.8 ppm and that of aromatic hydrocarbons, including benzene (<0.01–9,6 ppm; <0.03–31 mg/m^3), from below 0.01 to 36.7 ppm. [The Working Group was unable to determine if these workers were exposed mainly to gasoline or to diesel exhausts.]

(v) Ferry workers

Purdham *et al.* (1987) studied the potential exposure of stevedores employed in ferry operations to diesel and gasoline exhaust emissions. The constituents considered were total particles, PAHs, aldehydes, nitrogen oxides, sulfur dioxide and carbon monoxide. Exposures to particles averaged 0.50 mg/m^3 (range, 0.06–1.72 mg/m^3); carbon monoxide levels were detected, in the range of 20–100 ppm (23–115 mg/m^3), only when gasoline-powered vehicles were being loaded onto the ferries. The levels of the other constituents did not differ from the background.

Ulfvarson *et al.* (1987) measured personal exposures to airborne contaminants on two types of car ferries during loading and unloading. On the first one, a 2-h route, loading and unloading of vehicles took an average of 20 min; on the second, a 20-min crossing, loading and unloading times were not specified. The results are shown in Table 21.

Table 21. Levels of airborne contaminants measured on Sv otherwise specified)[a]

Contaminant	Car ferry (2-h run)[b]
Carbon monoxide	13–100
Nitrogen dioxide	<0.6
Sulfur dioxide	<1.8
Benzene	⩽0.2
Toluene	<0.2
Formaldehyde	0.03–0.31

Table 21.

Levels of airborne contaminants measured on Swedish car ferries (mg/m^3, unless otherwise specified).

(vi) Exhaust system mechanics

Chambers *et al.* (1984) measured the lead levels in airborne particles and deposited dusts in three centres for the replacement of passenger car exhaust systems. Airborne concentrations of lead collected with environmental and personal samplers ranged from 8.8 to 55.4 μg/m^3, with peak concentrations ranging from 20.2 to 92.7 μg/m^3 when floors were being swept during sampling. Dust concentrations in samples from floors and shelves ranged from 0.14 to 3.02% lead by weight. Dust in samples collected from inside exhaust systems ranged from 0.20 to 58.7% lead by weight, according to site.

(vii) Motor vehicle inspectors

An industrial hygiene survey of 38 motor vehicle inspection stations in New Jersey, USA, in 1973–74 indicated that inspectors were exposed to carbon monoxide at a TWA average of 10–24 ppm (11–28 mg/m^3); measurements in semi-open and enclosed stations were 11–40 ppm (13–46 mg/m^3) and those in outdoor stations, 4–21 ppm (5–24 mg/m^3). Average COHb levels in nonsmokers were 2.1% before a shift and 3.7% after a shift ($p > 0.01$) (Stern *et al.*, 1981).

(viii) Parking garage attendants

Ramsey (1967) determined both airborne carbon monoxide levels and blood COHb levels for 38 parking attendants in six garages in Dayton, OH, USA. These garages typically had four floors and a capacity of 300–500 cars. Hourly air sampling revealed a carbon monoxide concentration in the range of 8–275 mg/m^3, with a mean of 67.4 ± 28.5 mg/m^3 for 18 daily averages. COHb levels were determined in employees prior to and after the work day on Monday; a group of control students was also monitored. The 8:00 and 17.00 h levels were 1.5 ± 0.83 (SD) and 7.3 ± 3.46 for 14 nonsmokers; and 2.9 ± 1.88 and 9.3 ± 3.16 for 24 smokers. In controls, the levels were 0.81 ± 0.54 for ten nonsmokers and 3.9 ± 1.48 for 17 smokers. The differences between 8.00 and 17.00 h levels in garage workers, and between garage workers at 17.00 h and controls are highly significant ($p < 0.0001$).

(ix) Lumberjacks

Nilsson *et al.* (1987) studied the composition of exhaust emissions from two-stroke chain-saw engines run on gasoline and estimated operator exposure to chain-saw exhaust under snow-free conditions and with snow on the ground (Table 22). The presence of snow affects techniques used in cutting.

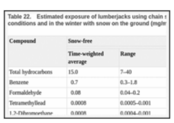
Table 22. Estimated exposure of lumberjacks using chain s
conditions and in the winter with snow on the ground (mg/m

Compound	Snow-free	
	Time-weighted average	Range
Total hydrocarbons	15.0	7–40
Benzene	0.7	0.3–1.8
Formaldehyde	0.08	0.04–0.2
Tetramethyllead	0.0008	0.0005–0.001
1,2-Dibromoethane	0.0008	0.0004–0.001

Table 22.

Estimated exposure of lumberjacks using chain saws during loggng under snow-free conditions and in the winter with snow on the ground (mg/m^3).

2.2. Environmental exposure

In many studies, levels have been reported of combustion products of fossil fuels (including gasoline and diesel fuel) in ambient air. The most frequently determined combustion products have been particles, carbon monoxide, nitrogen oxides, hydrocarbons and lead. These data are difficult to use in assessing the adverse health effects of engine exhausts, for several reasons: (i) the occurrence of these combustion products in ambient air may arise from sources other than engine exhausts; (ii) primary engine emissions may undergo further reactions in the environment at variable rates; and (iii) exposed populations tend to be transient, with variable and poorly characterized exposures (for review, see Holmberg & Ahlborg, 1983). Thus, the occurrence in the environment of the components of engine exhausts has only limited relevance to this monograph and the data have not been reviewed in detail.

Environmental emissions of fossil fuel combustion products from various sources, including engine exhausts, have been estimated for the major categories of pollutants (National Air Pollution Control Administration, 1970; National Research Council, 1972a,b; Howard & Durkin, 1974; National Research Council, 1977a,b; US Environmental Protection Agency, 1979; Bradow, 1980; Cuddihy *et al.*, 1980; Morandi & Eisenbud, 1980; Cuddihy *et al.*, 1981; US Environmental Protection Agency, 1982; Cuddihy *et al.*, 1984; The Motor Vehicle Manufacturers Association of the United States, Inc. and the Engine Manufacturers Association, 1986; US Environmental Protection Agency, 1986).

On the basis of estimates made by the National Research Council (1972a,b, 1977a,b), Hinkle (1980) estimated the environmental contribution of motor vehicle emissions for four categories of air pollutants, as a percentage of total emissions from all sources (and, in parentheses, from man-made sources): carbon monoxide, 7.7% (70%); nitrogen oxides, 2.3% (51%); particles, 1×10^{-6}% (1.8%); and lead, 98% (98%). It has been estimated that motor vehicle emissions contribute 80% or more of the polynuclear organic matter in the air of some cities (IARC, 1983).

Other authors have placed the contribution of motor vehicle emissions to carbon monoxide and nitrogen oxides in the environment at higher levels, the principal basis for uncertainty being the global input of these oxides from natural sources. In the USA, vehicle engine exhausts were estimated to produce 83% of the carbon monoxide and 44% of the nitrogen oxides from man-made sources in 1976 (US Environmental Protection Agency, 1979, 1982). Very similar estimates were reported for carbon monoxide (86%) and nitrogen oxides (42%) in the UK in 1984, with vehicle exhausts accounting for much higher percentages (up to 85%) of nitrogen oxides at street level in urban environments (Williams, 1987).

Concentrations of a number of engine exhaust components have been measured in ambient air in urban and rural environments. Representative data for particles, hydrocarbons, lead and oxides of nitrogen are given in Table 23. Concentrations of particle-associated PAHs in ambient air have also been reported by others (Sawicki, 1976; Egan *et al.*, 1979; Edwards, 1983; Chuang & Petersen, 1985). Benzo[*a*]pyrene concentrations in the air of over 200 cities in 25 countries worldwide were summarized by Sawicki (1976).

Table 23.

Table 23. Measured concentrations in ambient air of selected pollutants associated with engine exhausts.

Apportionment studies using receptor modelling methods have been used to estimate that the contribution of motor vehicle emissions to inhalable airborne particulate matter (<2.5 μmdiameter) is 5–10% (Lioy & Daisey, 1986) or 15% of total fine particles (Bradow, 1980); mutagenicity was 50–74%. These studies were conducted in winter when domestic heating is the other major source of the pollutants in cities (Lewtas & Williams, 1986). Therefore, motor vehicles would be expected to make an even larger contribution to these pollutants during the rest of the year or on an annual average.

In the 1960s and early 1970s, typical average levels of lead in air in the USA ranged from 11.3 $\mu g/m^3$ or higher near busy motorways, to 1–4 $\mu g/m^3$ in the central areas of many cities, 0.1–0.5 $\mu g/m^3$ in suburban and rural areas, and as low as 0.02 $\mu g/m^3$ in remote areas (National Research Council, 1972b). These ranges appear to be typical for other industrialized nations where leaded gasoline is used in motor vehicles (Lahmann, 1969; Maziarka *et al.*, 1971; Bini, 1973; Fisher & LeRoy, 1975; Ball & Hume, 1977; El-Shobokshy, 1985; Al-Mutaz, 1987). With the increasing use of lead-free gasoline and increasing restrictions on use of leaded gasoline, these levels are declining (Fishbein, 1976; Falk, 1977; US Environmental Protection Agency, 1986).

Motor vehicles have been identified as significant sources of ambient air concentrations of a number of specific volatile hydrocarbons, such as benzene, toluene, xylenes and acetylene (Seifert & Ullrich, 1978; Whitby & Altwicker, 1978; Häsänen *et al.*, 1981; Tsani-Bazaca *et al.*, 1981). The inventory of the Japanese Environmental Agency for total hydrocarbon emissions in 1978 indicates that 39% of hydrocarbon emissions in Japan were from mobile sources (Wadden *et al.*, 1986). In the UK, vehicle emissions were estimated to account for approximately 33% of the volatile organic compounds (mainly hydrocarbons) released to the environment in 1984

(Williams, 1987).

1,2-Dichloroethane and 1,2-dibromoethane are also present in engine exhausts, and the time-dependent concentrations of benzene and 1,2-dibromoethane near roads are reported to be closely correlated (Tsani-Bazaca *et al.*, 1981). Formaldehyde, the principal aldehyde component of engine exhausts, is generally found in ambient air at 12–18 $\mu g/m^3$, but concentrations of 107–180 $\mu g/m^3$ have been reported in heavy traffic or photochemical smog (National Research Council, 1981; Grosjean, 1982; Anon., 1984).

Limits have been set on motor vehicle emissions in many parts of the world. The Council of the European Communities (Commission of the European Communities, 1988) has, for example, adopted a phased programme for the implementation of emission standards for carbon monoxide, hydrocarbons and oxides of nitrogen from gasoline- and diesel-powered vehicles. The US Environmental Protection Agency is also proceeding with the phased implementation of standards for gasoline- and diesel-powered vehicles specifying decreasing limits for exhaust emissions of carbon monoxide, hydrocarbons, oxides of nitrogen and particles (diesel only); evaporative hydrocarbon emissions are regulated for gasoline-powered vehicles only (US Environmental Protection Agency, 1987).

2.3. Analysis

(a) Sampling

Vehicle exhaust cannot be sampled correctly at temperatures that occur in or just behind the exhaust pipe because (i) the adsorption/desorption ratio on filter materials is disadvantageous at elevated temperatures and (ii) various exhaust constituents may be converted into artefacts on the filter, depending upon conditions, such as conversion of PAHs into nitroarenes (Pitts *et al.*, 1978; Lee, F.S.-C. *et al.*, 1980; Gibson *et al.*, 1981; Schuetzle & Perez, 1983; Grimmer *et al.*, 1988). Furthermore, exhaust is a heterogeneous material consisting of a gaseous phase and a particulate phase, and different techniques have been used for their collection, which can be classified into dilution tube sampling and raw gas sampling.

Measurements of vehicle emissions are typically made under laboratory conditions using chassis or engine dynamometer testing. Specified driving cycles are used to simulate on-road conditions. The Federal Test Procedure (FTP — also referred to as the LA-4, US-72 and the Urban Cycle; National Research Council, 1982) is the primary cycle used in the USA to approximate urban driving conditions (US Environmental Protection Agency, 1977). A similar test cycle is used in Europe (EEC Regulation 15/04; Commission of the European Communities, 1970).

Emissions collected for the purpose of chemical analysis and bioassays are typically referred to as particulate-phase emissions, gas-phase emissions and condensate emissions. ‘Particulate emissions’ are defined as all materials collected on a filter from a dilution tube at a dilution ratio of ≃15:1 and at ≃35°C (see below; Hare *et al.*, 1979). ‘Gas-phase emissions’ are defined as all materials which pass through a filter from the dilution tube under the conditions specified above. ‘Condensate/extract’ comprises: (i) material extractable by organic solvents (toluene, acetone) from particles collected on filters; (ii) residue obtained by evaporation of condensed water; and (iii) the evaporation residue after washing the condenser with organic solvents. Therefore, ‘condensate extract’ refers to organic compounds collected from exhaust by this procedure. In general, these compounds are less volatile than naphthalene and do not include nitrogen oxides, sulfur dioxide, C_1–C_9 hydrocarbons, benzene, most alkylbenzenes or inorganic substances such as elemental carbon and lead.

(i) Dilution tube sampling

Vehicle exhaust generated by driving schedules under standard conditions on a chassis dynamometer is diluted with a well-defined quantity of filtered air in a dilution tunnel, from which samples can be taken isokinetically after they have been cooled to about 50°C (Hare & Barnes, 1979). It has been shown that this device (presented schematically in Figure 3) closely simulates the process of dilution (Lee & Schuetzle, 1983; Schuetzle, 1983) under actual atmospheric conditions. The residence time of exhaust in the tunnel before being trapped on filters has been estimated to be less than 5 sec. Particles may be collected on filters, such as Teflon, or by electrostatic precipitators (Lee & Schuetzle, 1983). Hallock *et al.* (1987) recommended a liquid electrostatic aerosol precipitator which preserves submicronic particle size. Semivolatile compounds in the gaseous phase can be trapped by adsorption filter systems containing inorganic silica or, more satisfactorily, organic materials (e.g., XAD-2, Tenax, Chromosorb 102, Porapak; Jones *et al.*, 1976; Lee *et al.*, 1979; Lee & Schuetzle, 1983; Schuetzle, 1983). Schuetzle (1983) recommended XAD-2, since this material, in contrast to Tenax, does not react with nitrogen oxides.

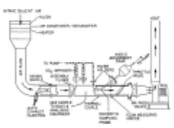

Fig. 3.

Dilution tube used for monitoring and collecting gas- and particulate-phase vehicle emissions[a].

Gases are sampled in bags either before entering the filter system or after having passed the adsorbent trap (see Figure 3). Stenberg *et al.* (1983) described a cryogradient technique which allows the separation of NO by cooling with a liquid nitrogen condenser.

(ii) Raw gas sampling

In most of these devices, the exhaust is partially condensed before separation by filter combinations. Initially, steel condensers were used (Stenburg *et al.*, 1961); since that time, a collecting device consisting of a vertical glass cooler and a micron filter of impregnated glass fibre with a separation degree of over 99.9% for particle sizes of 0.3–0.5 μm has been described (Grimmer *et al.*, 1973a; Kraft & Lies, 1981; VDI-Kommision, 1987; see Figure 4).

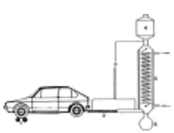

Fig. 4.

System for collecting undiluted vehicle exhaust[a].

Proportional raw gas sampling, resulting in samples of more manageable size, has been described (Stenberg *et al.*, 1981; Johnson, 1988). Various filter materials, as such or in combination, have been used to separate particles and semivolatile compounds from exhausts. Quartz and glass fibre, cellulose acetate (Millipore), polyvinylidene fluoride (Duropore), polytetrafluoroethylene (Teflon, Zefluor, Fluoropore), polyvinyl chloride, polyethylene and polycarbonate (Nucleopore) can separate >99.9% of submicrometer particulates (John & Reischl, 1978; Lee, F.S.-C. *et al.*, 1980; Lee & Schuetzle, 1983). Teflon has been cited as being superior to other materials in terms of separation efficiency and chemical inertness (Lee & Schuetzle, 1983; Schuetzle, 1983).

Semivolatile compounds in the gaseous phase can be separated out using polymer materials, such as Tenax, XAD-2 and Porapak, or with Chromosorb. Purification of these materials may be time-consuming since repeated washing (or Soxhlet extraction) with various solvents is required to remove organic impurities which interfere with analysis. Trapping of the gaseous phase can be carried out as in the case of dilution tube sampling, by (i) the cryogradient technique or (ii) gas bag collection.

One of the main problems described in the literature regarding the correct sampling of exhaust is avoidance of chemical conversion of sensitive compounds (e.g., PAHs) to artefacts (e.g., ketones, quinones, phenols, halides and nitroarenes). Losses of pyrene and perylene were studied after direct injection into exhaust near the end of the exhaust pipe, with recoveries of only 20–60% by gas chromatography and high-performance liquid chromatography (Lee *et al.*, 1979). Schuetzle (1983) found that more than 90% of pyrene and benzo[*a*]pyrene was lost through oxidation under the same conditions.

PAHs can react with nitrogen oxides, ozone or sulfuric acid under sampling conditions. Photooxidation during sample analysis may result in the formation of endoperoxides which then undergo rearrangement to yield hydroquinones and subsequently quinones, or in the formation of exoperoxides which yield ketones (Schuetzle, 1983). In the presence of nitric acid, nitrogen dioxide reacts with PAHs to yield nitroarenes (Pitts *et al.* 1978; Brorström *et al.*, 1983). On the assumption that nitroarene formation is acid-catalysed, diesel exhaust was collected with and without injection of ammonia during sampling; significantly higher amounts of 1-nitropyrene were found without ammonia injection at a sampling temperature of 100°C When passed through an exhaust-loaded filter, the particle-free gaseous phase enhanced the concentration of 1-nitropyrene. No such effect was observed when collecting filters were maintained at below 35°C (Grimmer *et al.*, 1988).

The artificial formation of nitroarenes during sampling procedures is still a matter of controversy (Gaddo *et al.*, 1984) and has been critically reviewed (Lee & Schuetzle, 1983).

It should be noted that the invariance of the PAH profile over the collection period is the essential precondition for correct sampling, since certain individual compounds are more sensitive to chemical reactions and/or evaporation effects.

(b) Extraction

Extraction of organic material from exhaust collected on filters is often incomplete owing to an inadequate choice of solvent or extraction time (Köhler & Eichhoff, 1967; Stanley *et al.*, 1967; for reviews see Jacob & Grimmer, 1979; Griest & Caton, 1983; Lee & Schuetzle, 1983). The recommended extraction procedure is on a Soxhlet apparatus or hot-solvent extraction with toluene, benzene, xylene (Köhler & Eichhoff, 1967; Grimmer *et al.*, 1982), benzene/ethanol (methanol, propanol; Swarin & Williams, 1980), dichloro-methane/methanol (Schuetzle *et al.*, 1985), toluene/ethanol (Schuetzle & Perez, 1981) or toluene/2-propanol (Lee & Schuetzle, 1983). Under these conditions, not only PAHs but also their more polar derivatives exhibit optimal extractability. This method also obviates the artefact formation that can occur with chloroform, dimethyl sulfoxide and other solvents used for extraction. In addition, Soxhlet solvent extraction results in higher recoveries of various PAHs than with cold ultrasonic extraction. If not analysed immediately after collection, the extract should be stored under nitrogen in the dark at 0°C or below.

(c) Clean-up and fractionation

After extraction, a small amount of organic material is obtained in a large volume of solvent. In order not to lose low-boiling constituents, the solution must be evaporated carefully. Vacuum rotatory evaporators with vacuum controller or specially designed devices are recommended (Dünges, 1979).

A fractionation scheme for vehicle exhaust combining condensed water, cooler washing (acetone) and filter extract (see Figure 5) has been described, which is based on liquid/liquid partition and chromatography on silica gel and Sephadex LH 20 (Grimmer & Böhnke, 1972; Grimmer *et al.*, 1973b, 1977; Lee & Schuetzle, 1983). An additional fractionation step using Sephadex LH 20 partition chromatography may be used. This method has also been used to characterize biologically active fractions; in some cases, the silica gel chromatography step has been deleted (Brune *et al.*, 1978; Grimmer *et al.*, 1984, 1987). A fractionation scheme for the preparation of biologically active fractions from diesel exhaust is given in Figure 6; nitroarenes are also separated by this method. A more complex fractionation scheme (Figure 7) can be used to separate the original exhaust extract into aliphatic compounds, aromatic compounds and moderately and highly-polar fractions after the removal of acidic and basic fractions (Petersen & Chuang, 1982). A similar scheme was used by Lee and Schuetzle (1983; see Fig. 1).

Fig. 5.

One scheme for fractionating automotive exhaust[a].

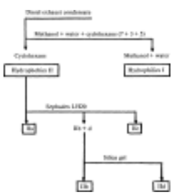

Fig. 6.

One scheme for fractionating diesel exhaust condensate[a].

Fig. 7.

One scheme for extraction and fractionation of organic material in diesel particulate[a].

Methods for the separation and identification of nitroarenes are given in the monograph on 1-nitropyrene. Organic halides, such as methyl bromide, chloroform, carbon tetrachloride, trichloroethane, tetrachloroethane and various brominated PAHs, have also been analysed in the exhaust of gasoline- and diesel-fueled vehicles (Harsch & Rasmussen, 1977; Alsberg *et al.*, 1985).

(d) Chemical analysis

In order to separate further the various fractions obtained by clean-up methods and to characterize and/or identify individual compounds simultaneously, thin-layer chromatography (TLC), high-performance liquid chromatography (HPLC) and gas chromatography (GC) have been used in combination with ultra-violet, visible and fluorescence spectrophotometry, mass spectrometry (MS) and more or less specific detection methods, such as flame ionization, nitrogen flame ionization and sulfur-specific and electron-capture detectors (Kunte, 1979; Lee & Schuetzle, 1983; Nielsen, 1983; White, 1985).

(i) Thin-layer chromatography (TLC)

Two-dimensional cellulose TLC with fluorescence detection is the recommended TLC method for PAH fractions from vehicle exhaust and has given results in good agreement with those obtained by GC (Kraft & Lies, 1981). A simple TLC screening method for the determination of benzo[*a*]pyrene, which is also applicable to vehicle exhaust, has recently been recommended by the International Union of Pure and Applied Chemistry (Grimmer & Jacob, 1987). The use of TLC for the analysis of PAHs has been reviewed (Daisey, 1983).

(ii) High-performance liquid chromatography (HPLC)

The basic advantages and disadvantages of HPLC in comparison to other techniques such as GC have been reviewed (Wise *et al.*, 1980; Wise, 1983). The method has been widely used for the detection and identification of organic constituents of vehicle exhaust, and results of determinations of PAHs in automotive exhaust condensate using HPLC have been compared with those obtained using capillary GC (Doran & McTaggart, 1974). A comparative study of different HPLC methods for the analysis of PAHs in diesel emissions has been carried out (Eisenberg & Cunningham, 1984). Using HPLC/GC-MS, 74 polycyclic aromatic compounds were identified or tentatively identified in diesel particulate extracts (Tong & Karasek, 1984). A normal-phase HPLC method using silica gel columns and *n*-hexane:benzene (3:1) as eluent has been developed to isolate PAHs and their nitro derivatives (Nielsen, 1983). A very precise, routine, on-line reverse-phase HPLC/fluorescence method has been reported for the analysis of nitroarenes in the picogram range by their reduction to highly fluorescent amines (Tejada *et al.*, 1983). A 'pyrenebutyric acid amide phase' has been applied to a multidimensional HPLC method with on-line peak identification by ultra-violet-visible spectrometry, which allows the detection of 1-nitropyrene in the range of 3–100 ng per mg of soot collected on a filter (Lindner *et al.*, 1985). HPLC has been used to compare the concentrations of some PAHs and their nitro derivatives in exhausts from four diesel cars (Gibson *et al.*, 1981). A semipreparative HPLC analysis of a soluble organic fraction of diesel engine exhaust particulates has been reported, together with unsatisfactory results using HPLC/MS coupling (Levine *et al.*, 1982).

(iii) Gas chromatography (GC) and gas chromatography /mass spectrometry (GC/MS)

GC methods for the determination of PAHs from exhaust condensates have been reviewed (Olufsen & Björseth, 1983), as have GC and GC/MS analyses of nitroarenes (White, 1985). Collaborative studies have been carried out to analyse PAHs in vehicle exhaust (Janssen, 1976; Metz *et al.*, 1984) in which GC methods were compared with those of HPLC (Metz *et al.*, 1984).

Packed-column GC has been largely replaced by high-resolution glass capillary column GC using fused silica columns and careful sample injection procedures (on-column injection at low temperatures of 50–80°C or thermal desorption cold trap injection procedure). Detection limits down to the picogram level have been reached with GC when single-ion monitoring mass spectrometry is used as the detection system (Ramdahl & Urdal, 1982).

Various classes of organic compounds from vehicle exhausts have been analysed by GC and GC/MS, including paraffins, olefins, PAHs, thia-arenes, aza-arenes, oxo-arenes and aldehyde, phenol, quinone and nitro derivatives of PAHs and their acid anhydrides (Hites *et al.*, 1981; Schuetzle *et al.*, 1981; Lee & Schuetzle, 1983; Alsberg *et al.*, 1984; Ramdahl, 1984; White, 1985). More than 70 individual nitroarenes were found in diesel particulate extracts by means of fused-silica capillary column GC and a nitrogen-specific detector, with detection limits of 0.2–0.5 mg/kg (Paputa-Peck *et al.*, 1983). The emission of PAHs and nitroarenes by diesel engines from PAH-containing and other well defined fuels (hexa-decane) were studied using GC/MS and tandem triple-quadrupole MS (Fulford *et al.*, 1982; Henderson *et al.*, 1983, 1984).

The rapid analysis of gaseous and other combustion-related compounds in hot gas streams by atmospheric-pressure chemical ionization/MS has been reported (Sakuma *et al.*, 1981).

(iv) Other methods

Photometric, infra-red, colorimetric, electrochemical and chemiluminescence techniques have been used for the analysis of gases such as sulfur dioxide, carbon monoxide, carbon dioxide, nitrogen oxides and formaldehyde (Hare & Baines, 1979; Deutsche Forschungs-gemeinschaft, 1985). Test tubes in which various colour reactions are seen are available for the analysis of various constituents of vehicle exhaust such as carbon monoxide, carbon dioxide, sulfur dioxide and nitrogen dioxide (Leichnitz, 1986).

3. Biological Data Relevant to the Evaluation of Carcinogenic Risk to Humans

3.1. Carcinogenicity studies in animals

Diesel engine exhaust

During the past decade, there has been worldwide interest in developing an improved data base for evaluating the potential carcinogenic effects of exposure to diesel exhaust. One of the earliest initiatives in this area was undertaken by the US Environmental Protection Agency (Pepelko & Peirano, 1983). The Working Group took cognizance of these preliminary studies which involved exposure by inhalation of SENCAR or strain A mice to whole diesel exhaust or by intraperitoneal injections of extracts of diesel exhaust particles. Only increases in the incidence of pulmonary adenomas were measured as the end-point. In some cases, animals were also administered known carcinogens. The Working Group noted that the exposure and observation times in these studies were generally short as compared with those in later studies that yielded positive results.

(a) Inhalation exposure

Mouse: Heinrich *et al.* (1986a) exposed two groups of 96 female NMRI mice, eight to ten weeks old, to filtered or unfiltered exhaust from a 1.6–1 displacement diesel engine operated according to the US-72 (FTP; see p. 80) test cycle to simulate average urban driving, or to clean air, for 19 h per day on five days per week for life.The unfiltered and filtered exhausts were diluted 1:17 with air and contained 4.24 mg/m^3 particles. Levels of 1.5 ± 0.3 ppm (3 ± 0.6 (SD) mg/m^3) nitrogen dioxide and 11.4 ± 2.1 ppm nitrogen oxides were found in whole exhaust and 1.2 ± 0.26 ppm (2.4 ±0.5 mg/m^3) nitrogen dioxide and 9.9 ± 1.8 ppm nitrogen oxides in filtered exhaust. Exposure to total diesel exhaust and filtered diesel exhaust significantly increased the number of animals with lung tumours (adenomas and carcinomas) to 24/76 (32%) and 29/93 (31%), respectively, as compared to 11/84 (13%) in controls. When the incidences of adenomas and carcinomas were evaluated separately, significantly higher numbers of animals in both diesel exhaust-exposed groups had adenocarcinomas (13 (17%) and 18(19%), respectively) than in controls (2.4%); no increase was seen in the numbers of animals with adenomas. [The Working Group noted that the incidence of lung tumours in historical controls in this laboratory could reach 32% (Heinrich *et al.*, 1986b).]

Groups of ICR and C57B1/6N mice (total number of treated and untreated animals combined alive at three months, 315 and 297, respectively) [initial numbers and sex distribution unspecified] were exposed to the exhaust from a small diesel engine (269 cm^3 displacement, run at idling speed) used as an electric generator; the exhaust was diluted 1:2 to 1:4 in air (Takemoto *et al.*, 1986). The mice were exposed within 24 h after birth for 4 h per day on four days per week (2–4 mg/m^3 particles; size, 0.32 μm; 2–4 ppm, 4–8 mg/m^3 nitrogen dioxide). Between months 13 and 28, lung tumours (adenomas and adenocarcinomas) were found in 14/56 exposed ICR mice and in 7/60 controls and in 17/150 treated C57B1/6N mice and 1/51 controls. The authors reported that the differences were not statistically significant. [The Working Group calculated that the difference in C57B1/6N mice was statistically significant at $p < 0.05$.]

Rat: Karagianes *et al.* (1981) exposed groups of male specific-pathogen-free Wistar rats [numbers unspecified], 18 weeks old, for 6 h per day for 20 months to one of five experimental atmospheres: clean air (controls); 8.3 ± 2.0 (SD) mg/m^3 soot from diesel exhaust; 8.3 ± 2.0 mg/m^3 soot from diesel exhaust plus 5.8 ± 3.5 mg/m^3 coal dust; 6.6 ± 1.9 mg/m^3 coal dust; or 14.9 ± 6.2 mg/m^3 coal dust. The diesel exhaust was produced by a three-cylinder, 43-brake horse power diesel engine driving a 15 kW electric generator. The fuel injection system of the engine was modified to simulate operating patterns of such engines in mines and was operated on a variable duty cycle (dilution, approximately 35:1). Six rats per group were killed after four, eight, 16 or 20 months of exposure. Complete gross necropsy was performed, and respiratory tract tissues, oesophagus, stomach and other tissues with lesions were examined histopathologically. Significant non-neoplastic lesions were restricted primarily to the respiratory tract and increased in severity with duration of exposure. In the six rats examined from each group after 20 months of exposure, two bronchiolar adenomas were observed — one in the group exposed to diesel exhaust only and one in the group exposed to diesel exhaust and coal dust. None was observed in controls or in the two groups exposed to coal dust only. [The Working Group noted the limited number of animals studied at 20 months.]

Groups of 72 male and 72 female or 144 male Fischer 344 weanling rats were exposed for 7 h per day on five days per week for 24 months to either clean air (controls); 2 mg/m^3 coal dust (<7 μm); 2 mg/m^3 diesel exhaust particles, with specific limits on gaseous/vapour constituents; or 1 mg/m^3 coal dust plus 1 mg/m^3 diesel exhaust particles (Lewis *et al.*, 1986). The nitrogen dioxide concentration in the diesel exhaust was 1.5 ± 0.5 ppm (3 ± 1 mg/m^3); the exhaust was generated by a 7–1 displacement, four-cycle, water-cooled, 'naturally aspirated' (open-chamber) diesel engine. The exhaust was diluted by a factor of 27:1 before entering the exposure chambers. Following three, six, 12 and 24 months of exposure, at least ten male rats per group were removed for ancillary studies. After 24 months of exposure, all survivors were killed. The numbers of rats necropsied and examined histologically in each of the four groups were 120–121 males and 71 –72 females. No difference in survival was noted among treatment groups, chambers or sexes [data on survival unavailable]. No statistical difference in tumour incidence was noted among the four groups. [The Working Group noted that no detailed information on tumour incidence was available and that the animals were killed at 24 months, a shorter observation period than used in other inhalation studies with rats that gave positive results.][1]

Female specific-pathogen-free Fischer 344 rats [initial number unspecified], aged five weeks, were exposed to diesel exhaust from a small diesel engine (269 cm^3 displacement) run at idling speed; rats were treated for 4 h per day on four days per week for 24 months, at which time they were killed or were left untreated (Takemoto *et al.*, 1986). The exhaust was diluted 1:2 to 1:4 with air. The concentration of particulates (size, 0.32 μm) ranged from 2–4 mg/m^3, and those of nitrogen dioxide were 2–4 ppm (3–8 mg/m^3). No lung tumour was observed in either the 26 treated or 20 control rats; 15 and 12 rats in the two groups, respectively, survived 18–24 months. [The Working Group noted the small group sizes.]

Iwai *et al.* (1986) exposed two groups of 24 female specific-pathogen-free Fischer 344 rats, seven weeks of age, to either diluted diesel exhaust or diluted filtered diesel exhaust for 8 h per day on seven days a week for 24 months, at which time some rats were sacrificed and the remainder were returned to clean air for a further six months of observation. The diesel exhaust was produced by a 2.4–1 displacement small truck engine; it was diluted ten times with clean air and contained 4.9 ± 1.6 mg/m^3 particles, 1.8 ± 1.8 ppm (3.6 ± 3.6 mg/m^3) nitrogen dioxide and 30.9 ± 10.9 ppm nitrogen oxides. Another group of 24 rats was exposed to fresh air only for 30 months. Incidences of lung tumours, diagnosed as adenomas, adenocarcinomas, squamous-cell carcinomas and adenosquamous carcinomas, were significantly higher in the group exposed to whole diesel exhaust, with or without a subsequent observation period (in 8 /19 rats, including five with malignant tumours) than in the control group (one adenoma in 1 /22 rats; $p < 0.01$). No lung tumour was observed in the group exposed to filtered exhaust (0/16 rats). Incidences of malignant lymphomas and tumours at other sites did not differ among the three groups. [The Working Group noted the small group sizes.]

Ishinishi *et al.*, (1986a) exposed groups of 64 male and 59 female specific-pathogen-free Fischer 344 rats, four weeks of age, to diesel exhaust from either a light-duty 1.8–1 displacement, four-cylinder engine (particle concentrations, 0.11,0.41,1.08 or 2.32 mg/m^3; nitrogen dioxide concentrations, 0.08, 0.26, 0.70 or 1.41 ppm (0.2, 0.5, 1.4 or 2.8 mg/m^3); nitrogen oxide concentrations, 1.24, 4.06, 10.14 or 20.34 ppm) or a heavy-duty 11–1 displacement, six-cylinder engine (particle concentrations, 0.46, 0.96, 1.84 or 3.72 mg/m^3; nitrogen dioxide concentrations, 0.46, 1.02, 1.68 or 3.00 ppm (0.9, 2.1, 3.4 or 6 mg/m^3); nitrogen oxide concentrations, 6.17, 13.13, 21.67 or 37.45 ppm). Exposure was for 16 h per day on six days per week for up to 30 months. The diesel emissions were diluted about 10–15 times (v/v) with air. Separate control groups for the light-duty and heavy-duty series were exposed to clean air. The incidence of lung tumours diagnosed as adenocarcinomas, squamous-cell carcinomas or adenosquamous carcinomas was significantly increased only in the highest-dose group (in 5/64 males and 3/60 females) of the heavy-duty diesel exhaust-exposed series compared to controls (in 0/64 males and 1/59 females; $p<0.05$). The incidences in the next highest-dose group in this series were 3/64 males and 1/59 females. [The Working Group noted that, although this incidence was not statistically different from that in the controls, it suggested an overall positive response for the two highest exposure levels.] No statistically significant increase in the incidence of lung tumours was noted in the groups exposed to light-duty diesel engine exhaust. [The Working Group noted that the highest level of exposure in the light-duty series was approximately one-half of the highest concentration used in the heavy-duty series, and that the incidence (3.3%) of lung tumours in the control animals of the light-duty diesel engine exhaust-exposed series was higher than that in the heavy-duty diesel controls (0.8%).]

Groups of 72 male and 72 female Fischer 344 rats, six to eight weeks old, were exposed to one of three concentrations of diesel engine exhaust or particle-filtered diesel engine exhaust from a 1.5–1 displacement engine operated according to the US-72 (FTP) driving cycle which simulates average urban driving; exposure was for 16 h per day on five days per week for two years (Brightwell *et al.*, 1986). The exposure concentrations were reported as a dilution of the exhaust with a constant volume of 800 m^3 of air (high dose), a further dilution of this mixture in air of 1:3 (medium dose) and a dilution of 1:9 (low dose). The particle concentrations in the unfiltered diesel exhaust atmosphere were 0.7, 2.2 and 6.6 mg/m^3 for the low, medium and high doses (with 8 ± 2 ppm nitrogen oxides in the high dose), respectively. Two control groups of 144 rats of each sex were exposed to conditioned air. Following the exposure period, the animals were maintained for a further six months in clean air. An exposure concentration-related increase in the incidence of primary lung tumours [detailed histopathology unspecified] was reported only in groups exposed to unfiltered diesel exhaust. [The Working Group noted that no information of tumour incidence was given for rats exposed to filtered diesel exhaust.][1]

Heinrich *et al.* (1986a) exposed two groups of 96 female Wistar rats, eight to ten weeks old, to filtered or unfiltered exhaust, as described on p. 89. A significantly increased incidence of lung tumours (histologically identified as eight bronchioalveolar adenomas and nine squamous-cell tumours) was observed in rats exposed to unfiltered diesel exhaust (17/95(18%) *versus* 0/96 controls). No lung tumour was reported in rats exposed to filtered exhaust.

Mauderly *et al.* (1986, 1987) exposed groups of 221–230 male and female specific-pathogen-free Fischer 344 rats, 17 weeks old, to one of three concentrations of diesel engine exhaust generated by a 1980 model 5.7–1 V8 engine operated according to US FTP cycles; exposure was for 7 h per day on five days per week for up to 30 months. The exposure concentrations were reported as a dilution of the whole exhaust to measured soot concentrations of 0.35 (low), 3.5 (medium) or 7.0 (high dose) mg/m^3. Levels of nitrogen dioxide were 0.1 ± 0.1 (0.2 ± 0.2), 0.3 ± 0.2 (0.6 ± 0.4) and 0.7 ± 0.5 ppm (1.4 ± 1 mg/m^3), respectively. Sham-exposed controls received filtered air. The soot particles were approximately 0.25 μm mass median diameter, and approximately 12% of their mass was composed of solvent-extractable organics. Subgroups of animals were removed at six, 12, 18 and 24 months for ancillary studies; all rats surviving after 30 months of exposure were killed. All rats that died or were killed were necropsied and examined histologically for lung tumours. Exposures did not significantly affect the survival of animals of either sex. The median survival time ranged from 880 (low) to 897 (medium) days of age for males and from 923 (high) to 962 (low) days for females. A total of 901 rats were examined for lung tumours; four types were found: bronchoalveolar adenomas, adenocarcinomas, squamous cysts (mostly benign) and squamous-cell carcinomas. None of the tumours was found to have metastasized to other organs. The incidences of lung tumours in males and females combined were 0.9% in controls, 1.3% in low-dose, 3.6% in medium-dose and 12.8% in high-dose groups. The authors noted that the prevalences at the medium and high levels were significantly increased (p<0.05). A total of 42 rats developed 46 lung tumours; four females in the high-dose group had two lung tumours each. Lung tumours were found in two male controls, in one low-dose male, in four mid-dose males and in 13 high-dose males; in females, the respective incidences were zero, two, four and 20. Adenomas predominated in the medium-exposure group. Adenocarcinomas, squamous-cell carcinomas and squamous cysts were observed predominantly at the high dose. The tumours were observed late in the study: 81% after two years of exposure. The authors observed no exposure-related difference in cause of death; the tumours were found incidentally at death or at termination of the experiment.

Hamster: Groups of 48 female Syrian golden hamsters, eight weeks of age, were exposed to diluted (1:7 air) unfiltered diesel exhaust (mass median particle diameter, 0,1 μm; mean particle concentration, 3.9 ± 0.5 mg/m^3; nitrogen dioxide, 1.2 ± 1.7 ppm (2.4 ± 3.4 mg/m^3); nitrogen oxides, 18.6 ± 5.8 ppm) or filtered diesel exhaust (nitrogen dioxide, 1.0 ± 1.5 ppm (2 ± 3 mg/m^3); nitrogen oxides, 19.2 ± 6.1 ppm); exposure was for 7–8 h per day on five days per week for life (Heinrich *et al.*, 1982). The exhaust was generated by a 2.4–1 displacement engine operating at a steady state. A group of 48 hamsters inhaling clean air served as controls. There was no effect of diesel exhaust on survival; median lifespan was 72–74 weeks in all groups, and no lung tumour was reported in treated or control animals.

Groups of 48 female and 48 male Syrian golden hamsters, eight to ten weeks of age, were exposed to diluted (1:17 air) filtered or unfiltered exhaust as described on p. 89 (Heinrich *et al.*, 1986a). A control group of 48 females and 48 males inhaled clean air. Median lifespan was not significantly influenced by diesel exposure and was 75–80 weeks for females and 80–90 weeks for males. No lung tumour was observed in treated or control animals.

Groups of 52 female and 52 male Syrian hamsters, six to eight weeks of age, were exposed to one of three concentrations of unfiltered or filtered exhaust as described on p. 91 (Brightwell *et al.*, 1986). Two control groups of 104 hamsters of each sex were exposed to clean air only. The authors reported that there was no increase in the incidence of respiratory-tract tumours in treated hamsters. [The Working Group noted the incomplete reporting of tumour incidence and survival.]

Monkey: Groups of 15 male cynomolgus monkeys (*Macacafascicularis*) were exposed by Lewis *et al.* (1986) to coal dust and/or diesel exhaust particles for 7 h per day on five days per week for 24 months, as described on p. 90. Following the exposure period, all survivors (59/60) were necropsied and examined histologically. No significant difference in tumour incidence was reported among the four groups. [The Working Group noted the short duration and inadequate reporting of the study.]

(b) Intratracheal or intrapulmonary administration

Rat: Four groups of 31,59,27 and 53 female specific-pathogen-free Fischer 344 rats, six weeks of age, received ten weekly intrapulmonary instillations of 1 mg/animal activated carbon or 1 mg/animal diesel exhaust particles [source unspecified] in phosphate buffer with 0.05% Tween 80, 2 ml of buffer alone or were untreated (Kawabata *et al.*, 1986). Rats surviving 18 months constituted the effective numbers. The experiment was terminated 30 months after instillation. The survival rate was 71–83%, with the lowest value in the diesel particle-treated group. The numbers of animals with malignant lung tumours [histological type unspecified] were significantly higher ($p<0.01$) in the groups treated with activated carbon (7/23) and with diesel particles (20/42) than in untreated (0/44) or vehicle controls (1/23). Similarly, the numbers of animals with benign and malignant lung tumours were also significantly increased in the groups treated with activated carbon (11/23) and diesel particles (31/42). [The Working Group noted the high incidence of pulmonary tumours observed after treatment with activated carbon, a material which is normally considered to be inert.]

Groups of 35 female inbred Osborne-Mendel rats, three months old, received lung implants of organic material from a diesel exhaust or a reconstituted hydrophobic fraction (Grimmer *et al.*, 1987). The organic material was collected from a 3–1 diesel passenger car engine, operated under the first cycle of the European test cycle (see p. 80), and was separated by liquid-liquid distribution into a hydrophilic fraction (approximately 25% by weight of the total condensate) and a hydrophobic fraction (approximately 75% by weight). The hydrophobic fraction was separated by column chromatography into several further fractions: (i) nonaromatic compounds plus PAHs with two and three rings (72% by weight of the total condensate), (ii) PAHs with four or more rings (0.8% by weight), (iii) polar PAHs (1.1% by weight) and (iv) nitro-PAHs (0.7% by weight). Animals received 6.7 mg hydrophilic fraction, 20 mg hydrophobic fraction, 19.2, 0.2, 0.3 or 0.2 mg of the four hydrophobic fractions, respectively, or 19.9 mg of reconstituted hydrophobic fraction. Two groups of 35 animals were untreated or received implants of the vehicle (beeswax:tri-octanoin, 1:1) only. All animals were observed until spontaneous death (mean survival time, 24–140 weeks). Six lung tumours (squamous-cell carcinomas) were found in animals treated with the hydrophobic subfraction containing PAHs with four to seven rings. Similar carcinogenic potency was seen with the reconstituted hydrophobic subfractions (seven carcinomas) and with the hydrophobic fraction (five carcinomas). A low carcinogenic potential was observed with the subfraction of nitro-PAHs (one carcinoma); the polar PAH produced no tumour; and one bronchiolar-alveolar adenoma was observed in animals treated with the nonaromatic subfraction with two- and three-ring PAHs. One adenoma of the lung occurred in the vehicle control group.

Hamster: Shefner *et al.* (1982) gave groups of 50 male Syrian golden hamsters, 12–13 weeks of age, intratracheal instillations once a week for 15 weeks of 1.25, 2.5 or 5 mg diesel particles (obtained from US Environmental Protection Agency; 90% by mass <10 åm) or diesel particles plus the same amounts of ferric oxide in 0.2 ml propylene glycol/gelatine/-saline; or a dichloromethane extract of diesel particles plus ferric oxide in 0.2 ml propylene glycol/saline once a week for 15 weeks. Ten animals in each group were sacrificed at 12 months. At the time of reporting (61 weeks), one lung adenoma had been found in the group receiving the high dose of diesel particles and one in the group receiving the high dose of diesel particle extract plus ferric oxide. No lung tumour was reported in various untreated or solvent-treated controls. [The Working Group noted the short observation period and the preliminary reporting of the experiment.]

Three groups of 62 male Syrian golden hamsters, eight weeks of age, were given intratracheal instillations of 0.1 ml of a suspension of 0.1,0.5 or 1 mg of an exhaust extract in Tween 60:ethanol:phosphate buffer (1.5:2.5:30 v/v) from a heavy-duty diesel engine (V6 11–1) once a week for 15 weeks and observed for life (Kunitake *et al.*, 1986). A control group of 59 animals received instillations of the vehicle only and a positive control group of 62 animals received 0.5 mg benzo[*a*]pyrene weekly for 15 weeks. Survival rates were 95%, 92%, 71% and 98% in the three treated groups and the vehicle controls, respectively. No significant difference in the incidences of tumours of the lung, trachea or larynx was observed between untreated control and treated groups; respiratory tumours occurred in 88% benzo[*a*]pyrene-treated hamsters. [The Working Group noted that length of survival was not reported.]

(c) Skin application

Mouse: A group of 12 male and 40 female C57B1 mice [age unspecified] received skin applications of 0.5 ml of an acetone extract of particles collected from a diesel engine [unspecified] running at zero load during the warm-up phase; treatment was given three times a week for life (Kotin *et al.*, 1955). Groups of 50 male and 25 female strain A mice [age unspecified] received similar applications of an extract of particles derived from the warmed-up engine running at full load. Of the mice in the first group, 16 had died by ten weeks; 33 mice survived to the appearance of the first skin tumour (13 months), and two skin papillomas developed. Of the male strain A mice, eight survived to the appearance of the first skin tumour (16 months), and one papilloma and three squamous-cell carcinomas were observed. Of the female strain A mice, 20 survived to the appearance of the first skin tumour (13 months), and 17 skin tumours [unspecified] were observed between 13 and 17 months. Both experiments were terminated after 22–23 months. No skin tumour occurred in 69 C57B1 controls (37 alive after 13 months) or in 34 (24 female and 10 male) strain A controls.

In a study reported before completion (Depass *et al.*, 1982), groups of 40 male C3H/HeJ mice [age unspecified] received skin applications of 0.25 ml of a 5 or 10% solution in acetone or 5,10,25 or 50% dichloromethane extracts of diesel particles collected from a [5.7–1] diesel engine; treatment was given three times per week for life. A positive control group received 0.2% benzo[*a*]pyrene in acetone, and a negative control group received acetone only. One squamous-cell carcinoma of the skin was observed in the group treated with the highest dose of dichloromethane extract after 714 days of treatment. All 38 mice receiving benzo[a]pyrene developed skin tumours. [The Working Group noted the inadequate reporting of the study.]

In a series of promotion-initiation studies (Depass *et al.*, 1982), groups of 40 male C3H /HeJ mice received a single initiating dose of 0.025 ml 1.5% benzo[*a*]pyrene in acetone, followed one week later by repeated applications of the 10% solution of diesel particles in acetone described above, 50% dichloromethane extract, 25% dichloromethane extract, acetone only or 0.015 μg phorbol 12-myristyl 13-acetate (TPA) five times per week for life. An additional group received no further treatment after the initiating dose of benzo[*a*]pyrene. In initiation studies, a single initiating dose of 0.025 ml of the 10% solution of diesel particles in acetone, 50% dichloromethane extract, acetone or TPA was followed after one week by of 0.015 μg TPA three times per week. The concentration of TPA used in the initiation and promotion studies was changed after eight months to 1.5 μg. In the promotion study, one mouse receiving the 50% dichloromethane extract had a squamous-cell carcinoma and two mice receiving the 25% extract had one squamous-cell carcinoma and one papilloma. In the initiation study, three (two papillomas, one carcinoma), three (two papillomas, one fibrosarcoma), one (papilloma) and two (one carcinoma, one papilloma) tumours were observed in the groups that received diesel particles, dichloromethane extract, acetone and TPA, respectively. [The Working Group noted the preliminary reporting of the study.]

Nesnow *et al.* (1982a,b) gave skin applications to groups of 40 male and 40 female SENCAR mice, seven to nine weeks of age, of 0.1, 0.5, 1.0, 2 or 10 mg of dichloromethane extracts of particles obtained from the exhausts of five diesel engines, A, B, C, D and E (E being a heavy duty engine) in 0.2 ml acetone; the 10-mg dose was given in five daily doses. The benzo[*a*]pyrene content ranged from 1173 ng/mg in the exhaust from engine A to 2 ng/mg in that from engines B and E. One week later, all mice received 2 μg TPA in 0.2 ml acetone twice a week for 24–26 weeks. A control group was treated with TPA only. The sample from engine A produced a dose-related increase in the incidence of skin papillomas, with 5.5 and 5.7 papillomas/mouse, 31% of males and 36% of females at the highest dose having skin carcinomas. With samples from engines B, C and D, responses of 0.1–0.5 papilloma/mouse were observed compared to 0.05–0.08 papilloma/mouse in TPA controls. The sample from engine E produced a response similar to that in controls (0.05–0.2 papilloma/mouse).

Similar groups of 40 male and 40 female SENCAR mice received weekly skin applications of 0.1, 0.5, 1, 2 or 4 mg extracts of particles from the emissions of engines A, B and E for 50–52 weeks (Nesnow *et al.*, 1982b, 1983). The high dose was given in two split doses. At that time, skin carcinomas had occurred in 3% of male and 5% of female mice given the 4-mg dose of the sample from engine A, in 3% of males given the 0.5-mg dose of the sample from engine B and in 3% of females given the 0.1-mg dose of the sample engine E. Doses of 12.6–202 μgper week benzo[*a*]pyrene produced skin carcinoma responses of 10–93%.

Groups of 50 female specific-pathogen-free ICR mice, aged eight to nine weeks, received skin applications of extracts of diesel particles collected from a V6 11–1 heavy-duty displacement diesel engine in 0.1 ml acetone onto shaved back skin every other day for 20 days (total doses, 5, 15 or 45 mg/animal; Kunitake *et al.*, 1986). A further group of 50 mice treated with acetone only served as controls. Beginning one week after the last diesel extract treatment, each animal received applications of 2.5 μg TPA in 0.1 ml acetone three times a week for 25 weeks, at which time they were autopsied. No skin 'cancer' was found in either treated or control groups; skin papillomas were seen in 1/48 and 4/50 surviving animals in the 15- and 45-mg dose groups, respectively [The Working Group noted the short duration of both the treatment and observation time.]

(d) Subcutaneous administration

Mouse: Groups of 15–30 female specific-pathogen-free C57B1/6N mice, six weeks of age, received subcutaneous injections into the intrascapular region of suspensions in olive oil containing 5% dimethyl sulfoxide of 10, 25, 50, 100, 200 or 500 mg/kg bw of diesel particles collected from a V6 11–1 heavy-duty displacement diesel engine; the treatment was given once a week for five weeks (Kunitake *et al.*, 1986). A control group of 38 mice received injections of the vehicle only. Animals were killed 18 months after the beginning of the experiment. The first tumours were palpated in week 47 (a total dose of 25 mg/kg bw), week 30 (50 mg/kg bw), week 27 (100 mg/kg bw) and week 39 (200 and 500 mg/kg bw) in the five treated groups, respectively. A significant increase in the incidence of subcutaneous tumours, diagnosed as malignant fibrous histiocytomas, was observed only in 5/22 mice receiving the 500-mg/kg bw dose ($p < 0.05$) in comparison with controls (0/38). [The Working Group noted the high dose required to produce a carcinogenic effect.]

(e) Administration with known carcinogens

Rat: Two groups of female specific-pathogen-free Fischer 344 rats [initial number unspecified], five weeks of age, were exposed to diesel exhaust, as described on p. 89 or to clean air for 4 h per day on four days per week for 24 months (Takemoto *et al.*, 1986). One month after the beginning of treatment, both groups received three weekly intraperitoneal injections of 1 g/kg bw *N*-nitrosodipropanolamine. Rats were killed at six, 12, 18 and 24 months after the start of treatment. A slight but nonsignificant increase in the incidences of lung adenomas and adenocarcinomas was observed in rats exposed to both exhaust and the nitrosamine compared to those exposed to the nitrosamine alone. After 12–24 months of observation, 16 lung tumours (12 adenomas and four carcinomas) were observed in 29 *N*-nitrosodipropanolamine-treated rats and 34 tumours (24 adenomas and 10 carcinomas) were observed in 36 rats exposed to both exhaust and *N*-nitrosodipropanolamine. The authors interpreted this result as an 'overadditive' effect on lung tumour incidence.

Heinrich *et al.* (1986a) gave groups of 48 female specific-pathogen-free Wistar rats, eight to ten weeks of age, 25 weekly subcutaneous injections of 250 or 500 mg/kg bw *N*-nitrosopentylamine during the first 25 weeks of exposure by inhalation to unfiltered diesel engine exhaust, to filtered diesel engine exhaust or to clean air, as described on p. 89. Significant increases in the incidences of squamous-cell carcinomas of the lung were observed in animals treated with the nitrosamine and exposed to total exhaust (22/47 low-dose nitrosamine; 15/48 high-dose nitrosamine compared to 2/46 and 8/48 clean air controls, respectively), although overall lung tumour rates were comparable in the groups exposed to the nitrosamine and to engine exhaust or clean air. The incidence of benign tumours (papillomas) of the upper respiratory tract was significantly reduced in nitrosamine-treated rats exposed to unfiltered or filtered diesel exhaust compared to controls exposed to nitrosamine and clean air.

Hamster. Heinrich *et al.* (1982) gave groups of 48–72 female Syrian golden hamsters, eight weeks old, weekly intratracheal instillations of 0.1 or 0.3 mg dibenzo[*a,h*]anthracene for 20 weeks or a single subcutaneous injection of 1.5 or 4.5 mg/kg bw *N*-nitrosodiethyl-amine (NDEA) and exposed them concomitantly by inhalation to unfiltered or filtered diesel exhaust or clean air, as described on p. 92. The incidence of tumours in the larynx/trachea was increased in animals treated with the higher dose of NDEA and exposed concomitantly to total exhaust (70.2%) or filtered exhaust (66%) as compared to controls (44.7%). The lower dose of NDEA and treatment with dibenzo[*a,h*]anthracene resulted in a lower incidence of these tumours. Only two lung tumours were found: one with the high dose of dibenzo[*a,h*]anthracene and filtered exhaust, the other with the low dose of NDEA and total exhaust.

Groups of 48 male and 48 female Syrian golden hamsters, eight to ten weeks of age, received a single subcutaneous injection of 4.5 mg/kg bw NDEA or 20 intratracheal instillations of 0.25 mg benzo[*a*]pyrene with concomitant exposure by inhalation to filtered or unfiltered diesel engine exhaust or to clean air, as described on p. 89 (Heinrich *et al.*, 1986a). Treatment with NDEA or benzo[*a*]pyrene produced respiratory tract tumour incidences of 10% or 2%, respectively, in animals exposed to clean air; rates were not significantly increased by concomitant exposure to filtered or unfiltered diesel engine exhaust.

Groups of 52 female and 52 male Syrian hamsters, six to eight weeks old, received a single subcutaneous injection of 4.5 mg/kg bw NDEA three days prior to exposure by inhalation to unfiltered or filtered diesel engine exhaust, as described on p. 91 (Brightwell *et al.*, 1986). The authors reported a nonsignificantly increased incidence of tracheal papillomas. [The Working Group noted that no information on tumour incidence was given.]

Gasoline engine exhaust

(a) Inhalation exposure

Mouse: Campbell (1936) exposed two groups of 37 male and 38 female mice [strain unspecified], three months old, by inhalation for 7 h per day on five days per week for about two years to one of two gasoline engine exhaust emissions: A was from a four-cylinder, 23-horse power, ordinary gasoline engine and B from a six-cylinder, 24-horse power engine run on gasoline with tetraethyllead 1:1800. Exposure was to a dilution of 1:145 in air for 4 h in the morning and to a dilution of 1:83 for 3 h in the afternoon. [The total particulate content of the exhaust and the lead concentration were not specified.] Of the animals exposed to exhaust emissions from car A, 9/75 had primary lung tumours compared to 8/74 controls; of those exposed to emissions from car B, primary lung tumours were seen in 12/75 animals compared to 6/70 controls. [Survival data not given.] Other types of tumours observed included mammary tumours and skin cancers among both treated groups and controls. [The Working Group noted the inadequate reporting of the study.]

Two groups of female ICR mice [initial numbers and age unspecified] were either exposed by inhalation to 0.1 mg/m^3 gasoline exhaust (1:250 dilution of emission from a small gasoline engine; carbon monoxide, 300 ± 50 ppm (350 ± 60 mg/m^3); nitric oxide, 0.21 ppm (0.3 mg/m^3); nitrogen dioxide, 0.08 ppm (0.16 mg/m^3) [total particulate concentration unspecified]) for 2 h per day on three days per week for six to 12 months, or were administered urethane (0.01%) in the drinking-water until sacrifice (Yoshimura, 1983). No untreated control group was included. Lung adenomas were found in 2/19 exposed mice killed between seven and 12 months; the incidence of tumours (adenomas and adenocarcinomas) in the urethane-treated group was 21/25. [The Working Group noted the short period of treatment, the short observation time and the absence of a control group.]

Rat: Groups of 72 male and 72 female Fischer 344 rats, six to eight weeks old, were exposed to one of three dilutions of gasoline engine exhaust from a 1.6–1 displacement engine operated according to the US-72 (FTP) driving cycle; exposure was for 16 h per day on five days per week for two years (Brightwell *et al.*, 1986). Further groups were exposed to exhaust from a gasoline engine fitted with a three-way catalytic converter. The exhaust was diluted by a constant volume of 800 m^3 air or at further dilutions of 1:3 or 1:9 of this mixture in air; the particulate concentration was less than the detection limit of 0.2 mg/m^3. The concentration of nitrogen oxides in the high dose of exhaust from the engine without a converter was 49 ± 5 ppm and that of carbon monoxide was 224 ± 32 ppm (260 ± 36 mg/m^3). Two control groups of 144 rats of each sex were exposed to conditioned air. After the exposure period, animals were maintained for a further six months in clean air. No increase in lung tumour incidence was reported among rats exposed to gasoline engine exhaust as compared with controls. [The Working Group noted the inadequate reporting of the study.]

Three groups of 80–83 female Bor: WISW rats, ten to 12 weeks old, were exposed by inhalation to 1:61 or 1:27 dilutions with clean air of leaded gasoline engine exhaust generated by a 1.6–1 engine operated according to the US-72 (FTP) driving cycle or to clean air (Heinrich *et al.*, 1986c). The lead content of the fuel was 0.3–0.56 g/l. Mean concentrations of exhaust components measured in the inhalation chambers were (high [low]): carbon monoxide, 350 ± 24 [177.5 ± 12.5] mg/m^3; nitric oxide, 28 ± 3 [13.7 ± 1.5] mg/m^3; nitrogen dioxide, 1.9 ± 0.4 [1.0 ± 0.2] mg/m^3; particles, 95.8 ± 16.5 [47.9 ± 20.2] 25g/m^3. About 35% of the particulate mass was lead. Exposure was for 18–19 h per day on five days per week for two years, followed by a maximal observation period of six months in clean air. Mean survival time of exposed and control animals was 105 weeks. Exposure to either concentration (1:61 or 1:27) of gasoline exhaust did not produce a significant increase in lung tumour incidence: 1/83 exposed to 1:61 had a squamous-cell carcinoma and 3/78 exposed to 1:27 had two squamous-cell carcinomas and one adenoma; 1/78 controls had an adenoma. In addition, one animal in each of the three exposure groups showed a tumour in the nasal cavities. [The Working Group noted that the nonlead particulate concentration was less than 1/20 the lowest level of particulates that produced an excess of lung tumours in the studies of diesel exhaust. The highest levels of gasoline engine exhaust that can be tested are limited by the toxicity of carbon monoxide.]

Hamster: Three groups of 80–83 female Syrian golden hamsters, ten to 12 weeks old, were exposed to gasoline engine exhaust, as described above but without the six-month observation period (Heinrich *et al.*, 1986c). Median survival in treated and control groups was 70 weeks. One of 75 animals exposed to the high concentration of exhaust (1:27) and three of 80 exposed to the low concentration (1:61) had a tumour of the respiratory tract. No respiratory tract tumour occurred in the 83 controls. [The Working Group noted that the nonlead particulate concentration was less than 1/20 the lowest level of particulates that produced an excess of lung tumours in the studies of diesel exhaust. The highest levels of gasoline engine exhaust that can be tested are limited by the toxicity of carbon monoxide.]

Brightwell *et al.* (1986) exposed groups of 52 male and 52 female Syrian hamsters, six to eight weeks of age, to gasoline engine exhaust, as described on p. 98. Two control groups of 104 hamsters of each sex were exposed to conditioned air only. The authors reported that respiratory tract tumours in treated hamsters were rare and not related to treatment. [The Working Group noted the inadequate reporting of the data.]

Dog: Stara *et al.* (1980) exposed seven groups of 12 female beagle dogs, four months of age, to exhaust from a six-cylinder, 2.4–1 gasoline engine run on leaded fuel and operated to simulate urban driving, and to specific pollutants found in gasoline engine exhaust (dilution, 1:570 in air). The groups were exposed to nonirradiated exhaust, to exhaust irradiated with ultra-violet, to sulfur dioxide and sulfuric acid, to nonirradiated exhaust plus sulfur dioxide and sulfuric acid, to exhaust irradiated with ultra-violet plus sulfur dioxide and sulfuric acid, to nitrogen oxides with high nitrogen dioxide and to nitrogen oxides with high nitric oxide. A group of 20 dogs was exposed to clean air. The exhaust contained 100 ppm (115 mg/m^3) carbon monoxide and 24–30 ppm hydrocarbon expressed as methane. The irradiated exhaust contained 0.5–1.0 ppm (1–2 mg/m^3) nitrogen dioxide, 0.1 ppm (0.12 mg/m^3) nitric oxide and 0.2–0.4 ppm oxygen expressed as 0_3. The concentration of lead measured in the different exposure atmospheres was 14–26 μg/m^3. The dogs were exposed for 16 h per day for 68 months and then held in clean air for 29–36 months. Complete necropsies were performed on 85 dogs. No lung tumour was observed in the 40 exposed or 17 control dogs. [The Working Group noted that the concentrations of particles in the exposure atmospheres were not given.]

(b) Intratracheal or intrapulmonary administration

Rat: Groups of 34–35 inbred female Osborne-Mendel rats, three months old, received a single implantation of 5.0 or 10.0 mg/animal of gasoline engine exhaust condensate, 4.36, 8.73 or 17.45 mg/animal of a PAH-free fraction, 0.50, 0.99 or 1.98 mg/animal of a fraction of PAHs with two to three rings, 0.14, 0.28 or 0.56 mg/animal of a fraction of PAHs with more than three rings, or 0.03, 0.10 or 0.30 mg benzo[*a*]pyrene in beeswax:trioctanoin (1:1) into the left lobe of the lung and were observed until natural death (Grimmer *et al.*, 1984). The exhaust was produced by a 1.5–1 passenger car engine operated on the European test cycle. One control group of 34 rats received an injection of the vehicle only, and another control group of 35 animals remained untreated. At death, animals were autopsied and lungs were examined histopathologically. Mean survival times in the treated groups and controls were similar, ranging from 80–111 weeks. Only the fraction containing PAHs with more than three rings produced lung tumour (carcinomas and sarcomas) incidences comparable to those induced by total exhaust condensate (4/35, 17/34 and 24/35 *versus* 7/35 and 20/35). No lung tumour was observed in the untreated or vehicle controls. A dose-response relationship was obtained with the total condensate and with the fraction of

PAHs with more than three rings.

Hamster: In an experiment by Mohr *et al.*, (1976) and Reznik-Schüller and Mohr (1977), two groups of six male Syrian golden hamsters, 12 weeks old, each received intratracheal instillations of 2.5 or 5 mg gasoline exhaust condensate, prepared from emissions of a common German passenger car operating according to the European test cycle and containing 340 μg/g benzo[*a*]pyrene, in Tris-HCI and EDTA solution. Treatment was every two weeks for life. Moribund animals were killed and their lungs examined histologically for tumours. A further group of six animals was treated with solvent only and were sacrificed after the last exhaust condensate-treated animal had died. Survival times ranged from 30–60 weeks, during which time animals had received 15–30 instillations of condensate. All condensate-treated animals developed pulmonary adenomas.

Groups of 30 male Syrian golden hamsters, 16 weeks of age, received intratracheal instillations of 0.2 ml of a gasoline exhaust condensate from a 1.5–1 engine, its fractions, including the methanol phase, the cyclohexane phase II and the nitromethane phase, a reconstitution product of these fractions, a synthetic mixture of pure carcinogenic PAHs or 40 μgbenzo[*a*]pyrene in Tris-buffer/saline; treatment was every two weeks until natural death (Künstler, 1983). One group of 30 untreated animals and one group of 30 solvent-treated animals served as controls. Tracheas and lungs of all hamsters were examined histologically by light microscopy. Survival time was 68–87 weeks. No lung tumour was found in animals treated with the condensate or its fractions. In the benzo[*a*]pyrene-treated group, one mucoepidermoidal carcinoma of the respiratory tract and one lung adenoma were found; one animal treated with cyclohexane phase II (0.13 mg/animal; 10.7 μg benzo[*a*]pyrene equivalents) had a lung adenoma.

(c) Skin application

Mouse: A group of 108 C57B1 mice [age and sex unspecified] received skin applications of a concentrated benzene extract of particles from a V8 gasoline engine [procedures unspecified] (Kotin *et al.*, 1954). Among 86 mice surviving at the appearance of the first skin tumour (390 days), 38 developed 68 skin tumours, including 22 skin carcinomas. Among 69 benzene-treated controls, 42 survived to the time of appearance of the first skin tumour in treated mice; no skin tumour was reported.

Wynder and Hoffmann (1962) gave groups of 50 female Swiss (Millerton) mice, six weeks of age, skin applications of 5,10,25, 33 or 50% solutions in acetone of the ‘tar’ from a V8 gasoline engine (Hoffmann & Wynder, 1962b) exhaust extracted with benzene. Treatment was given three times a week for 15 months; the mice were observed for a further three months, at which time they were killed. Thirty mice painted with acetone served as controls. The numbers of mice with skin papillomas at 18 months were 0,4,50,60 and 60% in the control, 5, 10, 25 and 33% dose groups, respectively; the corresponding incidences of skin carcinomas were 0, 4, 32, 48 and 54, respectively. In the high-dose group, all mice had died by ten months; 70% had skin papillomas and 4% had skin carcinomas.

In similar studies by Hoffmann *et al.* (1965), the incidence of skin papillomas and carcinomas was higher in 20 Swiss ICR mice treated with extracts of exhaust from a V8 engine that used approximately 1 1 of engine oil/200 miles (0.3 1/100 km) than in those treated with exhausts from an engine that used approximately 1 1 of oil/1600 miles (0.04 1/100 km).

Brune *et al.* (1978) gave groups of 50 or 80 female random-bred CFLP mice, approximately 12 weeks of age, skin applications of an exhaust condensate produced from a 1.5–1 gasoline engine during a European test cycle, fractions of this condensate or benzo[*a*]pyrene in 0.1 ml dimethyl sulfoxide:acetone (3:1) twice a week for life. The groups treated with the total condensate received doses of 0.526, 1.579 or 4.737 mg/animal (0.15, 0.45 or 1.35 μg/animal benzo[*a*]pyrene equivalents) per treatment; the two groups treated with the methanol phase (66% of the total condensate) received doses of 1.389 or 4.168 mg/animal (0.60 or 1.80 μg/animal benzo[*a*]pyrene equivalents); those treated with the cyclohexane phases I and II (34% and 17% of the total condensate), the nitromethane phase (17% of the total condensate) and a reconstitution of the fractions received 0.30 and 0.90 μg/animal benzo[*a*]pyrene equivalents. Three further groups of 50 mice received applications of 1.92, 3.84 or 7.68 μg/animal benzo[*a*]pyrene. One control group received applications of the vehicle alone and another remained untreated. Animals with advanced malignant tumours were killed; all other animals were observed until natural death. Statistical analysis of the results revealed a linear relationship between the percentage of animals with local tumours (squamous-cell papillomas or carcinomas) and dose for the nitromethane phase (16.4 and 68.9%), the cyclohexane phase I (13.7 and 68.8%), the reconstitution (7.9 and 54.7%) and the total condensate (3.9, 35.1 and 76.9%). Local tumour rates in mice treated with total condensate were significantly higher than those in mice treated with benzo[*a*]pyrene (19.5, 15.2 and 60%) or the PAH-free fractions (methanol phase (2.6 and 5.9%) and cyclohexane phase II (2.8 and 1.5%)), which did not differ significantly from controls (1.3 and 0%). A second experiment by the same group using 40 mice per group gave similar results; however, local tumour incidences were significantly higher in the first experiment, probably due to minor differences in experimental techniques.

Grimmer *et al.* (1983a) gave groups of 65 or 80 female CFLP mice, seven weeks old, dermal applications of extracts of an exhaust condensate from a 1.5–1 gasoline engine run on the European test cycle, its fractions or benzo[*a*]pyrene in 0.1 ml dimethyl sulfoxide:acetone (1:3) solvent; treatment was given twice a week for 104 weeks. Doses administered were: total condensate — 0.292, 0.875 or 2.626 mg/animal (0.12, 0.36 or 1.09 μg/animal benzo[*a*]pyrene equivalents); benzo[*a*]pyrene, 0.0039, 0.0077 or 0.0154 mg/animal; the methanol phase (PAH-free fraction), 0.97 or 2.9 mg/animal (0.48 or 1.45 μg/animal benzo[*a*]pyrene equivalents); the PAH-fraction containing PAHs with two and three rings, 0.152 or 0.455 mg/animal (0.46 or 1.39 μg/animal benzo[*a*]pyrene equivalents); the PAH-fraction containing PAHs with more than three rings, 0.02 or 0.06 mg/animal (0.24 or 0.73 μg/animal benzo[*a*]pyrene equivalents); and a mixture of 15 PAHs in a ratio corresponding to that of the automobile exhaust, 0.003 or 0.009 mg/animal (0.24 or 0.73 μg/animal benzo[*a*]pyrene equivalents). One group treated with 0.1 ml of the solvent only and one untreated group served as controls. Animals with advanced tumours were killed; the remaining animals were observed until natural death. The PAH-free fraction (methanol phase) and the fraction of PAHs with two or three rings produced low rates of skin tumours (carcinomas and papillomas): 11 [13.9%] and one [1.3%] animals with local tumours, respectively, in the high-dose groups. Clear dose-response relationships were demonstrated for tumour incidence in the groups treated with total condensate (six [7.7%], 34 [44.3%] and 65 [83.3%]), in those given the fraction containing PAHs with more than three rings (seven [8.9%] and 50 [63.5%]), in those given the mixture of 15 PAHs (one [1.3%] and 29 [38.7%]) and in benzo[*a*]pyrene-treated animals (22 [34.4%], 39 [60.9%] and 56 [89.1%]). No local skin tumour was seen in controls. Similar results were obtained by Grimmer *et al.* (1983b).

Groups of 40 male and 40 female SENCAR mice, seven to nine weeks of age, received single skin applications in 0.2 ml acetone of 0.1,0.5,1,2 or 3 mg of dichloromethane extracts of particulates collected from the emission of an unleaded gasoline engine (of a 1977 model passenger car [engine volume unspecified]) with a catalytic converter (Nesnow *et al.*, 1982a). One week later, all mice received 2 μg TPA in 0.2 ml acetone twice weekly for 24–26 weeks. At that time, the percentages of mice with papillomas and the numbers of papillomas/-mouse in TPA-treated controls were 8% and 0.08 in males and 5% and 0.05 in females, respectively. In the groups treated with both TPA and the gasoline extract, the respective percentages and numbers were: males — 5% and 0.05 (0.1 mg), 13% and 0.15 (0.5 mg), 18% and 0.18 (1 mg), 22% and 0.24 (2 mg) and 18% and 0.24 (3 mg); females — 13% and 0.23 (0.1 mg), 18% and 0.24 (0.5 mg), 10% and 0.13 (1 mg), 21% and 0.23 (2 mg) and 23% and 0.28 (3 mg).

(d) Subcutaneous administration

Mouse: Groups of 87 or 88 female NMRI mice [age unspecified] received a single subcutaneous injection in 0.5 ml tricaprylin of 20 or 60 mg exhaust condensate from a gasoline engine [unspecified] (Pott *et al.*, 1977). A third group of 45 mice was injected three times with 60 mg condensate containing 0.163 μg/mg benzo[*a*]pyrene. A group of 89 mice that received 0.5 ml tricaprylin alone and a further group of 87 untreated mice served as controls. Animals that developed tumours up to 10 mm in diameter at the application site were killed. The mean survival time in the low- and medium-dose groups was in the range of that of the control groups (80–88 weeks), but was 57 weeks in the high-dose group. The numbers of animals with sarcomas at the injection site were 10/87 (11.5%), 6/88 (6.8%) and 5/45 (11.1%) in the condensate-treated groups and 3.4% in the tricaprylin-treated group.

(e) Administration with known carcinogens

Mouse: Groups of 60 female NMRI mice, eight to ten weeks old, received ten intratracheal instillations of 100 μg benzo[*a*]pyrene, 20 intratracheal instillations of 50 μg benzo[*a*]pyrene or ten intratracheal instillations of 50 μgdibenzo[*a,h*]anthracene, with concomitant exposure to gasoline engine exhaust, as described on p. 99, for 53 weeks only and were observed for a further 40 weeks (Heinrich *et al.*, 1986c). Administration of benzo[*a*]pyrene or dibenzo[*a,h*]anthracene with clean air induced a high basic lung tumour rate of 70–90% (adenomas and adenocarcinomas). Mean survival times (75–85 weeks) of exhaust-exposed animals were clearly shorter, with the exception of the groups treated ten times with 100 μg benzo[*a*]pyrene, in which gasoline exhaust exposure induced a higher incidence of adenocarcinomas (22/38 and 28/40 in the 1:27 and 1:61 dilution groups) but a significantly reduced incidence of adenomas (4/38 and 3/40) compared to clean air controls (20/42 adenocarcinomas, 16/42 adenomas). The total numbers of tumour-bearing animals in clean air and exhaust-exposed groups were not, however, significantly different. In the groups exposed 20 times to 50 μg benzo[*a*]pyrene, adenocarcinoma induction by the exhaust was inhibited significantly (3/35, 5/36, 15/42 in the 1:27, 1:61 and control groups, respectively). Additional groups of 61–83 newborn NMRI mice received a single subcutaneous injection of 4 μg (females and males) or 10 μg (females only) dibenzo[*a,h*]anthracene followed by inhalation exposure to one of the two dilutions of gasoline exhaust for six months, after which they were killed; the number of lung tumours per animal was not significantly different from that in controls exposed simultaneously to clean air.

Groups of 86–90 female NMRI mice [age unspecified] were injected subcutaneously with 10,30 or 90 μgbenzo[*a*]pyrene alone or together with 6.6 or 20 mg exhaust condensate from a gasoline engine [unspecified] (Pott *et al.*, 1977). The dose-response relationship for local sarcomas produced by benzo[*a*]pyrene (20%, 54%, 76%) was reduced significantly by the addition of both doses of the condensate. The difference was seen most clearly 30 weeks after treatment.

Rat: Two groups of female Sprague-Dawley rats [initial numbers unspecified] were either administered *N*-nitrosodiisopropanolamine in the drinking-water (0.01%) or were exposed concomitantly by inhalation for 2 h per day on three days per week to gasoline engine (generator EM300) exhaust diluted 1:250 in air for six to 12 months, at which time the animals were killed (Yoshimura, 1983). In animals killed between seven and 12 months, the number of lung tumours (11/37) in the combined treatment group (one adenoma and ten undifferentiated carcinomas, squamous-cell carcinomas, adenocarcinomas and mixed tumours) was significantly greater than that in the 24 nitrosamine controls (two carcinomas; $p < 0.05$).

Groups of 60 female Bor: WISW rats, ten to 12 weeks old, received 25 daily subcutaneous injections of 0.25 or 0.5 g/kg bw *N*-nitrosodipentylamine and were exposed to gasoline engine exhaust, as described on p. 99 (Heinrich *et al.* 1986c). The treatments induced significant increases in the incidences of benign tumours of the whole respiratory tract (in 9/47 and 14/48 rats given the 1:27 and 1:61 dilutions of exhaust and receiving 0.5 g/kg bw nitrosamine, and in 15/50 and 14/45 rats given the 1:27 and 1:61 dilutions and receiving0.25 g/kg bw nitrosamine, respectively) compared with clean air controls (5/48 and 4/46 rats), but decreases in the incidences of malignant tumours (33/47 and 34/48, respectively, compared to 43/48 controls; and 13/50 and 18/45 rats, compared to 29/46 in the groups receiving 0.5 and 0.25 g/kg bw nitrosamine). When lung tumour rates were evaluated separately, the incidences of malignant tumours (mostly squamous-cell carcinomas and adenocarcinomas) were also reduced in nitrosamine-treated rats by exposure to either concentration of exhaust (in 24/48, 25/49 and 40/49 rats in the 0.5 g/kg bw groups and in 11/54, 14/47 and 26/48 rats in the 0.25 g/kg bw groups exposed to 1:27 and 1:61 dilutions and clean air, respectively), whereas the incidence of benign tumours remained unchanged. Rats given the low dose of *N*-nitrosodipentylamine exposed to 1:61 or 1:27 dilutions of gasoline exhaust showed overall lung tumour rates of 15/47 and 13/54, respectively, *versus* 27/48 rats treated with nitrosamine but exposed to clean air. In animals given the high dose of *N*-nitrosodipentylamine, these rates were 33/49 and 28/48, respectively, *versus* 44/49 controls.

Hamster: Groups of 80–81 female Syrian golden hamsters, ten to 12 weeks old, received a single subcutaneous injection of 3 mg/kg bw *N*-nitrosodiethylamine (NDEA) or 20 intratracheal instillations of 0.25 mg benzo[*a*]pyrene and were exposed to gasoline engine exhaust, as described on p. 99 (Heinrich *et al.* 1986c). Administration of NDEA or benzo[*a*]pyrene to hamsters exposed to clean air resulted in basic rates of benign respiratory tract tumours of 12.8 and 6.5% of animals, respectively; one malignant tumour of the paranasal cavity was also seen in the group exposed to benzo[*a*]pyrene. The basic tumour rate was not significantly increased by exposure to either dilution of exhaust. Tumour rates in NDEA- and benzo[*a*]pyrene-treated animals inhaling the 1:27 dilution of exhaust were approximately 50% lower than those in treated animals inhaling the 1:61 dilution or clean air.

Groups of 52 male and 52 female Syrian hamsters, six to eight weeks old, received a single subcutaneous injection of 4.5 mg/kg bw NDEA three days prior to exposure by inhalation to gasoline engine exhaust, as described on p. 98 (Brightwell *et al.* 1986). The authors reported that NDEA-treated hamsters had a nonsignificantly increased incidence of tracheal papillomas. [The Working Group noted the inadequate reporting of the data.]

3.2. Other relevant data

(a) Experimental systems

(i) Deposition, clearance, retention and metabolism

Engine exhaust contains material in gaseous, vapour and particulate phases, and the absorption, distribution and excretion of individual constituents is influenced by the phase in which they occur and by the properties of each compound. After inhalation, highly soluble compounds in the gaseous phase, such as sulfur dioxide, are absorbed in the upper airways and do not penetrate significantly beyond the level of the bronchioles. Compounds that interact biochemically with the body are also retained in significant quantities; thus, processes such as binding of carbon monoxide to haemoglobin normally occur in the gas-exchange (pulmonary) region of the lung.

Retention characteristics of materials not associated with the particulate phase are highly compound-specific. The factors affecting the uptake of a wide variety of vapours and gases have been summarized (Davies, 1985).

As described on p. 47, a proportion of a compound in the vapour phase condenses onto the particulate material produced in the engine exhaust. The association of a compound with the particulate phase modifies the deposition pattern and affects its lung retention; the lung burden of a compound following continuous exposure to that compound coated on particles may be many times that of continuous exposure to the compound alone (Bond *et al.*, 1986).

Deposition in the respiratory tract is a function of particle size. The median particle size in a variety of long-term exposure systems has been between 0.19 and 0.54 μm (Yu & Xu, 1986), representative of that in an urban environment (Cheng *et al.*, 1984). However, some of the carbonaceous mass in environmental samples results from airborne suspension of material collected in automobile exhaust pipes and is >5 μmin size (Chamberlain *et al.*, 1978); such particles are unlikely to be produced in a static exposure system. Dilution has little effect on the size distribution of particles used in long-term studies (0.3–7 mg/m^3; Cheng *et al.*, 1984), although rapid dilution (<1 sec) can lead to a smaller size (0.10–0.15 μm; Chan *et al.*, 1981), The presence of sulfates in the particulate phase (Lies *et al.*, 1986) may lead to enlargement of individual particles in the high humidity of the respiratory tract, thereby altering the deposition pattern (Pritchard, 1987).

Diesel engine exhaust

Deposition: Studies of the deposition of diesel engine exhaust, representative of fresh urban exhaust, are summarized in Table 24; the particle sizes used were in the lower part of the range found in long-term exposure chambers. Deposition following nose-only exposure was measured by radiotracer technique. Data are quoted as a proportion of the amount of inhaled aerosol, which is based on estimates of ventilation rates. [The Working Group noted that the data on deposition of diesel particles in rats are in broad agreement with data for other particulate materials of similar size (Raab *et al.*, 1977; Wolff *et al.*, 1984).]

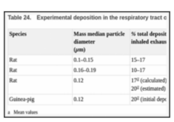
Table 24. Experimental deposition in the respiratory tract c

Species	Mass median particle diameter (μm)	% total deposit inhaled exhaus
Rat	0.1–0.15	15–17
Rat	0.16–0.19	10–17
Rat	0.12	17[a] (calculated) 20[a] (estimated)
Guinea-pig	0.12	20[a] (initial depc

a Mean values

Table 24.

Experimental deposition in the respiratory tract of diesel engine exhaust particles.

A model for the deposition of diesel exhaust particles predicts that, as the median size increases from 0.08 to 0.30 μm,total deposition in rats falls from 25 to 15%, tracheo-bronchial deposition from 5 to 2% and pulmonary deposition from 12 to 5%; upper respiratory tract deposition remains constant at 8% (Yu & Xu, 1986). The model predicts that pulmonary deposition will vary only with (body weight)$^{-0.14}$, since diffusion is the predominant mechanism (Xu & Yu, 1987). [The Working Group noted that this model is in good agreement with the observed deposition of other particles (e.g., Raab *et al.*, 1977; Wolff *et al.*, 1981, 1984)].

Following exposure of rats for six, 12, 18 and 24 months to 0.4, 3.5 and 7.1 mg/m^3 diesel exhaust particles, there was no significant effect of length of exposure or exposure concentration on the deposition of 0.1 μm gallium oxide particles (Wolff *et al.*, 1987).

Mucociliary clearance: The clearance of particles from the lung following a single exposure to radiolabeled diesel particles is summarized in Table 25. The fast phase of clearance is conventionally assumed to be due to mucociliary action, the remainder (slow phase) to pulmonary clearance. The variation in the fraction of the lung deposit cleared by mucociliary action (i.e., the tracheobronchial deposit) is linked to particle size and hence deposition pattern. [The Working Group noted that Gutwein *et al.* (1974) give no information on particle size and that, without this, the high tracheobronchial deposit cannot be accounted for.]

Table 25.

Clearance of diesel exhaust particles from rat lung following single exposures.

In rats exposed for short periods (4–100 h) to diesel exhaust with particulate concentrations in the range 0.9–17 mg/m^3, a dose-dependent reduction in mucociliary clearance occurred, although the effect was less marked on exposure to the gas phase alone (Battigelli *et al.*, 1966). No such effect occurred in sheep exposed for 30 min to concentrations of 0.4–0.5 mg/m^3 of resuspended diesel particles, i.e., in the absence of the gas phase (Abraham *et al.*, 1980). Exposure-related differences in tracheal mucociliary clearance have also been reported over 1–12 weeks in rats exposed to 1 and 4.4 mg/m^3 particulates in diesel exhaust. However, in another study, there was no effect on tracheal mucociliary clearance of exposures of six to 24 months to particulate concentrations of 0.4–7.1 mg/m^3 (Wolff *et al.*, 1987). [The Working Group noted that there may be some impairment of mucociliary clearance, possibly caused by the gas phase of engine exhaust, but that its effect is of limited significance in the long term.]

Pulmonary (alveolar) clearance: The pulmonary clearance of diesel particles is very much slower than the mucociliary clearance (see Table 25). On the basis of these data, the lung burden of rats during protracted exposure should tend exponentially toward an equilibrium value at 12 months. In rats exposed to diesel exhaust with a particulate concentration of 0.3 mg/m^3, there was evidence of equilibration after 12 months (only a 2.5-fold increase over 24 months); however, with exposures of 3.5 and 7.0 mg/m^3, lung burdens increased steadily (five to 11 fold) over 24 months. This has been referred to as the ‘overload’ phenomenon (Wolff *et al.*, 1987). The clearance rate of insoluble particles following prolonged exposure to diesel exhaust at a variety of concentrations and durations also indicates impaired long-term clearance (Wolff *et al.*, 1984). Thus, it appears that the normal clearance mechanisms become seriously impaired, leading to very long-term retention of material in the lung, usually referred to as ‘sequestration’.

Results of studies on particulate clearance in rats following repeated exposures to diesel exhaust are summarized in Table 26. Lung clearance was estimated either by exposure to a pulse of ^{14}C-labelled diesel exhaust particles at the end of the cumulative exposure (Chan *et al.*, 1984; Lee *et al.*, 1987) or by measuring the lung burden of soot spectrophotometrically (Griffis *et al.*, 1983). Also included are data on the clearance of a pulse of radiolabeled fused aluminosilicate particles following exposure to diesel exhaust for two years at particulate concentrations between 0.4 and 7.0 mg/m^3 (Wolff *et al.*, 1987). [The Working Group noted that pulse techniques measure only the clearance of the material that has most recently entered the lung. Since there is no difference between this and total soot measurements, deposition, and hence ventilation, must continue to occur in those areas where clearance is impaired, confirming the findings of Wolff *et al.* (1987) that deposition is unaffected by prolonged exposure to diesel exhaust.]

Table 26.

Pulmonary clearance in rats of insoluble particles following exposure to diesel exhaust.

Pulmonary clearance as a function of contemporary lung burden has also been considered (McClellan, 1986). In an analysis of the published data, Wolff *et al.* (1986) concluded that in rats sequestration becomes a significant burden at a certain level [about 1 mg/lung] and is related to the rate of accumulation; i.e., short exposure to a high concentration produces an effect at a lower lung burden than more protracted exposure at a lower concentration. Thus, there is no strong relationship between the half-time of clearance and cumulative exposure.

[The relationship between half-times for pulmonary clearance of diesel exhaust particles and other insoluble particles in the rat following exposure to diesel exhaust and an ‘exposure rate’, calculated by the Working Group from cumulative exposure, mg/m^3 × weeks × (h/week)/168, is plotted in Figure 8. The Working Group noted that there is an effect on clearance at ‘exposure rates’ above 10 mg/m^3 × week (i.e., continuous exposure to 0.2 mg/m^3 or exposure for 40 h per week to 0.8 mg/m^3 for one year) and a strong suggestion that impaired clearance occurs over the whole range of ‘exposure rates’ studied.]

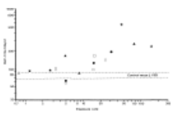

Fig. 8.

Pulmonary clearance in rats of diesel exhaust particles and other insoluble particles following exposure to diesel exhaust.

Studies in rats on the effect of exposure to diesel exhaust on the clearance of metal oxide particles containing a γ-emitting isotope are summarized in Table 27 (Bellmann *et al.*, 1983; Heinrich *et al.*, 1986a; Lewis *et al.*, 1986; Wolff *et al.*, 1987). The control animals cleared the metal oxide particles much faster than they did diesel particles or fused aluminosilicate particles (see Table 26; Wolff *et al.*, 1987). [The Working Group noted that this suggests that clearance of metal oxides involves a significant soluble component.]

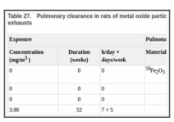

Table 27.

Pulmonary clearance in rats of metal oxide particles following exposure to diesel engine exhausts.

[The relationship between half-times for pulmonary clearance of metal oxide particles in rats following exposure to diesel exhaust and an ‘exposure rate’ calculated by the Working Group is plotted in Figure 9. The Working Group noted that impaired clearance of metal oxide particles does not become apparent until significantly higher values of ‘exposure rate’ than in the studies on diesel and fused aluminosilicate particles and considered that the differences in the results could be explained by continuing solubility masking an impairment in mechanical clearance, implying that sequestration is primarily a mechanical effect. For comparison, data for gasoline from Bellmann *et al.* (1983) have been added.]

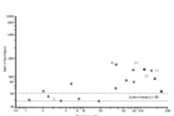

Fig. 9.

Pulmonary clearance of metal oxide particles in rats following exposure to engine exhaust.

After only two months' exposure of rats to a diesel exhaust particulate concentration of 2 mg/m^3, clearance of metal oxide particles was significantly faster than in controls, suggesting a stimulated lung response; no such effect was observed subsequently (Oberdoerster *et al.*, 1984; Lewis *et al.*, 1986). [The Working Group noted that overloading had probably occurred.]

The rate of clearance of ferric oxide in hamsters was slightly lower (75 ± 40 days) following one year's exposure to diesel exhaust particles (4 mg/m^3) than that in clean-air controls (55 ± 17 days; Heinrich *et al.*, 1986a). In another study, only 10% clearance of ^{14}C-labelled diesel particles was observed 400 days after a single exposure of guinea-pigs (Lee *et al.* 1983). Six months after a three-month exposure of mice, rats and hamsters to diesel exhaust (particles, 1.5 mg/m^3), the mice appeared to have a slower clearance than rats and hamsters (Kaplan *et al.*, 1982).

The gas phase alone appears to have no effect on pulmonary clearance in rats or hamsters (Heinrich *et al.*, 1986a). Clearance of diesel particles following prolonged exposure to a carbon black aerosol of similar size showed a pattern of impairment similar to that observed after diesel exposure (see Fig. 8), strongly suggesting that dust overloading *per se* impairs mechanical clearance (Lee *et al.*, 1987). [The Working Group noted that the half-time lung clearance of carbon black is shorter than that of diesel exhaust at similar 'exposure rates'. This may reflect a local effect of diesel particles on the alveolar macrophages which mediate mechanical clearance; diesel particles depress the phagocytic capacity of macrophages, whereas coal dust activates them (see below and Castranova *et al.*, 1985).]

The majority of the particles that are cleared by macrophages from the pulmonary region leave *via* the ciliated epithelium and are excreted *via* the gut. However, a proportion penetrate the lymphatic system, borne by macrophages, and are filtered by the lymph nodes to form aggregates of particles (Vostal *et al.*, 1981). It has been estimated that one-third of clearance occurred *via* this route during the first 28 days after exposure of rats to diesel exhaust (Chan *et al.*, 1981). [The Working Group noted that there is no information on how this proportion changes with time or with prolonged exposure.]

Retention: The retention of the organic compounds associated with exhaust particles has been reviewed (McClellan *et al.*, 1982; Vostal *et al.*, 1982; Holmberg & Ahlborg, 1983; Vostal, 1983; Wolff *et al.*, 1986). Organic compounds adsorbed on exhaust particles can be extracted by biological fluids, as has been observed in assays for mutagenesis (Claxton, 1983; Lewtas & Williams, 1986; see p. 121). The half-time of the slow phase of lung clearance for ^{14}C derived from labelled diesel exhaust was 25 days in rats (Sun & McClellan, 1984), and that for ^{3}H-benzo[*a*]pyrene coated on diesel particles was 18 days (Sun *et al.*, 1984). The retention of 1-nitropyrene adsorbed onto diesel exhaust particles is described in the monograph on that compound.

No data were available on changes in the retention of individual compounds after prolonged exposure to diesel exhaust.

Metabolism: The metabolism of several components of engine exhausts has been reported previously: some polycyclic aromatic hydrocarbons (IARC, 1983), formaldehyde (IARC, 1982a), lead (IARC, 1980), nitroarenes (IARC, 1984) and benzene (IARC, 1982b). The metabolism of 1-nitropyrene associated with diesel exhaust particles is described in the monograph on that compound.

The metabolism of benzo[*a*]pyrene coated on diesel exhaust particles has been studied in different experimental systems. Fischer 344 rats were exposed for 30 min by nose-only inhalation to ^{3}H-benzo[*a*]pyrene adsorbed onto diesel engine exhaust particles. The majority (65–76%) of the radioactivity retained in the lungs (as determined by high-performance liquid chromatography) 30 min and 20 days after exposure was associated with benzo[*a*]pyrene. Smaller amounts of benzo[*a*]pyrene-phenols (13–18%) and benzo[*a*]-pyrene-quinones (5–18%) were also detected. No other metabolite was found (Sun *et al.*, 1984).

The pulmonary macrophages of dogs metabolized 1 μM ^{14}C-benzo[*a*]pyrene, either in solution or coated on diesel particles, into benzo[*a*]pyrene-7,8-, -4,5- and -9,10-dihydrodiols (major metabolites) as well as into benzo[*a*]pyrene-phenols and benzo[*a*]pyrene-quinones (minor metabolites). The total quantity of metabolites did not differ when macrophages were incubated with either benzo[*a*]pyrene in solution or benzo[*a*]pyrene coated on diesel particles (Bond *et al.*, 1984).

Fischer 344 rats were exposed to diesel engine exhaust (7.1 mg/m^3 particles) for about 31 months. After sacrifice, DNA was extracted from the right lung lobe and analysed for adducts by ^{32}P-postlabelling: more DNA adducts were found in the exhaust-exposed group than in the unexposed group (Wong *et al.*, 1986).

Fischer 344 rats and Syrian golden hamsters were exposed to different dilutions of diesel engine exhaust for six months to two years, when blood samples were analysed for levels of haemoglobin adducts (2-hydroxyethylvaline and 2-hydroxypropylvaline) by gas chromatography-mass spectrometry. A dose-dependent increase in the level of haemoglobin adducts was found, corresponding to the metabolic conversion of about 5–10% of inhaled ethylene and propylene to ethylene oxide and propylene oxide, respectively (Törnqvist *et al.*, 1988).

Gasoline engine exhaust

Deposition: In a study on the deposition of particles from inhaled gasoline exhausts (mass median diameter, 0.5 μm) in rats, mean total deposition of particles was 30.5%. Most deposition occurred in the alveolar region and in the nasal passages (Morgan & Holmes, 1978). In this study, the concentration of carbon monoxide in the gasoline exhaust was reduced before inhalation, and the particles were larger than those of the diesel exhausts reported. [The Working Group noted that the greater deposition of gasoline exhaust particles is consistent with the larger size of the particles and does not imply any fundamental difference in deposition between diesel and gasoline exhausts particles.]

Clearance: The results of a study on pulmonary clearance of ferric oxide by rats and hamsters following exposure to gasoline engine particles (0.04 and 0.09 mg/m^3) for two years are summarized in Table 28 (Bellmann *et al.*, 1983). Clearance was similar to that in controls and in animals exposed to diesel exhaust (see Table 27). [The Working Group noted that, on the basis of the data concerning exposure to diesel exhaust, clearance of metal oxide particles would not be impaired by exposures to such low concentrations.]

Table 28. Pulmonary clearance by rats and hamsters of fer to gasoline engine exhausts[a]

Exposure		
Concentration (mg/m^3)	Duration (months)	h/day × days/week
0	0	0
0.04	12	19 × 5
0.09	(US—72 cycle)	19 × 5

Table 28.

Pulmonary clearance by rats and hamsters of ferric oxide particles following exposure to gasoline engine exhausts.

Metabolism: As reported in an abstract, crude extracts of gasoline exhaust were applied topically to male BALB/c mice over a period of one to two weeks and DNA was isolated from the treated skin for analysis by ^{32}P-postlabelling. The major DNA adduct derived from benzo[*a*]pyrene-7,8-dihydrodiol-9,10-epoxide was found in exposed mice(Randerath *et al.* 1985).

Fischer 344 rats and Syrian golden hamsters were exposed to different dilutions of gasoline engine exhaust for six months to two years, and blood samples were analysed for levels of 2-hydroxyethylvaline and 2-hydroxypropylvaline in haemoglobin by gas chromatography-mass spectrometry. A dose-dependent increase in the level of haemoglobin adducts was found, corresponding to the metabolic conversion of about 5–10% of inhaled ethylene and propylene to ethylene oxide and propylene oxide, respectively (Törnqvist *et al.*, 1988).

(ii) Toxic effects

Diesel engine exhaust

After about 480 days, NMRI mice exposed to unfiltered, diluted (1:17) diesel exhaust (particles, 4 mg/m^3; carbon monoxide 14.3 ± 2.5 mg/m^3) had lost body weight in comparison with animals exposed to filtered exhaust (carbon monoxide, 12.7 ± 2.2 mg/m^3) or with controls. Under the same circumstances, rats had a lower weight increase (Heinrich *et al.*, 1986a).

The livers of Syrian golden hamsters exposed for five months to diesel exhaust diluted 1:5 and 1:10 in air had enlarged sinusoids with activated Kupffer's cells. Nucleoli were frequently fragmented or irregularly shaped. Fat deposition was observed in the sinusoids. Mitochondria from animals exposed to the 1:5 dilution had frequently lost cristae. Giant microbodies were observed in hepatocytes, and gap junctions between hepatocytes were disturbed (Meiss *et al.*, 1981).

In an initiation-promotion assay in rat liver using induction of 7-glutamyl transpeptidase-positive foci as the endpoint, Pereira *et al.* (1981a) exposed partially hepatectomized Sprague-Dawley rats to diesel exhaust (particles, 6 mg/m^3) for up to six months. The animals were also fed choline-supplemented or choline-deficient diets. Exposure to diesel exhaust did not alter the number of foci or induce 'remarkable' liver toxicity.

Lung function: Short-term exposure to diesel exhaust (28 days) led to a 35% increase in pulmonary air flow resistance in Hartley guinea-pigs (Wiester *et al.*, 1980) but increased vital capacity and total lung capacity in Sprague-Dawley rats (Pepelko, 1982a).

Prolonged exposure of rats to diluted diesel exhaust has led to impairment of lung function in some studies (Gross, 1981; Heinrich *et al.*, 1986a; McClellan, 1986) but not in others (Green *et al.*, 1983). No significant impairment of lung function was reported in hamsters (Heinrich *et al.*, 1986a).

A classic pattern of restrictive lung disease was observed in cats after 124 weeks of exposure to diesel exhaust (weeks 1–61: dilution factor, air:diesel, 18; particles, ~6 mg/m^3; weeks 62–124: dilution factor, 9; particles, ~12 mg/m^3; Moorman *et al.*, 1985). No such effect was observed during the first 61 weeks of the study (Pepelko *et al.*, 1980, 1981; Moorman *et al.*, 1985).

Lung morphology, biochemistry and cytology: After two years of exposure, the wet and dry weights of lungs from both mice and rats exposed to unfiltered, diluted (1:17) diesel exhaust (particles, 4 mg/m^3; carbon monoxide, 14.3 ± 2.5 mg/m^3) were two to three times higher than those of controls. The lung weights of Syrian golden hamsters exposed similarly had increased by 50 and 70% (Heinrich *et al.*, 1986a). An increased lung to body weight ratio was also observed in guinea-pigs following an eight-week exposure to a dilution of 1:13 (Wiester *et al.*, 1980).

Exposure of rats for 30 months to diesel exhaust (particles, 1–4 mg/m^3) resulted in dose-dependent irregularity, shortening and loss of cilia in ciliated epithelia, particularly the trachea and the main bronchi (Ishinishi *et al.*, 1986a).

Increased numbers of alveolar macrophages containing diesel particles and of type II pneumocytes and accumulation of inflammatory cells within the alveoli and septal walls were observed after a 24-h exposure of Fischer 344 rats to high concentrations of diesel exhaust (particles, 6 mg/m^3; White & Garg, 1981). Macrophage aggregates were still present six weeks after a two-week exposure (Garg, 1983).

Following prolonged exposure of rats to diesel exhausts (particles, 2–5 mg/m^3), particle-containing alveolar macrophages and type II cell hyperplasia were observed (Heinrich *et al.*, 1986a; Iwai *et al.*, 1986; Vallyathan *et al.*, 1986). Increases in both the number and size of macrophages and in the number of polymorphonuclear leukocytes were also observed in rats and hamsters (Chen *et al.*, 1980; Vostal *et al.*, 1982; Strom, 1984; Heinrich *et al.*, 1986a). Elevated levels of lymphocytes have also been reported in rats and hamsters (Strom, 1984; Heinrich *et al.*, 1986a). Particle accumulation and cellular proliferation have been observed in guinea-pigs (Chen *et al.*, 1980; Wiester *et al.*, 1980; Barnhart *et al.*, 1981; Weller *et al.*, 1981), and granulocyte counts were increased dramatically (up to ten-fold) in hamsters (Heinrich *et al.*, 1986a).

In Fischer 344 rats exposed to diesel engine exhaust (particles, 2 mg/m^3) for two years, depressed chemiluminescence and decreased surface ruffling of alveolar macrophage membranes were observed, indicating a depression of the phagocytic activity of the macrophages (Castranova *et al.*, 1985).

In specific-pathogen-free Wistar rats exposed to diesel exhaust (soot, 8.3 ± 2.0 mg/m^3) continuously for up to 20 months, slight focal and diffuse macrophage accumulation and alveolar cell hypertrophy were observed after four months. After 20 months' exposure, focal macrophage accumulation was moderate and diffuse accumulation was slight to moderate. Alveolar cell hypertrophy was more marked (up to severe), and interstitial fibrosis and alveolar emphysema were more pronounced than after four months. Alveolar bronchiolization was seen in one group at four months, but was present in four of six groups up to a moderate degree after 20 months (Karagianes *et al.*, 1981). In a long-term inhalation study with pathogen-free Fischer 344 rats exposed for up to 30 months to whole exhaust diluted to contain soot concentrations of 0.35, 3.5 or 7.0 mg/m^3, focal accumulation of soot was dose-dependent and was paralleled by an active inflammation involving alveolar macrophages adjacent to terminal bronchioli. Progressive fibrosis was present in areas of soot accumulation. Epithelial hyperplasia and squamous metaplasia occurred adjacent to fibrotic foci (Mauderly *et al.*, 1987). However, although there was accumulation of particles, no histopathological sign of fibrotic change was observed after 12 or 24 months' exposure of Fischer 344 rats to diesel emissions (particles, 2 mg/m^3; Green *et al.*, 1983; Vallyathan *et al.*, 1986).

Fibrotic changes in the lungs of Hartley guinea-pigs exposed to diesel exhaust (particles, 0.25–6 mg/m^3) began after six months' exposure at a particulate concentration of about 0.75 mg/m^3; ultrastructural changes were concentration-dependent and started to appear after two weeks of exposure at this level. Alveolar septa were thickened following exposures above 0.25 mg/m^3 particles (Barnhart *et al.*, 1981, 1982).

After exposure of cats to diesel exhaust for 27 months (particles, 6 mg/m^3 for weeks 1–61; 12 mg/m^3 for weeks 62–124), bronchiolar epithelial metaplasia and peribronchial fibrosis were observed; the latter became more severe after an additional six months' exposure to clean air, but the bronchiolar epithelium returned to normal (Hyde *et al.*, 1985).

Biochemical changes in the lung associated with the changes described have been discussed by McClellan (1986). Lavage fluids from hamsters and rats after one and two years' exposure to unfiltered, diluted (1:17) diesel exhaust (particles, 4 mg/m^3; carbon monoxide, 14.3 ± 2.5 mg/m^3) contained increased levels of lactate dehydrogenase, alkaline and acid phosphatase, and glucose-6-phosphate dehydrogenase and of collagen and total protein (Heinrich *et al.*, 1986a). In contrast, acid phosphatase activity was reduced in rats and guinea-pigs exposed for one day to 12 months to diesel engine exhaust (particles, 0.25–6 mg/m^3); the effects were directly related to duration and levels of exposure (Weller *et al.*, 1981). Protein content and β-glucuronidase and acid phosphatase activities were elevated in lavage fluid cells from rats exposed to diesel exhaust for 48 weeks (particles, 1.5 mg/m^3) or 52 weeks (particles, 0.75 mg/m^3; Strom, 1984). Rats exposed to filtered diesel exhaust showed only small increases in glucose-6-phosphate dehydrogenase activity, collagen and protein content, while hamsters showed no increase (Heinrich *et al.*, 1986a). The total lung collagen level was elevated in the lungs of cats six months after exposure to diesel exhaust for 27 months. The cross-linked collagen content was more than doubled at the end of the exposure to air, and the collagen aldehydes:hydroxyproline ratio was elevated (Hyde *et al.*, 1985).

Sequestration (discussed above, p. 107) can be correlated with histopathological changes observed after prolonged exposure. Strom (1984) concluded that the apparent threshold of exposure of rats for increased influx of cells into the lung, beginning with alveolar macrophages, followed by polymorphonuclear leukocytes and lymphocytes, was 0.25–0.75 mg/m^3 for 28 weeks. [The Working Group noted that this would correspond to a calculated 'exposure rate' of 9 mg/m^3 × week, 110 h/week, which is not dissimilar to the point at which marked sequestration occurs (see Fig. 8).]

In Fischer 344 rats, DNA synthesis in lung tissue was increased four-fold after two days of continuous exposure by inhalation to diesel exhaust (particles, 6 mg/m^3). DNA synthesis returned to control levels one week after exposure. The labelling index of type II cells was significantly greater than that in controls after two and three days of exposure to diesel exhaust. After one day of exposure, palmitic acid incorporation into phosphatidylcholine in lung tissue increased by three fold when tissue palmitic acid content decreased. Total lung fatty acid content decreased by 23% after one day of exposure (Wright, 1986).

Effects on metabolism: Exposure to diesel particles or diesel particulate extracts has been reported to have no effect (Chen & Vostal, 1981 ; Rabovsky *et al.*, 1984) or a moderate (<two-fold change) effect (Lee, I.P. *et al.*, 1980; Pepelko, 1982b; Dehnen *et al.*, 1985; Chen, 1986) on aryl hydrocarbon hydroxylase activity in the lung and liver of mice and rats and in the lung of hamsters.

Exposure of Fischer 344/Crl rats by inhalation to diesel engine exhaust (particles, 7.4 mg/m^3) for four weeks doubled the rate of 1-nitropyrene metabolism in both nasal tissue and perfused lung. In addition, the amount of ^{14}C covalently bound to lung macromolecules was increased four fold (Bond *et al.*, 1985). (See also the monograph on 1-nitropyrene.)

One week after instillation, there was significantly more residual benzo[*a*]pyrene in the lungs of A/Jax mice exposed to diesel engine exhaust (particles, 6 mg/m^3) for nine months, probably because benzo[*a*]pyrene had bound to exhaust particles. The amounts of free benzo[*a*]pyrene and of different unconjugated and conjugated metabolite fractions in lungs, liver and testis were similar to those in diesel exhaust-exposed and control mice (Cantrell *et al.*, 1981;Tyrer *et al.*, 1981).

Immunology and infection: In guinea-pigs exposed to diesel engine exhaust (particles, 1.5 mg/m^3) for up to eight weeks, B- and T-cell counts in lymph nodes were not altered (Dziedzic, 1981). No change was observed in the immunological function of splenic B- or T-cells from Fischer 344 rats exposed for up to 24 months to diesel engine exhaust (particles, 2 mg/m^3; Mentnech *et al.*, 1984).

CD-1 mice and Fischer 344 rats exposed to high (particles, 7 mg/m^3), medium (particles, 3.5 mg/m^3) or low (particles, 0.35 mg/m^3) levels of diesel engine exhaust for up to 24 months had exposure-related pathological changes in lung-associated lymph nodes, including enlargement, with histiocytes containing particles in the peripheral sinusoids and within the cortex. The total number of lymphoid cells in lung-associated lymph nodes was significantly increased after six months of exposure. In groups of mice and rats immunized at six-monthly intervals by intratracheal instillation of sheep red blood cells and analysed for IgM antibodies in lymphoid cells in rats and mice and for IgM, IgC and IgA antibodies in serum of rats, mice had an increased number of antibody-forming cells in lymph nodes from six months, but differences from controls were not statistically significant. In rats, the total number of IgM antibody-forming cells in lymph nodes was significantly elevated after six months of exposure to the high level of diesel exhaust and after 12 months of exposure to all levels. Antibody titres to sheep red cells in rat serum were not altered (Bice *et al.*, 1985).

The IgE antibody response of BDF_1 mice was increased after five intranasal inoculations at intervals of three weeks of varying doses of a suspension of diesel engine exhaust particles in ovalbumin solution. Antiovalbumin IgE antibody titres, assayed by passive cutaneous anaphylaxis, were enhanced by doses as low as 1 µg particles given at a three-week interval (Takafuji *et al.*, 1987).

Exposure to diesel engine exhaust may increase the susceptibility of mice to infection (Campbell *et al.*, 1981; Hahon *et al.*, 1985).

Gasoline engine exhaust

Lifetime exposure of specific-pathogen-free Sprague-Dawley rats to gasoline engine exhaust (carbon monoxide, 57 mg/m^3; nitrogen oxides, 23 ppm) reduced body weight (Stupfel *et al.*, 1973). Body growth rate was also reduced among Sprague-Dawley rats exposed for up to 88 days to exhaust (dilution, 1:11) from a gasoline engine operated with (carbon monoxide, 80 mg/m^3) or without (carbon monoxide, 240 mg/m^3) a catalytic converter (Cooper *et al.*, 1977).

Haematocrit and haemoglobin and erythrocyte counts were increased in Wistar rats exposed to gasoline engine exhaust (carbon monoxide, 583 mg/m^3) for five weeks (Massad *et al.*, 1986). Sprague-Dawley rats were exposed to diluted (∼1:10) exhaust from a gasoline engine with and without a catalytic converter (particles, ∼1.2 mg/m^3 irradiated, 1.1 mg/m^3 nonirradiated; carbon monoxide, 47 and 53 mg/m^3; and particles, 0.77 mg/m^3 nonirradiated, 3.59 mg/m^3 irradiated; carbon monoxide, 631 and 640 mg/m^3, respectively) for seven days. Haematocrit and serum lactate dehydrogenase activities were elevated in both groups exposed to emissions generated without a catalyst; no such change was observed in the groups exposed to emissions generated with a catalyst. No change was observed in serum glutamate oxaloacetate transaminase activity (Lee *et al.*, 1976).

Beagle dogs exposed for 61 months to gasoline engine exhaust (carbon monoxide, 114 mg/m^3; Malanchuk, 1980) developed arrhythmia and bradycardia (Lewis & Moorman, 1980).

Lung function: Long-lasting functional disturbances of the lung were observed in beagle dogs after exposure to raw or irradiated gasoline engine exhaust (carbon monoxide, 114–126 mg/m^3) for 68 months (Lewis *et al.*, 1974; Gillespie, 1980). In contrast, no impairment in lung function was detected in Crl:COBS CD(SD)BR rats exposed for 45 or 90 days to diluted (1:10) exhaust from a catalyst-equipped gasoline engine (particles, 11.32 ± 1.27 mg/m^3; carbon monoxide, 19.5 ± 3.5 mg/m^3; Pepelko *et al.*, 1979).

Lung morphology, biochemistry and cytology: In several reports of studies in beagle dogs, atypical epithelial hyperplasia was observed in animals exposed for 68 months to raw or irradiated gasoline engine exhaust (carbon monoxide, 114 mg/m^3). Increases in alveolar air space and cilia loss were observed after a long recovery period following exposure to irradiated exhaust (Hyde *et al.*, 1980). The collagen content of lung tissues following exposure to raw or irradiated exhaust, with and without a 2.5–3-year recovery period was not significantly different from that in unexposed animals; prolyl hydroxylase levels in the lung were highest in groups exposed to irradiated exhaust. Exposure to a mixture of sulfur oxides and irradiated exhaust also increased the level of this enzyme (Orthoefer *et al.*, 1976; Bhatnagar, 1980). Phosphatidyl ethanolamine content was lower in liver tissues of some dogs exposed for 68 months, and lung tissue phosphatidyl ethanolamine content was 90% of the mean control value. Lysobisphosphatidic acid and phosphatidyl glycerol levels in the lungs were increased (Rouser & Aloia, 1980).

Effects on metabolism: Extracts of gasoline engine particles instilled into hamster lungs increased aryl hydrocarbon hydroxylase activity of lung tissue by three to five fold (Dehnen *et al.*, 1985).

Immunology and infection: Increased sensitivity to infection has been demonstrated following exposure of mice to the exhaust of a gasoline engine with a catalytic converter, but the effect was less than that in mice following similar exposure to diesel engine exhaust (Campbell *et al.*, 1981).

(iii) Effects on reproduction and prenatal toxicity

Diesel engine exhaust

A three-fold increase in sperm abnormalities was observed in male Chinese hamsters exposed to diesel engine exhaust [dose unspecified] for six months, as compared to controls exposed to fresh air (Pereira *et al.*, 1981b). As reported in an abstract, a statistically significant dose-related increase in sperm abnormalities was observed in male (C57B1/6 × C3H)F_1 mice receiving 50, 100 or 200 mg/kg bw diesel engine exhaust particles by intraperitoneal injection for five days. An eight-fold increase in sperm abnormalities over the spontaneous level was observed in mice receiving the highest dose. A significant decrease in the number of sperm was observed only at the highest dose; testicular weight was not affected (Quinto & De Marinis, 1984).

Gasoline engine exhaust

Fertilized white Leghorn eggs were incubated with diluted (1:11, exhaust:air) light-irradiated or unirradiated exhaust from a gasoline engine operated with and without a catalytic converter. Exposure was maintained for about 14 days at particulate levels of approximately 0.7 or 15 mg/m^3. Exposure to unirradiated exhaust resulted in decreased survival and embryonic weight; irradiated exhaust had a less pronounced effect. Similar effects were seen with the catalytic converter, but they were less pronounced (Hoffman & Campbell, 1977, 1978).

Two studies have shown decreased fertility in mice following exposure to irradiated automobile exhaust [unspecifed] (Hueter *et al.*, 1966; Lewis *et al.*, 1967).

(iv) Genetic and related effects

The genetic and related effects of diesel and gasoline engine exhausts have been reviewed (Lewtas, 1982; Claxton, 1983; Holmberg & Ahlborg, 1983; Ishinishi *et al.*, 1986b; Lewtas & Williams, 1986).

Since engine exhaust is difficult to administer in short-term tests, studies have been conducted on several components and fractions of exhausts. Early studies were conducted on exhaust condensates; recent dilution sampling methods have permitted the collection of soot particles. Biological studies have been conducted on collected particles and on various extracts of particles, primarily extractable or soluble organic matter. Several solvents are effective for extracting organic material from diesel and gasoline particles (Claxton, 1983); dichloromethane is that used most commonly. More volatile organic compounds are collected on adsorbent resins and extracted for bioassay. Only limited studies have been conducted on direct exposure to gaseous and whole exhausts.

Studies of genotoxicity are thus conducted on particles, particulate extracts, volatile organic condensates or whole emissions, and the results are expressed as activity per unit mass. In order to compare different emissions, genotoxicity is often expressed as emission rate or genotoxicity per unit distance driven or per mass of fuel consumed. Thus, for example, the mutagenic activity in *Salmonella typhimurium* TA98 of several gasoline particulate extracts is greater than that of diesel particulate extracts per unit mass of organic extract, while the mutagenic emission factor per kilometre driven for gasoline automobiles is less than that for diesel engines (Lewtas & Williams, 1986). The data on gasoline engine exhausts are considered together, whether or not the engine used was equipped with a catalyst and regardless of the type of fuel used (e.g., leaded or unleaded). When this information was available to the Working Group, however, it is noted in the text.

The genotoxic activity of diesel particulate extracts is generally decreased by the addition of a metabolic activation system (e.g., Aroclor 1254-induced or uninduced liver 9000 × *g* supernatant (S9), lung S9, microsomal preparations). In contrast, the genotoxicity of gasoline particulate extracts is generally increased by the addition of metabolic activation (Claxton, 1983; Lewtas & Williams, 1986).

Diesel engine exhaust

The soluble organic matter extracted from diesel particles obtained from the exhaust of several types of diesel engines induced DNA damage in *Bacillus sub tills* in the absence of an exogenous metabolic system at doses of 60–500 µg/ml (Dukovich *et al.*, 1981).

The majority of studies on the mutagenicity of diesel exhaust have been conducted in *S. typhimurium* on soluble or extractable organic matter removed from soot particles. The dichloromethane extractable organic matter from soot particles collected from two diesel engines was mutagenic to *S. typhimurium* TA1537, TA1538, TA98 and TA100 in the presence and absence of an exogenous metabolic system from Aroclor 1254-induced rat liver. In the presence of activation, one soot extract was weakly mutagenic to TA1535 (Huisingh *et al.*, 1978). Other studies of particulate extracts from the exhausts of various diesel engines and vehicles also induced mutation in *S. typhimurium* TA1537, TA1538, TA98 and TA100 with and without an exogenous metabolic system, but not in TA1535 (Clark & Vigil, 1980; Clark *et al.*, 1981; Claxton, 1981; Claxton & Kohan, 1981; Dukovich *et al.*, 1981; Belisario *et al.*, 1984). Diesel engine exhaust particulate extracts were also mutagenic in *S. typhimurium* TM677 and TA100 in a forward mutation assay using 8-azaguanine resistance (Claxton & Kohan, 1981; Liber *et al.*, 1981) and in mutagenesis assays in *Escherichia coli* WP2 and K12 (Lewtas, 1983; Lewtas & Williams, 1986). In these assays, except in *E. coli* K12 where metabolic activation was required, the particulate extracts were mutagenic both in the absence and presence of an exogenous metabolic system.

Fractionation of diesel engine exhaust particulate extracts resulted in fractions (aliphatic hydrocarbons in a paraffin fraction) that were not mutagenic to *S. typhimurium* TA1535, TA1537, TA1538, TA98 or TA100, as well as in fractions that were highly mutagenic and contained most of the activity (moderately polar and highly polar neutral fractions; Huisingh *et al.*, 1978). Similar studies in *S. typhimurium* TA98 using different fractionation procedures showed that most of the mutagenic activity of diesel engine exhaust particulate extracts was in neutral and acidic fractions (Petersen & Chuang, 1982; Pitts *et al.*, 1982; Handa *et al.*, 1983; Schuetzle, 1983; Austin *et al.*, 1985). Separation of the neutral fraction on the basis of polarity resulted in concentration of the mutagenic activity in the aromatic, moderately polar and highly polar oxygenated fractions (Huisingh *et al.*, 1978; Rappaport *et al.*, 1980; Pederson & Siak, 1981; Petersen & Chuang, 1982; Schuetzle, 1983; Austin *et al.*, 1985).

Chemical characterization by the use of bioassays has been reviewed (Schuetzle & Lewtas, 1986). Such studies have shown that nitrated PAHs contribute to the mutagenicity of diesel particulate extracts. The first evidence for the presence of nitroarenes in diesel particulate extracts was provided when a decrease in mutagenicity was observed in nitroreductase-deficient strains of *S. typhimurium* (Claxton & Kohan, 1981; Löfroth, 1981a;Pederson & Siak, 1981; Rosenkranz *et* *al.*, 1981; Pitts *et al.*, 1982). The contribution of mono- and dinitro-PAHs to the mutagenicity of these extracts (20–55%) was estimated by measuring both nitro-PAH and mutagenicity in *S. typhimurium* TA98 in the same diesel particulate extracts (Nishioka *et al.*, 1982; Salmeen *et al.*, 1982; Nakagawa *et al.*, 1983; Schuetzle, 1983; Tokiwa *et al.*, 1986). Other oxidized PAHs in diesel particulate extracts, such as PAH epoxides (Stauff *et al.*, 1980), pyrene-3,4-dicarboxylic acid anhydride (Rappaport *et al.*, 1980) and 5*H*-phenanthro[4,5-*bcd*]pyran-5-one (Pitts *et al.*, 1982), have been shown to be mutagenic to *S. typhimurium*. The formation of both nitro- and oxidized PAH has been reviewed (Pitts, 1983).

The use of the *S. typhimurium* mutagenesis assay to investigate the bioavailability of mutagens has also been reviewed (Claxton, 1983; Lewtas & Williams, 1986). Diesel particles dispersed in dipalmitoyl lecithin, a component of pulmonary surfactant, in saline were mutagenic to *S. typhimurium* TA98 (Wallace *et al.*, 1987). One diesel soot particulate sample collected by electrostatic precipitation from a diesel automobile was directly mutagenic to *S. typhimurium* TA98, TA100, TA1538 and TA1537 in the absence and presence of an exogenous metabolic system from Aroclor 1254-induced rat liver when particles were added directly to the top agar (1–20 mg/plate) without prior extraction or suspension in dimethyl sulfoxide. The sample was not mutagenic to *S. typhimurium* TA1535 when tested at up to 20 mg/plate (Belisario *et al.*, 1984). Diesel soot particles were either not mutagenic or weakly mutagenic to *S. typhimurium* when incubated with physiological fluids such as serum, saline, albumin, lung surfactant and lung lavage fluid (Brooks *et al.*, 1980; King *et al.*, 1981; Siak *et al.*, 1981). Serum and lung cytosol (proteinaceous fluids) inhibited mutagenicity of diesel particulate extracts in *S. typhimurium* (King *et al.*, 1981). Engulfment and incubation of diesel particles with lung macrophages decreased their mutagenic activity (King *et al.*, 1983).

Filtered diesel exhaust was mutagenic to *S. typhimurium* TA100 and to *E. coli* WP2*uvr*A/pkM101 in the absence but not in presence of an exogenous metabolic system; a marginal response was obtained in *S. typhimurium* TA104 in the presence of an Aroclor 1254-induced liver metabolic system (Matsushita *et al.*, 1986). Gaseous emissions from diesel exhaust collected by condensation after dilution and filtration of the particles were mutagenic to *S. typhimurium* TA98 and TA100 in the absence of an exogenous metabolic system; addition of an Aroclor-induced liver metabolic system reduced their mutagenic activity (Rannug, 1983; Rannug *et al.*, 1983). These two approaches to testing the gaseous emissions from diesel engine exhaust thus both show that they are mutagenic to *S. typhimurium* TA98 and TA100 in the absence of an exogenous metabolic system. The studies differ in the quantitative estimates of the contribution that the gaseous emissions make to the total mutagenicity of diesel exhaust: direct testing of gaseous emissions suggests that the gas phase contributes at least 30 times more to the total mutagenicity than the particles (Matsushita *et al.*, 1986); testing of the condensation extract indicated that the gaseous emissions contributed less (up to 30%) than the particles to the total mutagenicity (Rannug, 1983). [The Working Group noted that the latter procedure could result in loss of some volatile components during sampling, extraction or preparation for bioassay.]

The urine of female Swiss mice exposed for 8 h per day on five days per week to whole diesel exhaust (dilution, 1:18; particles, 6–7 mg/m^3) for seven weeks (Pereira *et al.*, 1981c) or of Fischer 344 rats exposed to diesel exhaust particles (1.9 mg/m^3) for three to 24 months (Green *et al.*, 1983; Ong *et al.*, 1985) was not mutagenic to *S. typhimurium*. However, positive responses were obtained with the urine of Sprague-Dawley rats given 1000–2000 mg/kg bw diesel exhaust particles by gastric intubation or by intraperitoneal or subcutaneous administration (Belisario *et al.*, 1984, 1985). [The Working Group noted that this result can be taken as evidence for the bioavailability of mutagens from diesel particles.]

Particulate extracts of diesel engine exhaust emissions increased the number of mitotic recombinants in *Saccharomyces cerevisiae* D3 (Lewtas & Williams, 1986). Mitchell *et al.* (1981) also found a slight elevation in the number of recombinants with concentrations of 100–2000 μg/ml diesel exhaust, but the authors concluded that the results overall were negative. An 8-h exposure to an approximately five-fold dilution of exhaust (particles, 2.2 mg/m^3) from a diesel engine did not increase the incidence of sex-linked recessive lethal mutations in *Drosophila melanogaster* (Schuler & Niemeier, 1981).

Extracts from the emissions of diesel engines (up to 250 μg/ml did not induce DNA damage in cultured Syrian hamster embryo cells, as determined by alkaline sucrose gradient centrifugation (Casto *et al.*, 1981). However, diesel exhaust particles (1 and 2 mg/ml) induced unscheduled DNA synthesis in tracheal ring cultures prepared from female Fischer 344 rats (Kawabata *et al.*, 1986).

As reported in an abstract, diesel engine emission particles and particulate extracts were more cytotoxic for excision repair-deficient xeroderma pigmentosum fibroblasts than for normal human fibroblasts (McCormick *et al.*, 1980).

Particulate extracts (2.5–150 μg/ml) from the exhaust of one light-duty diesel engine induced mutation to ouabain resistance in mouse BALB/c 3T3 cells in the absence and presence of an exogenous metabolic system, while no significant increase in mutation frequency was found with particulate extracts from another light-duty or from a heavy-duty diesel engine (Curren *et al.*, 1981). Another diesel engine exhaust extract induced mutation in the absence of metabolic activation (Lewtas & Williams, 1986).

In two separate studies, particulate extracts of diesel engine emissions from several passenger cars and one heavy-duty engine all induced mutations in mouse lymphoma L5178YTK$^{+/-}$ cells. Maximal increases in mutation frequency occurred at concentrations of 20–300 μg/ml (Rudd, 1980; Mitchell *et al.*, 1981).

Particulate extracts (60 μg/ml) from the exhaust emission of five light-duty diesel passenger cars induced mutations to 6-thioguanine resistance in Chinese hamster CHO cells both in the absence and presence of an exogenous metabolic system from Aroclor 1254-induced rat liver (Li & Royer, 1982). In another study, similar particulate extracts from two light-duty diesel engines (tested at 25–100 and 100–400 μg/ml) induced mutation in Chinese hamster CHO cells, but no mutagenic activity was observed with samples from one light-duty (up to 300 μg/ ml) or one heavy-duty diesel engine (up to 750 μg/ ml; Casto *et al.*, 1981). In a third study, extracts from the exhaust of a light-duty diesel engine (25–75 μg/ml) induced mutation in Chinese hamster CHO cells in the presence, but not in the absence, of an exogenous metabolic system (Brooks *et al.*, 1984). In a study on whole particles from diesel engines (500–750 μg/ml), mutations were induced in Chinese hamster CHO cells in the absence of an exogenous metabolic system (Chescheir *et al.*, 1981).

Diesel particulate extracts (100–200 μg/ml) from emissions of light-duty and heavy-duty diesel engines induced 8-azaguanine and ouabain resistance in Chinese hamster V79 cells. The light-duty samples were more mutagenic than the heavy-duty samples (Morimoto *et al.*, 1986). In another study, particulate extracts (up to 100 μg/ml) generated by a light-duty diesel engine did not induce mutation to 6-thioguanine, 8-azaguanine or ouabain resistance in Chinese hamster V79 cells (Rudd, 1980). [The Working Group noted the small number of plates used.]

Particulate extracts (100 μg/ml) of diesel exhaust induced mutation to trifluorothymidine and 6-thioguanine resistance in human TK6 lymphoblasts in the presence, but not in the absence of an exogenous metabolic system (Liber *et al.*, 1980; Barfknecht *et al.*, 1981).

Particulate extracts of emissions from three light-duty and one heavy-duty diesel engines

(100–400 µg/ml) induced sister chromatid exchange in Chinese hamster CHO cells (Mitchell *et al.*, 1981; Brooks *et al.*, 1984).

When whole diesel exhaust was bubbled through cultures of human peripheral lymphocytes from four healthy nonsmokers, sister chromatid exchange was induced in two of the samples (Tucker *et al.*, 1986). Sister chromatid exchange was also induced in cultured human lymphocytes by a light-duty diesel particulate extract (5–50 µg/ml;Lockard *et al.*, 1982) and by diesel particulate extracts (10–200 µg/ml) from emissions of light-duty and heavy-duty diesel engines (Morimoto *et al.*, 1986). In the last study, light-duty samples were more potent in inducing sister chromatid exchange than heavy-duty samples.

A particulate extract (20–80 µg/ml from the exhaust emission of one light-duty diesel engine induced structural chromosomal abnormalities in Chinese hamster CHO cells (Lewtas, 1982), but an extract from a similar engine did not (Brooks *et al.*, 1984).

A particulate extract (0.1–100 µg/ml from the exhaust of a light-duty diesel engine induced chromosomal aberrations in cultured human lymphocytes in the absence of an exogenous metabolic system. In the presence of metabolic activation, no increase in the total percentage of cells with aberrations was observed, although an increase in the number of chromosomal fragments and dicentrics was observed (Lewtas, 1982, 1983).

Particulate extracts (2.5–100 µg/ml) from the exhaust of one light-duty diesel engine induced morphological transformation in BALB/c 3T3 cells in the absence, but not in the presence, of an exogenous metabolic system from Aroclor 1254-induced rat liver (Curren *et al.*, 1981). Similar extracts from two other light-duty diesel engines and a heavy-duty diesel engine did not induce morphological transformation in these cells in the absence or presence of a metabolic system (Curren *et al.*, 1981, up to 300 µg/ml; Zamora *et al.*, 1983, up to 40 µg/ml). An extract from a light-duty diesel engine (2–10 µg/ml) induced morphological transformation in BALB/c 3T3 cells initiated by treatment with 3-methylcholanthrene (Zamora *et al.*, 1983).

Particulate extracts (31–500 µg/ ml) from the emissions of three light-duty diesel engines enhanced transformation of Syrian hamster embryo cells in the presence of SA7 virus. No significant enhancement of transformation was observed with the corresponding extract (up to 500 µg/ml) from a heavy-duty engine (Casto *et al.*, 1981).

A particulate extract (5–10 µg/ml) of exhaust from a light-duty engine inhibited intercellular communication, as measured by metabolic cooperation in Chinese hamster V79 lung cells (Zamora *et al.*, 1983).

Primary cultures of 12-day-old hamster embryos from pregnant Syrian hamsters that received intraperitoneal injections of the neutral fractions of light-duty or heavy-duty diesel particulate extracts (2000–4000 mg/kg bw) on day 11 of gestation had an increased number of 8-azaguanine-resistant mutations (Morimoto *et al.*, 1986).

Exposure of B6C3F1 mice to whole diesel engine exhaust emission (12 mg/ m^3 particles) for one month did not induce sister chromatid exchange in bone-marrow cells, but injection [unspecified] of either diesel particles (300 mg/kg bw) or their extract (800 mg/kg bw) resulted in an increased incidence of sister chromatid exchange in the bone marrow of mice sacrificed two days after treatment (Pereira, 1982).

No increase in the frequency of sister chromatid exchange was observed in the peripheral lymphocytes of Fischer 344 rats exposed to whole diesel engine exhaust emission (1.9 mg/m^3 particles) for three months (Ong *et al.*, 1985), and no significant increase was observed in bone-marrow cells of rats exposed to 4 mg/kg whole emissions from light- or heavy-duty diesel engines for up to 30 months (Morimoto *et al.*, 1986). [The Working Group could not determine the accumulated dose.]

Intratracheal instillation of diesel engine exhaust particles (6–20 mg) in male Syrian hamsters increased the incidence of sister chromatid exchange in lung cells, as did exposure of Syrian hamsters for 3.5 months to whole diesel engine exhaust emissions (particles, 12 mg/m^3; Guerrero *et al.*, 1981). Exposure of pregnant Syrian hamsters to whole diesel engine exhaust emissions (particles, 12 mg/m^3) from day 1 of gestation, or intraperitoneal administration of diesel engine exhaust particles at the LD_{50} (300 mg/kg bw) on day 12 of gestation, did not result in increased frequencies of sister chromatid exchange in fetal liver, as determined on day 13. However, an increase was seen after intraperitoneal administration on day 12 of a dichloromethane extract of the particles (Pereira, 1982; Pereira *et al.*, 1982).

No increase in the frequency of micronuclei in bone marrow was found in male ICR mice exposed to whole exhaust emission from a light-duty diesel engine at particulate concentrations of 0.4 and 2.0 mg/m^3 for up to 18 months (Morimoto *et al.*, 1986), or in Swiss-Webster CD-1 mice or Fischer 344 rats exposed to whole emission (particles, 1.9 mg/m^3) for six months and two years, respectively (Ong *et al.*, 1985), or in B6C3F1 and Swiss mice and Chinese hamsters exposed to exhaust emissions for one to six months (particles, 6 mg/m^3) or for one month (particles, 12 mg/m^3); however, an increase was observed in Chinese hamsters exposed to 6 mg/m^3 for six months. There was a slight increase in the number of micronucleated bone-marrow cells in B6C3F1 mice, but not in Chinese hamsters, administered an extract of diesel particles (800 and 1000 mg/kg bw) intraperitoneally (Pereira *et al.*, 1981b,c; Pereira, 1982; Pepelko & Peirano, 1983). As reported in an abstract, extracts of diesel engine exhaust particles given intraperitoneally at concentrations of up to 1000 mg/kg bw to Chinese hamsters did not increase the frequencies of chromosomal aberrations, micronuclei or sister chromatid exchange in bone-marrow cells (Heidemann & Miltenburger, 1983).

No increase in the incidence of dominant lethal mutations was found when male T-stock mice exposed for 7.5 weeks to diesel exhaust (particulates, 6 mg/m^3; 8 h/day, 7 days/week) were mated with (101×C3H)F_1, (SEC×C57B1)F_1, (C3H×C57B1)F_1 or T-stock female mice or when female (101×C3H)F_1 mice were similarly exposed for 7 weeks prior to mating with untreated males. No increase in the frequency of heritable point mutations was found after T-stock males were similarly exposed to diesel exhaust [length of exposure not given] prior to mating, and no oocyte killing was observed in (SECXC57B1)F_1 female mice after exposure for eight weeks prior to mating (Pepelko & Peirano, 1983).

Gasoline exhaust

Gasoline exhaust emissions from both catalyst and noncatalyst automobiles, collected using several standard methods, were mutagenic to *S. typhimurium* TA98 and TA100 (Claxton & Kohan, 1981; Löfroth, 1981a,b; Ohnishi *et al.*, 1982; Zweidinger, 1982; Clark *et al.*, 1983; Handa *et al.*, 1983; Rannug, 1983; Rannug *et al.*, 1983; Brooks *et al.*, 1984; Norpoth *et al.*, 1985; Westerholm *et al.*, 1988). Addition of a catalyst, however, significantly decreases the rate of emission from gasoline engine vehicles of material that is mutagenic to these strains (Ohnishi *et al.*, 1980; Zweidinger, 1982; Rannug, 1983; Rannug *et al.*, 1983; Lewtas, 1985).

Extracts of particles collected from the exhaust pipes of gasoline automobiles [assumed to be noncatalyst, using leaded fuel] were mutagenic to *S. typhimurium* TA1537, TA98 and TA100 both in the absence and presence of an exogenous metabolic system from Aroclor-induced rat liver (Wang *et al.*, 1978). Particulate and condensate extracts of the exhausts of a noncatalyst gasoline engine and a catalyst (oxidizing) gasoline vehicle were mutagenic to *S. typhimurium* TA1538, TA98 and TA100 in the presence of an exogenous metabolic system from Aroclor-induced rat liver. The samples were either not mutagenic or weakly mutagenic to *S. typhimurium* TA1535 (Ohnishi *et al.*, 1980). Dichloromethane extracts of soot particles from a gasoline catalyst vehicle were mutagenic to *S. typhimurium* TA98 and TA100 in the absence and presence of an exogenous metabolic system but were not mutagenic to *S. typhimurium* TA1535 (Claxton, 1981). Particulate extracts of gasoline catalyst engine (unleaded fuel) emissions were mutagenic to *S. typhimurium* TA98 in the absence and presence of an exogenous metabolic system and in *S. typhimurium* TA100 only in the presence of an exogenous metabolic system (Westerholm *et al.*, 1988).

Gas-phase emissions collected from catalyst and noncatalyst engines by condensation after dilution and filtration were mutagenic to *S. typhimurium* TA98 and TA100 in the absence of an exogenous metabolic system, and the contribution of the gas phase to the total mutagenicity ranged from 50–90% in the absence of activation. In the presence of a metabolic system, the mutagenicity was decreased (Rannug, 1983; Rannug *et al.*, 1983; Westerholm *et al.*, 1988).

After fractionation of gasoline engine exhaust particulate and condensate extracts, the neutral aromatic fraction, which contains the PAHs, was found to be mutagenic to *S. typhimurium* TA98 in the presence of an exogenous metabolic system (Löfroth, 1981b; Handa *et al.*, 1983); the highest dose-dependent increase in mutagenicity was induced by the four- to seven-ring PAH fraction in *S*. typhimurium TA98 and TA100 (Norpoth *et al.*, 1985). Handa *et al.* (1983) found the acidic fraction to be significantly more mutagenic in *S. typhimurium* TA98 in the absence than in the presence of an exogenous metabolic system.

Nitro-PAH are either not detectable or present at much lower concentrations in particulate extracts from gasoline engine exhausts than in diesel particle extracts (Nishioka *et al.*, 1982; Handa *et al.*, 1983). In studies using strains of *S. typhimurium* that do not respond to nitro-PAH, gasoline engine exhaust particulate extracts (Brooks *et al.*, 1984) and whole catalyst gasoline engine emissions (Jones *et al.*, 1985) were less mutagenic than in TA98 (in the absence of activation), suggesting the presence of nitroaromatic compounds. Löfroth (1981a), however, using similar techniques, did not see a decrease in mutagenicity attributable to nitro-PAHs. [The Working Group noted that these results are not necessarily inconsistent, since different strains and sampling methods were used.]

Several studies of exhaust emissions from vehicles run on gasoline blended with alcohol (10–23% ethanol or methanol) have shown either no significant change or a decreased emission rate of material mutagenic to *S. typhimurium* TA98 and TA100 (Clark *et al.*, 1983; Rannug, 1983; Clark *et al.*, 1984).

Particulate extracts of one unleaded gasoline catalyst engine exhaust emission tested at up to 1500 µg/ml did not induce mitotic recombination in *S. cerevisiae* D3 (Mitchell *et al.*, 1981).

An extract of emissions from an unleaded gasoline catalyst engine (250 µg/ml) induced DNA damage in cultured Syrian hamster embryo cells, as measured by alkaline sucrose gradients, in the absence of an exogenous metabolic system (Casto *et al.*, 1981).

Particulate extracts from the exhaust of an unleaded gasoline catalyst engine (2.5–500 µg/l) induced mutation to ouabain resistance in mouse BALB/c 3T3 cells in the absence and presence of an exogenous metabolic system (Curren *et al.*, 1981). Particulate extracts from unleaded gasoline catalyst automobiles and leaded gasoline noncatalyst automobiles (20–350 µg/ml) were mutagenic to mouse lymphoma L5178Y $TK^{+/-}$ cells. Metabolic activation increased the mutagenic activity (Mitchell *et al.*, 1981 ; Lewtas, 1982). Particulate extracts from the exhaust emission from a gasoline engine with catalytic converter (50–400 µg/ml) induced mutations to 6-thioguanine resistance in CHO cells in the absence of an exogenous metabolic system (Casto *et* *al.*, 1981). In another study, extracts from an unleaded gasoline catalyst engine (25–75 µg/ml induced mutations to 6-thioguanine resistance in the *hgpt* locus in Chinese hamster CHO cells only in the presence of an exogenous metabolic system (Brooks *et al.*, 1984).

Particulate extracts of unleaded gasoline catalyst engine emissions (10–200 µg/ml) induced sister chromatid exchange in Chinese hamster CHO cells in the absence of an exogenous metabolic system (Mitchell *et al.*, 1981). Extracts from another unleaded gasoline catalyst engine exhaust (10–50 µg/ml) also induced sister chromatid exchange in Chinese hamster CHO cells both in the absence and presence of an exogenous metabolic system (Brooks *et al.*, 1984). Leaded gasoline noncatalyst engine exhaust particulate extracts induced sister chromatid exchange in Chinese hamster CHO cells in the presence of an exogenous metabolic system (Lewtas & Williams, 1986). [The Working Group noted that no data were provided on responses in the absence of an exogenous metabolic system.]

Extracts from an unleaded gasoline catalyst engine exhaust (20–60 µg/ml) induced chromosomal aberrations in Chinese hamster CHO cells in the presence of an exogenous metabolic system (Brooks *et al.*, 1984). Particulate extract [type of fuel and presence of catalyst unspecified] (0.6–5 µg/ml) induced aneuploidy and polyploidy in Chinese hamster V79 cells in the absence of an exogenous metabolic system (Hadnagy & Seemayer, 1986) and induced disturbance of the spindle apparatus (Seemayer *et al.*, 1987).

Dichloromethane particulate extracts from the exhaust of an unleaded gasoline catalyst engine (2.5–500 µg/ml) increased the frequency of morphological transformation of BALB/c 3T3 cells in both the absence and presence of an exogenous metabolic system from Aroclor 1254-induced rat liver (Curren *et al.*, 1981). Dichloromethane extracts of the particulate emissions of an unleaded gasoline catalyst engine (31–500 µg/ml) enhanced morphological transformation of Syrian hamster embryo cells in the presence of SA7 virus (Casto *et al.*, 1981).

In male BALB/c mice exposed to whole gasoline engine exhaust [type of fuel and presence of catalyst unspecified] emissions for 8 h per day for ten days and killed 18 h after the last exposure period, an increased frequency of micronucleated bone-marrow cells was found (Massad *et al.*, 1986).

(b) Humans

(i) Deposition, clearance, retention and metabolism

The factors affecting the uptake of gases and vapours, including model calculations for their absorption in the different regions of the human respiratory tract, have been summarized (Davies, 1985).

Diesel engine exhaust

No data on the deposition, clearance, retention or metabolism of diesel engine exhaust were available to the Working Group. A model has been developed to predict the deposition of diesel exhaust in humans (Yu & Xu, 1986; Xu & Yu, 1987; Yu & Xu, 1987).

Gasoline engine exhaust

The results of two laboratory experiments in which human volunteers inhaled the exhaust from an engine run on gasoline containing ^{203}Pb-tetraethyllead are summarized in Table 29. In one of the experiments, the exhaust was contained in a 600–1 chamber; the concentrations of carbon monoxide and carbon dioxide were reduced using chemical traps; median particulate size was about 0.4 µum (Chamberlain *et al.*, 1975) or 0.35 and 0.7 µm, resulting in an aerosol considered typical of urban environments (Chamberlain *et al.*, 1978). In the other experiment, the exhaust was rapidly diluted in a wind tunnel which prevented coagulation of the primary exhaust particles and resulted in aerosols with median particulate sizes of 0.02–0,09 µm. Both experiments were conducted with a variety of breathing patterns, which were monitored but not controlled. Total deposition was relatively constant at 30% over a wide range of breathing patterns for sizes typical of urban aerosols (Chamberlain, 1985). However, as the size of the primary particles decreased (below 0.1 µm), deposition increased sharply, and the length of the respiratory cycle (time between the start of successive breaths) significantly affected deposition. [The Working Group noted that these data are in broad agreement with those for other particulate materials of similar size (Heyder *et al.*, 1983; Schiller *et al.*, 1986.]

Table 29. Total deposition (%) of leaded gasoline particles pattern[a]

Particulate diameter (µm)	Tidal volume in litres (respiratory cycle in seco					
	0.5 (2)	0.5 (4)	1.0 (4)	1.5 (4)	0.5 (6)	1.0 (6)
0.02	53	64		86		82
0.04			42		40	58
0.09		35				32
0.35						
~0.4[b]		37	26		47	46

Table 29.

Total deposition (%) of leaded gasoline particles as a function of size and breathing pattern.

In a separate analysis of the same data, deposition was shown to increase with respiratory cycle in an approximately linear fashion — ranging from 10% at 3 sec to 55% at 20 sec; the slope of this line was somewhat dependent on tidal volume. A small, but significant effect of expiratory reserve volume on deposition was observed: total deposition dropped by a factor of 1.2 for an increase in expiratory reserve volume of 2.5 1 (Wells *et al.*, 1977).

In a third study, measurements of total deposition were performed in the field by comparing inhaled and exhaled airborne lead concentrations; the method was found to give results comparable to experimental measurements involving ^{203}Pb. Total deposition was measured for inhalation at an average breathing pattern of 0.81 and a respiratory cycle of 5.2 sec in persons seated by a motorway (61 %), by a roundabout (64%), in an urban street (48%) and in a car park (48%). Median particulate sizes in the breath of persons near quickly moving traffic (0.04 µm) were found to be much smaller than those in persons in the urban environment or in a car park (0.3 µm), although the air near roundabouts also contained a large proportion by mass of adventitious particles (2 µm) (Chamberlain *et al.*, 1978).

Lung clearance was best described by a four-component exponential clearance. The first two phases (half-times, 0.7 and 2.5 h) were similar for exhaust particles, lead nitrate (which is soluble) and lead oxide (which is insoluble), and therefore probably represent mucociliary clearance (Chamberlain *et al.*, 1975, 1978). On average, 40% of lung deposition of 0.35-µm aerosols was in the pulmonary region and 60% in the tracheobronchial region. The removal of lead compounds from the pulmonary region was described by a two-component exponential with half-times of 9 and 44 h; one exception was the removal of lead from highly carbonaceous particles, which exhibited half times of 24 and 220 h (Chamberlain *et al.*, 1978; Chamberlain, 1985).

No data on the metabolism in humans of gasoline engine exhaust were available to the Working Group.

(ii) Toxic effects

Early studies involving human volunteers showed that exposure to gasoline engine exhaust may cause headache, nausea and vomiting (Henderson *et al.*, 1921), Sayers *et al.* (1929) monitored the carbon monoxide content of gasoline engine exhaust gas-air mixtures and found a relationship between increasing carbon monoxide concentration, carboxyhaemoglobin (COHb) level and reports of headache in six men exposed to atmospheres containing 229–458 mg/m^3 carbon monoxide. In a more recent study of ten patients with angina (Aronow *et al.*, 1972), significant increases in COHb levels and significant reductions in exercise performance until onset of angina symptoms were observed in persons driving for 90 min in heavy traffic, as compared with tests both before the experiment and after breathing purified air for 90 min.

Among six volunteers exposed for 3.7 h to diesel engine exhaust gases containing about 4 mg/m^3 nitrogen dioxide, there was no increase in urinary thioether concentration (Ulfvarson *et al.*, 1987).

Effects of exposure to diesel engine exhaust on the lung have been reviewed (Calabrese *et al.*, 1981), Although bus garage and car ferry workers, exposed occupationally to mixtures of gasoline and diesel engine exhausts, had lower mean levels of respiratory function (forced respiratory volume in 1 sec (FEV_1) and forced vital capacity (FVC) than expected, they showed no change in these measures over working shifts (for exposure measurements, see Tables 17 and 21, respectively). In contrast, workers on roll-on roll-off ships, exposed mainly to diesel engine fumes, showed statistically significant reductions in FEV_1 and FVC during working shifts (for exposure measurements, see Table 18). These reductions were reversible, however, the levels returning to normal after a few days with no exposure. The work-shift concentrations of nitrogen dioxide and carbon monoxide in these three groups averaged 0.54 mg/m^3 and 1.1 mg/m^3, respectively (Ulfvarson *et al.*, 1987). A small reduction in FEV_1/FVC and in $FEF_{25–75\%}$ (forced expiratory flow at 25–75% of forced vital capacity) was also observed at the end of a work shift among a group of chain-saw operators (Hagberg *et al.*, 1983; for exposure measurements, see Table 22). Concentrations of diesel engine emissions in coal mines, involving, on average, 0.6 mg/m^3 nitrogen dioxide and 13.7 mg/m^3 carbon monoxide, were not associated with decrements in the miners' ventilatory function (Ames *et al.*, 1982).

Studies in which changes in COHb levels were investigated over the course of a work shift are summarized in section 2 (pp. 69–73).

Possible effects on the lung of chronic occupational exposures to low levels of diesel engine exhaust emissions were studied cross-sectionally in railroad engine house workers (Battigelli *et al.*, 1964), in iron ore miners (Jörgensen & Svensson, 1970), in potash miners (Attfield *et al.*, 1982), in coal miners (Reger *et al.*, 1982; for exposure measurements, see Table 15), in salt miners (Gamble *et al.*, 1983), in coal miners exposed to oxides of nitrogen generated (in part) by diesel engine emissions underground (Robertson *et al.*, 1984) and in bus garage workers (Gamble *et al.*, 1987b). Effects of relatively high concentrations of automobile emissions have been described among bridge and road tunnel workers in two large cities (Speizer & Ferris, 1963; Ayres *et al.*, 1973; for exposure measurements, see Table 19). Changes in lung function over a five-year period have also been studied longitudinally among coal miners working underground in mines with and without diesel engines (Ames *et al.*, 1984). Some, but not all, of the results from these various studies showed decrements in lung function and increased prevalence of respiratory symptoms in subgroups exposed to engine emissions.

Exposure to engine exhaust has also been associated with irritation of the eyes (Waller *et al.*, 1961; Battigelli, 1965; Hamming & MacPhee, 1967; Hagberg *et al.*, 1983).

A 15-year follow-up of 34 156 members of a heavy construction equipment operators' union showed a highly significant overall excess of deaths certified as due to emphysema (116 observed, 70.2 expected), and this excess appeared to be higher among men with longer membership in the union (Wong *et al.*, 1985). No data on smoking habits were included in the mortality analyses, and the authors noted that they were unable to estimate the degree to which exposure to diesel engine emissions (as distinct from other occupational factors, such as exposure to dust) might have contributed to the excess mortality from emphysema.

Another cohort study, of 1558 white motor vehicle examiners, yielded a slight excess of deaths from cardiovascular disease (124 observed, 118.4 expected) in a 29-year follow-up. The excess was more pronounced for deaths occurring during the first ten years of employment (28 observed, 20.9 expected; Stern *et al.*, 1981). [The Working Group noted that the excesses observed are easily attributable to chance ($p > 0.1$).] A 32-year follow-up of 694 Swedish bus garage employees also showed a small, statistically nonsignificant, excess of deaths from cardiovascular disease (121 observed, 115.9 expected) which showed no pattern to indicate a relation to probable intensity or duration of exposure to diesel emissions (Edling *et al.*, 1987). Moreover, Rushton *et al.* (1983) found no excess of deaths from cerebrovascular or ischaemic heart disease among maintenance workers in London bus garages. A 27-year follow-up of 3886 potash miners and millers also showed no excess mortality that could be attributed to the presence of diesel engines in some of the mines that were studied; in only two of eight mines had diesel engines been used (Waxweiler *et al.*, 1973). None of these four analyses of mortality included adjustments for the men's smoking habits. However, the authors noted that the US potash workers whom they had studied included a greater proportion of cigarette smokers than among all US males.

(iii) Effects on reproduction and prenatal toxicity

No data were available to the Working Group.

(iv) Genetic and related effects

The frequency of chromosomal aberrations in cultured lymphocytes from 14 male miners exposed to diesel engine exhaust (five were smokers) was no greater than in 15 male office workers (five smokers; Nordenson *et al.*, 1981). The incidence of chromosomal changes was also investigated in four groups of 12 men: drivers of diesel-engine trucks, drivers of gasoline-engine trucks, automobile inspectors and a reference group, matched with respect to age, smoking habits and length in the jobs. The frequencies of gaps, breaks and sister chromatid exchange in lymphocyte preparations were not significantly different in the four groups (Fredga *et al.*, 1982). [The Working Group noted the small number of subjects in both of these studies.]

Among workers with relatively heavy exposure to diesel engine exhaust — in particular, crews of roll-on roll-off ships and car ferries and bus garage staff (the latter two groups also having exposure to gasoline engine exhausts) — no difference in mutagenicity to *S. typhimurium* TA98 or *E. coli* WP2 *uvrA* was observed between urine collected during exposed periods and that collected during unexposed periods. Similarly, no increase in urinary mutagenicity was found among six volunteers before and after an experimental exposure to diesel engine exhaust gases from an automobile run for 3.7 h at 60 km/h, 2580 revolutions/min (Ulfvarson *et al.*, 1987).

3.3. Epidemiological studies of carcinogenicity to humans

(a) Introduction

Although population-based studies to detect a possible association between exposure to engine exhausts and cancer in humans are the most direct methods for detecting human carcinogenesis, for low levels of risk the approach is complicated by several factors. These factors can be divided broadly into problems related to the documentation of levels of exposure and the potential for unidentified confounding factors to influence the results.

Nonoccupational exposure to engine exhaust is nearly ubiquitous in urban areas and in the vicinity of vehicles. Because emissions are diluted in the nonoccupational environment, it is unlikely that investigations of the general population would reveal risks when groups with heavy exposure show only a small risk.

'Unexposed' reference populations used in epidemiological studies are likely to contain a substantial number of subjects who are exposed nonoccupationaly to engine exhausts. The 'exposed' group is often defined on the basis of job title, which may be an inadequate surrogate for exposure to exhaust emissions, and this may lead to an underestimation of risk. The situation is further complicated by the presence of possible confounding factors, such as smoking and other exposures (e.g., asbestos in railroad yards), which may influence results, especially when lung and bladder cancers are being studied. In addition, in many studies of the occupational setting, there is an inextricable link between exposure to exhaust emissions and to vapours from the fuels themselves. Some occupational groups, such as car-park attendants and toll-booth workers, which might be thought to be a source of more direct information due to their heavy exposure, are usually too small and/or too transient for a population-based study of cancer to be feasible.

Another important consideration is that occupational cohorts tend to have below-average mortality, both from all causes and from various major categories of specific causes. These deficits are, typically, manifestations of a selection process based on health status, referred to as the 'healthy worker effect'. In view of this overall deficit in cancer mortality in working cohorts, conventional statistical evaluation of site-specific standardized mortality ratios (SMRs) is usually conservative. That is, comparison of the SMR with an 'expected' value of 100 derived from the general population — rather than from some defined internal unexposed comparison group — may result in an underestimation of the true magnitude of any occupation-related increase in risk for specific cancers.

In the studies reviewed, retrospective assessment of an individual's exposure to engine exhausts is necessarily indirect, since there are generally no systematic or quantitative records of work-place or ambient exposures. In some studies, the title of a job or occupation with known or presumed exposure is used as a simple surrogate measure of exposure, and the cancer risk of groups of individuals in such jobs is compared with that of the general population or of persons in unrelated jobs. In some other studies, mainly of case-control design, each individual's past exposure is assessed by the use of a job-exposure matrix. In its simplest form, a job-exposure matrix is a two-way table in which each job or occupation is assigned a code indicating the presence (and sometimes the magnitude) of substances to which persons in that job would be exposed, on the basis of contemporary measurements and knowledge of working practices. The job history obtained from the subject is then used to construct his or her record of past exposure from the matrix. Among the limitations of this approach is the fact that individual exposures may differ widely even within narrowly defined occupations, because of differences in working practices between individuals and work sites, from country to country and over time. It should be noted, however, that while such problems in exposure assessment reduce the precision with which any effect can be measured, they are not likely to give rise to a spurious association where none exists; consistency of results between different studies of this kind is therefore of particular importance in assessing the relationship between exposure and disease.

Several of the available case-control studies are hospital-based rather than population-based; i.e., the control group consists of subjects hospitalized for diseases different from those of the cases. Because little is known about the etiology of many diseases, some of which may be associated with exposure to engine exhaust, it is difficult to rule out bias resulting from the choice of specific sets of controls.

(b) Mortality and morbidity statistics

The Working Group noted that surveys of mortality or morbidity statistics suffer from many limitations, which reduce their usefulness in the evaluation of carcinogenic risks. Comparison of the results of different studies is complicated by the varying definitions and groupings of occupations and cancer sites. Generally, these studies have been designed to generate hypotheses about potentially exposed groups. For example, a striking difference in the male:female sex ratio for tumours unrelated to hormonal status within a specific geographical region might suggest an area that should be explored in either cohort or case-control studies, in which exposure can be assessed more readily.

Studies of this type that may relate to exposure to exhaust fumes include the following: Menck and Henderson (1976), Decouflé *et al.* (1977), Office of Population Censuses and Surveys (1978), Petersen and Milham (1980), Howe and Lindsay (1983), Milham (1983), Dubrow and Wegman (1984), Malker and Weiner (1984), Baxter and McDowall (1986) and Olsen and Jensen (1987).

(c) Cohort studies

(i) Railroad workers

Kaplan (1959) evaluated 6506 deaths among railroad workers from the medical records of the Baltimore and Ohio Railroad relief department between 1953 and 1958, 818 of which were due to cancer and 154 of which were lung cancer. The cases were categorized into three groups by exposure to diesel exhaust. In comparison with national death rates, none of the groups had an excess risk for lung cancer. [The Working Group noted that, since changeover to diesel engines began in 1935 and was 95% complete by 1959 (Garshick *et al.*, 1988), few if any of the lung cancer deaths could have occurred in workers with more than ten years' exposure to diesel exhaust; in addition, smoking habits were not considered.]

Howe *et al.* (1983) studied a cohort of 43 826 male pensioners of the Canadian National Railway Company consisting of retired railroad workers who were known to be alive in 1965 plus those who retired between 1965 and 1977. Of the total of 17 838 deaths that occurred in 1965–77, 16 812 (94.4%) were successfully linked to a record in the Canadian mortality data base. The expected number of cancer deaths was estimated from that of the total Canadian population, adjusted for age and calendar period. Available information included birth date, province of residence, date of retirement and occupation at time of retirement. Occupational exposures were classified into three types: 'diesel fumes', coal dust and other. The two statistically significant results for the whole cohort were deficits in deaths from all causes (SMR, 95 [95% confidence interval (CI), 93–96]) and from leukaemia (SMR, 80 [95% CI, 65–97]). For exposure to diesel engine exhaust, the risk for cancer of the trachea, bronchus and lung increased with likelihood of exposure: the relative risks were 1.0 for unexposed, 1.2 [1.1–1.3] for 'possibly exposed' and 1.4 [1.2–1.5] for 'probably exposed' (p for trend < 0.001). The SMR for bladder cancer was 103 [88–119]. Similar results were found for the risk for cancer of the trachea, bronchus and lung from exposure to coal dust. Since there was considerable overlap in exposures to diesel fumes and coal dust, the risk was evaluated by calendar time during which one of these exposures predominated. The risk was largely accounted for by exposure to diesel exhaust. Since exposure to asbestos occurs during locomotive maintenance, workers thought to have had such exposure were removed from the analysis, with little effect on the risk associated with exposure to diesel engine exhaust. Exclusion of workers exposed to welding fumes did not alter the result. The authors noted that the data presented and the risks observed probably represent an underestimate of the true risk, for at least two reasons: exposure misclassification because of the use of job held last and failure to determine the cause of death for 5.6% of cases. [The Working Group noted that no data were available on duration of exposure, usual occupation or smoking habits and recognized the potential for competing biases in the way in which the cohort was composed.]

Garshick *et al.* (1988) studied a cohort of 55 407 white male railroad workers aged 40–64 in 1959 who had started railroad service ten to 20 years earlier. The cohort was traced from records of the pension scheme for US railway workers through to 1980; it was estimated that less than 2% left the industry during the period covered by the study. Death certificates were available for 88% of the 19 396 deaths, of which 1694 were from lung cancer; decedents for whom a death certificate was not obtained were classified as having died of unknown causes. Records of railroad jobs from 1959 through to death, retirement or 1980 were also available from the records of the pension scheme. Jobs were divided into regular exposure to diesel exhausts (train crews, workers in diesel repair shops) and no exposure (clerks, ticket and station agents, and signal maintenance workers). Job categories with recognized asbestos exposure, such as car repair and construction trades, were excluded from those selected for study. Information was available on duration of exposure. There was a significant excess risk for lung cancer in the groups exposed to diesel engine exhaust; this risk was highest in those who had the longest exposure: aged 40–44 (relative risk, 1.5; 95% CI, 1.1–1.9) and 45–49 (1.3; 1.0–1.7) and exposed to diesel exhaust in 1959. The groups aged 50–54 and 55–59 in 1959 also had excess risks, of 1.1 and 1.2, respectively, although these were not statistically significant. When workers with further potential asbestos exposure (shop workers) were excluded, similarly elevated lung cancer rates were observed. Although smoking habits were not considered directly, the authors pointed out that there was no difference in smoking habits by job title in comparison studies of current workers or in a case-control study in which smoking was assessed. [The Working Group noted that exclusion of shop workers would also have excluded men exposed to welding fumes.]

As part of this study, exposure was assessed on the basis of several hundred time-weighted samples of respirable dust taken in the early 1980s both at stationary sites in parts of four existing, smaller railroad yards and with personal samplers carried by railroad workers in different job categories (Woskie *et al.*, 1988a). Samples were taken from workers in 39/155 Interstate Commerce Commission job codes, and the results were used to classify the jobs; these 39 categories were subsequently combined into 13 job groups, which could be further combined into five: clerks, signal maintenance, engineers/firers, brakers/conductors and shop workers. The nicotine content was used to adjust the extractable respirable particulate content of each sample to account for the portion contributed by cigarette smoking. Mean exposure levels by national career groups in the five major categories of exposure suggested a five-fold range of exposure to respirable particles between clerks and shop workers (Woskie *et al.* 1988b). These values confirmed the a-priori assignment of the categories of diesel exposure used in the cohort study (Garshick *et al.*, 1988) and the assignment to appropriate exposure categories for the case-control study (Garshick *et al.*, 1987; see p. 140).

(ii) Bus company employees

Raffle (1957) determined deaths, retirements and transfers due to lung cancer in London Transport employees aged 45–64 years in jobs with presumably different exposures to exhaust fumes in 1950–54 and compared the figures with those for lung cancer mortality for men in England and Wales or in Greater London. No relationship between presumed exposure and lung cancer incidence was noted. In a subgroup of bus and trolley bus engineering staff aged 55–64, 30 deaths from lung cancer occurred while 21.2 were expected (observed:expected, 1.4) on the basis of the experience of other London Transport employees. [The Working Group noted that no information on smoking habits was available, and that all the deaths occurred in men over 55 years of age.] Waller (1981) compared lung cancer deaths and retirements or transfers to alternative jobs due to lung cancer in men aged 45–64 employed within five job categories of London Transport (bus drivers, bus conductors, engineers (garages), engineers (central works) and motor men and guards) to lung cancer mortality (age- and calendar time-adjusted) for men in Greater London. The study covered 25 years, ending in 1974, thus including some of the data described by Raffle (1957). A total of 667 cases of lung cancer were observed; although the risk was not elevated for any of the five job categories, the highest SMR occurred in the group that was presumably most heavily exposed to diesel exhaust (bus garage workers). [The Working Group noted that no data on smoking habits were available, and neither duration nor latency was examined.]

Rushton *et al.* (1983) examined a cohort of 8684 men employed as maintenance workers in 71 bus garages in London for at least one year in 1967–75. Follow-up until 31 December 1975 was completed for 8490 (97.8%) workers, and cause of death was known for 701 of 705 who had died. The SMRs were 84 [95% CI, 78–91] for all causes and 95 [83–109] for all neoplasms, 101 [82–122] for lung and pleural cancer, 151 [60–307] for leukaemia, 121 [49–250] for central nervous system tumours and 139 [72–244] for bladder cancer. None of the rates for cancer at individual sites was statistically significantly increased. The authors noted the short follow-up period.

Edling *et al.* (1987) studied 694 men, five of whom (0.7%) were lost to follow-up, who had been employed as clerks, bus drivers or bus garage workers in five bus companies in south-eastern Sweden at any time between 1950 and 1959, and followed for 1951–83. The SMRs, based on age-, sex- and calendar time-adjusted national rates, were 80 (195 deaths observed; 95% CI, 70–90) for deaths from all causes and 70 (50–90) for deaths from malignancy. Dividing the data by exposure category, exposure time or latency did not appreciably change the risk ratios. The small sample size did not allow detailed examination of cancers at specific sites, although six lung cancer cases were observed compared to nine expected. [The Working Group noted that smoking habits were not addressed.]

(iii) Professional drivers and some other groups exposed to vehicle exhausts

Ahlberg *et al.* (1981) identified a cohort of Swedish drivers said by the authors to be exposed to diesel exhaust (1865 or 1856 [*sic*] fuel oil tanker drivers and 34 027 other truck drivers) from the national census of 1960. In this cohort, 1143 cancers were registered within the Swedish Cancer Registry in 1961–73. The reference population consisted of 686 708 blue-collar workers from the 1960 census who were thought to have had no exposure to petroleum products or chemicals. The data were adjusted for age and residence. The relative risk for lung cancer was elevated in the whole cohort. (1.3; 95% CI, 1.1–1.6) and in Stockholm truck drivers in particular (1.6; 1.2–2.3). From a questionnaire study of 470 professional drivers in Stockholm, it was noted that 78% of fuel truck drivers and 31% of other truck drivers smoked. The authors cited an unpublished study indicating that the comparable smoking rate in Stockholm was 40% and concluded that the results could not be explained by smoking.

Wong *et al.* (1985) studied a cohort of 34 156 male members of a heavy construction equipment operators' union in the USA with potential exposure to diesel exhaust. Cohort members had to have been a union member for at least one year between 1 January 1964 and 31 December 1978, by which time 3345 had died and 1765 (5.2%) could not be traced. Death certificates were obtained for all but 102 (3.1%) decedents. No information was available for jobs held before 1967 and limited information was available on jobs held between 1967 and 1978. The SMRs, based on national figures, adjusted for age, sex, race and calendar time, were 81 (95% CI, 79–84) for all causes, 93 (87–99.6) for all cancers, 99 (88–110) for lung cancer (ICD7 162–163) and 118 (78–172) for bladder cancer. The data were also analysed by duration of union membership, latent period, retirement status, job category and exposure status. Significant upward trends in risk were detected for lung cancer with duration of union membership, used as a surrogate for duration of potential exposure to diesel exhaust, with SMRs for lung cancer of 45 [22–83], 75 [49–111], 108 [81–141], 102 [78–132]and 107 [91–125] for workers with <5, 5–9, 10–14, 15–19 and ⩾ 20 years of union membership, respectively. A significant upward trend was also noted for lung cancer with latent period. Mortality from cancers of the digestive system (SMR, 142; 116–173) and respiratory system (SMR, 162; 138–190) and from lymphosarcoma and reticulosarcoma (SMR, 231; 111–425) was elevated in retirees. Exclusion of early retirees did not remove the risks for respiratory cancer or lymphatic cancer. In general, groups with jobs with presumed high exposure to diesel fumes did not show the excesses reported above. A random sample of union members was surveyed to determine smoking habits, and no significant difference between members and the general population was revealed.

In a review, Steenland (1986) presented data on a preliminary study of the mortality experience of about 10 000 teamsters (truck drivers, dock workers, mechanics and jobs outside the trucking industry) who had died in 1982–83 and had worked for at least ten years in a teamster job. Using occupational data on death certificates, proportionate mortality ratios were calculated for lung cancer for 255 mechanics (226; 95% CI, 162–309), 5834 truck drivers(154; 144–166), 490 dock workers(132; 99–175) and 1064 others(116; 95–142). [The Working Group noted that this was an interim report and that judgement should be reserved until the final results are available.]

Gustafsson *et al.* (1986) studied 6071 Swedish ‘dockers’ assumed by the authors to have been exposed to diesel exhaust and first employed before 1974 for at least six months. The group had been followed for death from 1 January 1961 or from the date of first employment (if this date occurred later) through to 1 January 1981. Age-, calendar time-and region-specific rates were used to generate expected numbers of deaths. The SMRs were 89 (95% CI, 84–94) for all causes, 103 for all cancers, 132for lung cancer (105–166) and 110 (85–142) for urogenital tract cancer. Cancer morbidity was determined among 6063 workers who had been alive and without cancer on 1 January 1961 and were followed through to 1 January 1980; a standard morbidity ratio of 110 (101–120; 452 cases) was seen for cancers at all sites and of 168 (136–207; 86 cases) for lung cancer. [The Working Group noted that there was no consideration of duration, intensity or latency of exposure or of smoking habits in this study.]

Stern *et al.* (1981) examined mortality patterns among 1558 white male vehicle examiners who had been employed in New Jersey, USA, for at least six months between 1944 and 1973. The vital status of all but eight (0.5%) of these was ascertained as of 31 August 1973; these eight were assumed to be alive. Approximately 63% of the cohort members had begun employment prior to 1957. A modified life-table analysis was used to generate the expected number of cause-specific deaths on the basis of national rates, adjusting for age and calendar time. There were 52 deaths from cancer (47.8 expected [SMR, 109; 95% CI, 81–143]). The SMRs for malignant disease increased significantly with latency: 0–9 years, 69 [25–151]; 10–19 years, 98 [56–159]; 20–29 years, 107 [62–171]; >30 years, 189 [101–323]. Cancer at no specific organ site accounted for this excess. The exposure of interest was carbon monoxide, but the authors speculated that other components of automobile exhaust might have been responsible. No information on smoking habits was available for deceased workers, but COHb levels in currently nonsmoking workers increased during the work shift, indicating exposure to exhaust.

In a cohort study of white men enlisted in the US Navy (Garland *et al.*, 1988), 143 cases of testicular cancer were identified in the period 1974–79; age-specific incidence rates were similar to those for the US population, derived from the US National Cancer Institute Surveillance, Epidemiology and End Results (SEER) programme for 1973–77. Of 110 occupational groups in the Navy, three involving maintenance of gasoline and diesel engines and daily exposure to their exhaust emissions (aviation support equipment technicians, enginemen and construction mechanics) had significantly high standardized incidence ratios for testicular cancer: 3.4 (95% CI, 1.9–5.6) in comparison to SEER rates, and 3.8 (2.1–6.3) in comparison to men in the US Navy as a whole, based on 15 cases. The authors noted that this was a hypothesis-generating study and that the men also had potential daily exposure to solvents and other chemicals.

(iv) Miners

Although diesel engines have been used in many mines for a number of years, the Working Group decided not to consider all groups of miners because they may be exposed concurrently to other potential lung carcinogens such as radon decay products, heavy metals and silica, and there was no way that the possible confounding effects of such factors could be determined from the data available in published reports.

Waxweiler *et al.* (1973) studied potash miners and millers, who are exposed to no known carcinogens in the ore, who had been employed for at least one year between January 1940 and July 1967 by eight companies. The vital status of the cohort was identified to July 1967. Of a total of 3886 men, 31 could not be traced and were assumed to be alive. Causes of death were compared with those of the general US population, standardized for age, race, sex and calendar time. Of the cohort, 2743 men had worked at least one year underground and less than one year on the surface and 1143 men had worked at least one year on the surface and less than one year underground. In only two of the eight mines were diesel engines used; one mine changed to diesel in 1949 and the other in 1957. Death certificates were available for 433 of the 438 workers who had died. The effect of smoking was taken into account. No excess mortality from lung cancer was seen in either surface or underground miners. Mortality rates did not differ between the mines with diesel vehicles and those without. The authors noted the short follow-up, the small expected numbers of deaths and the broad classification of causes of death.

(d) Case-control studies

(i) Lung cancer

Williams *et al.* (1977) examined cancer incidence and its relationship to occupation and industry in a study based on the US Third National Cancer Survey. In this study, detailed personal interviews were sought for 13 179 cancer patients (a random 10% sample of all incident invasive tumours occurring in three years in eight areas in the USA) and obtained for 7518 (57%). The numbers of cases of cancer at various anatomical sites were compared with that of cases at all other sites combined. The interview included occupational history (main employment and recent employment), other demographic data and information on smoking and drinking habits; the analysis also controlled for age, sex, race and geographical location. A statistically nonsignificant lung cancer excess (odds ratio, 1.5; [CI could not be calculated]) was observed for truck drivers, which could not be accounted for by smoking. Intensity, duration of exposure and latency were not evaluated. [The Working Group noted the potential for bias due to the relatively low level of compliance with the questionnaire.]

In a population-based case-control study, Coggon *et al.* (1984) used the data on occupation on the death certificates of all men under the age of 40 years in England and Wales who had died of tracheobronchial carcinoma during the period 1975–79; 598 cases were detected, 582 of which were matched with two and the rest with one control who had died from any other cause, for sex, year of death, local authority district of residence and year of birth. Occupations were coded using the Office of Population Census and Surveys 1970 classification of occupations, and a job-exposure matrix was constructed by an occupational hygienist, in which the occupations were grouped according to likely exposure to each of nine known or putative carcinogens. All occupations entailing exposure to diesel fumes were associated with an elevated odds ratio for bronchial carcinoma (1.3; 95% CI, 1.0–1.6); however, for occupations with presumed high exposure, the odds ratio was 1.1 (0.7–1.8). [The Working Group noted the limited information on occupation from death certificates, the young age of the subjects and the consequent short times of exposure and latency, and the lack of information on smoking habits and on the possible confounding effects of other carcinogenic exposures.]

In a hospital-based case-control study (Hall & Wynder, 1984) in 18 hospitals in six US cities, 502 men with histologically confirmed primary lung cancer (20–80 years old) and 502 control patients, matched for age, race and hospital were identified. Patients were interviewed between December 1980 and November 1982. Half of the controls had cancer; patients with tobacco-related diseases were excluded. The questionnaire included items on smoking habits, demographic variables and usual occupation. Occupations were grouped either dichotomously as exposed to diesel exhaust (warehousemen, bus drivers, truck drivers, railroad workers and heavy equipment repairmen and operators) or nonexposed, or, in a separate evaluation, in three presumed categories of frequency of exposure in the job (high, moderate, little). Using the dichotomous division, the exposed group had a significantly elevated odds ratio (2.0; 95% CI, 1.2–3.2), which, however, decreased to 1.4 (0.8–2.4; not significant) when adjusted for smoking. The crude odds ratios were 1.7 (0.6–4.6) for a high probability of exposure to diesel exhaust and 0.7 (0.4–1.3) for a moderate probability of exposure. [The Working Group questioned the possible consequences on risk estimates of excluding patients with tobacco-related diseases from the control group.]

In a hypothesis-generating case-control study, Buiatti *et al.* (1985) investigated the occupational histories of histologically confirmed cases of primary lung cancer among residents of metropolitan Florence, Italy, diagnosed during 1981–83 in the regional general hospital and referral centre for lung cancers in the Province of Florence. For the 376 cases (340 men, 36 women), 892 controls (817 men, 75 women), matched by sex, age, date of admission and smoking status in seven categories, were selected from the medical service of the same hospital, excluding patients with lung cancer, attempted suicides and patients not resident in metropolitan Florence. Each case and control completed a structured questionnaire on demographic variables and on all jobs held for more than one year. The jobs were classified into 21 major classes and 251 subclasses, using the International Labour Office classification. Odds ratios for industries and occupations (ever *versus* never worked) were calculated using logistic regression, in which age and smoking status were included. Taxi drivers had an elevated relative risk for lung cancer after adjusting for tobacco smoking (1.8; 95% CI, 1.0–3.4). [The Working Group noted that multiple comparisons were made, increasing the probability that statistically significant results would be found.]

In a case-control study in northern Sweden, Damber and Larsson (1987) analysed the association between lung cancer and occupation. The cases were 604 male lung cancers reported to the Swedish Cancer Registry during 1972–77 and who had died before May 1979. For each case, a control was drawn from the National Registry for Causes of Deaths, and was matched for sex, year of death, age and municipality; cases of lung cancer and attempted suicide were excluded as controls. In addition, for each case, one living control (less than 80 years old) was drawn from the National Population Registry, matched for sex, year of birth and municipality. Information on residence, occupation, employment and smoking habits was collected by a questionnaire mailed to surviving relatives and to living controls; the response rates were 98% for cases and 96% and 97% for dead and living controls, respectively. Information was requested on all jobs held for at least one year and on lifetime smoking history. A linear logistic regression model, using three discrete levels of employment (<1 year, 1–20 years, and >20 years) and four levels of lifetime tobacco consumption, was used to calculate odds ratios. For professional drivers with more than 20 years' employment, the unmatched odds ratio was 1.5 (95% CI, 0.9–2.6) in comparison with dead controls; this was reduced to 1.2 (0.6–2.2) after adjustment for smoking. The figures obtained in comparison with living controls were 1.7 (0.9–3.2) and 1.1 (0.6–2.2), respectively.

Garshick *et al.* (1987) performed a case-control study on lung cancer deaths among employed and retired US male railroad workers with ten or more years of service, who had been born on 1 January 1900 or after and who had died between 1 March 1981 and February 1982. Cases of primary lung cancer (1256) were matched to two controls by age and date of death. Workers who had died from cancer, suicide, accident or unknown causes were not included among controls. Potential exposure to diesel exhaust was assigned on the basis of an industrial hygiene evaluation of the >150 railroad jobs and areas described by the US Interstate Commerce Commission. Job codes for each worker were available from the US Railroad Retirement Board starting in 1959 and ending with death or retirement. For workers who had retired between 1955 and 1959, the last railroad job held was available. Asbestos exposure prior to 1959 was categorized by job held in 1959 (end of steam locomotive era) or by the last job before retirement, if this was before 1959. Smoking history was obtained by questionnaire from the next-of-kin. Using multiple conditional logistic regression analysis to adjust for smoking and asbestos exposure, workers 64 years of age or younger at time of death who had worked in a diesel exhaust-exposed job for 20 years had a significantly elevated odds ratio for lung cancer (1.4; 95% CI, LI–1.9). No such effect was observed among older workers (0.91 ; 0.71–1.2), many of whom had retired shortly after the transition to diesel-powered locomotives and were therefore not exposed.

In a population-based case-control study (Lerchen *et al.*, 1987), all white and Hispanic white residents of New Mexico, USA, aged 25–84 years, with primary lung cancer, excluding bronchioalveolar carcinoma, diagnosed between 1 January 1980 and 31 December 1982, were identified from the New Mexico Tumor Registry. The cases (333 men and 173 women) were frequency matched with controls selected randomly from the telephone directory or, for persons 65 years or older, from the roster of participants in a health insurance scheme, for sex, ethnic group and ten-year age band at a ratio of approximately 1.5 controls per case (449 men and 272 women). Detailed occupational and smoking histories were obtained by personal interview, with response rates of 89% for cases and 83% for controls. Next-of-kin provided interviews for 50% of the male and 43% of the female cases and for 2% of the controls; the authors recognized the possible bias introduced by this practice. The odds ratio for exposure to diesel exhaust fumes, adjusted for age, ethnic group and smoking, was 0.6 (95% CI, 0.2–1.6). [The Working Group noted the possible bias in choosing controls from the telephone directory when cases are not required to have a telephone or to be listed.]

In a case-control study of lung cancer in France (Benhamou *et al.*, 1988), 1625 histologically confirmed cases and 3091 controls, matched for sex, age at diagnosis, hospital admission and interviewer, completed a questionnaire on residence, education, occupation, and smoking and drinking habits. All occupations held for more than one year were recorded and coded without knowledge of the case status of the patient, using the International Standard Classification of Occupations and according to chemical or physical exposures. The analysis was limited to men (1260 cases and 2084 controls); adjustment was made for age at starting smoking, amount smoked and duration of smoking. Several occupations were associated with increased odds ratios for lung cancer, including miners and quarry men (2.1; 95% CI, 1.1–4.3) and transport equipment operators (1.4; 1.1 – 1.8); the subcategory of motor vehicle drivers also had an increased risk (1.4; 1.1–1.9).

(ii) Bladder cancer

In a population-based case-control study in Canada (Howe *et al.*, 1980), all patients with bladder cancer newly diagnosed in three Canadian provinces between April 1974 and June 1976 were identified; 77% of the patients were interviewed, and for each patient one neighbourhood control, individually matched for age and sex, was interviewed. In the analysis, 632 case-control pairs (480 male and 152 female) were included. Lifetime smoking and employment histories were obtained, and exposure to dusts and fumes was elucidated. Elevated odds ratios were observed for railroad workers [not further defined] (9.0; 95% CI, 1.2–394.5; nine exposed cases) and for exposure to diesel and traffic exhaust (2.8; 0.8–11.8; 11 exposed cases).

In a death certificate-based case-control study (Coggon *et al.*, 1984; for details, see description on p. 139), the occupations of 291 bladder cancer cases and 578 hospital controls were compared. The odds ratio for all diesel fume-exposed occupations was 1.0 (95% CI, 0.7–1.3) and that for occupations with high exposure was 1.7 (0.9–3.3). [The Working Group had the same reservations about this study as expressed on p. 139.]

In a population-based case-control study, the relationship between truck driving and bladder cancer was investigated (Hoar & Hoover, 1985). Cases consisted of all white residents of New Hampshire and Vermont, USA, who had died from bladder cancer in 1975–79. One control per case was selected randomly from all other deaths among residents, excluding suicides, and matched for state, sex, age, race and year of death. A second control per case was selected with the additional matching criterion of county of residence. There were 230 and 210 eligible cases in the two states, respectively; the rate of response to interview was 87% for New Hampshire and 58% for Vermont, and the non-respondents were similar to the respondents with respect to case-control status, sex, age and county of residence. The odds ratio for ever having been a truck driver was 1.5 (95% CI, 0.9–2.6), and there was a significant trend between bladder cancer risk and number of years of truck driving: odds ratios, 1.4 (0.6–3.3), 2.9 (1.2–6.7) and 1.8 (0.8–4.1) for those employed as truck drivers for 1–4, 5–9 and >10 years, respectively. Additional adjustment for age, county, coffee drinking or cigarette smoking (six categories) did not alter these crude odds ratios. [The Working Group noted the nonlinearity of the trend.]

In a hospital-based case-control study in Turin, Italy (Vineis & Magnani, 1985), 512 male cases and 596 male controls randomly selected from among other patients in the main hospital of the city of Turin between 1978 and 1983 were interviewed for lifetime occupational and smoking histories. Occupations were coded using the International Labour Office classification, and associations between specific chemicals and bladder cancer were studied using a job exposure matrix. Adjusting for age and smoking, the odds ratio for bladder cancer for truck drivers was 1.2 (95% CI, 0.6–2.5).

In a hospital-based case-control study, Wynder *et al.* (1985) examined the occupational histories and life style factors (smoking, alcohol and coffee consumption, demographic factors) of 194 male cases of histologically confirmed bladder cancer, 20–80 years of age, diagnosed during two-and-a-half years (January 1981–May 1983) in 18 hospitals in six US cities, and of 582 controls, matched by age, race, year of interview and hospital of admission, hospitalized during the same period for diseases not related to tobacco use. The participation rate among eligible subjects was 75% among cases and 72% among controls. 'Usual' occupation was coded according to an abbreviated list of the US Bureau of Census codes. No significant association was detected between bladder cancer and occupations presumed to involve exposure to diesel exhaust: warehousemen and materials handlers, bus and truck drivers, railroad workers, heavy equipment operators and mechanics (odds ratio, 0.87; 95% CI, 0.47–1.6). [The Working Group questioned the possible consequences on risk estimates of excluding patients with tobacco-related diseases from the control group.]

Data from all ten areas of the US National Bladder Cancer Study were used to evaluate the association of motor exhausts with bladder cancer (Silverman *et al.*, 1986). The study group comprised 1909 white male cases with histologically confirmed bladder carcinoma or papilloma not specified as benign and 3569 frequency-matched controls. Significantly elevated age- and smoking-adjusted odds ratios for bladder cancer were observed for truck drivers or delivery men, and for taxi drivers or chauffeurs: 1.5 (95% CI, 1.1–2.0) and 6.3 (1.6–29.3) for 'usual' occupation, 1.3 (1.1–1.4) and 1.6 (1.2–2.2) for 'ever' occupation. For bus drivers, the odds ratios did not reach significance (1.3, 0.9–1.9 and 1.5, 0.6–3.9 for 'ever' and 'usual', respectively). When allowance was made for a 50-year latency, a significant trend with increasing duration of employment as a truck driver was observed: 1.2, 1.4, 2.1 and 2.2 for a duration of employment of <5, 5–9, 10–24 and >25 years, respectively (p <0.0001). Information on subsets of this cohort has been published elsewhere (Silverman *et al.*, 1983; Schoenberg *et al.*, 1984; Smith *et al.*, 1985). In the Detroit subset (Silverman *et al.*, 1983), the adjusted odds ratio for bladder cancer for truck drivers who had never driven a vehicle with a diesel engine was 1.4 (0.7–2.9) and that for men who had ever driven a vehicle with a diesel engine was 11.9 (2.3–61.1).

Occupational risk factors were investigated as part of a population-based case-control study in Copenhagen, Denmark (Jensen *et al.*, 1987). Between May 1979 and April 1981, a total of 412 live patients with bladder cancer (invasive tumours and papillomas) were reported in the study, 389 of whom were interviewed. Live controls were selected at random from the municipalities where the cases lived, and the sample was stratified to match the cases with regard to sex and age in five-year groups. Among the 1052 controls approached, the overall participation rate was 75%. Cases and controls were interviewed for information on occupational history coded according to the Danish version of the International Standard Industrial Classification. Cigarette smoking was adjusted for in the analysis by using two dichotomous variables (ever/never smoked, current/noncurrent smoker) and a continuous variable (logarithm of pack-years smoked). The adjusted odds ratio for bladder cancer was elevated in land transport workers (1.6; 95% CI, 1.1–2.3). The adjusted odds ratios for bladder cancer for bus, taxi and truck drivers were 0.7 (0.4–1.5), 1.6 (0.8–3.4), 3.5 (1.1–11.6) and 2.4 (0.9–6,6) for durations of employment of 1–9, 10–19, 20–29 and >30 years, respectively, representing a significant trend with duration of employment. The trend was not significant for land transport workers.

In a hospital-based case-control study in Argentina (Iscovich *et al.*, 1987), 120 patients with histologically confirmed bladder carcinoma admitted to ten general hospitals in Greater La Plata between March 1983 and December 1985 were identified. The 117 patients who could be interviewed represented approximately 60% of all incident cases. For each case, a hospital control from the same establishment was selected (patients with diseases associated with tobacco smoking constituted 12% of the control group); a neighbourhood control, matched for age and sex, was also selected. Information on smoking and past and present occupations was collected by questionnaire. An exposure index based on a job-exposure matrix was generated. The adjusted odds ratio for truck and railway drivers was 4.3 [95% CI, 2.1–29.6].

Covering the period 1960–82, Steenland *et al.* (1987) identified 731 male bladder cancer (ICD-9 188) deaths in the Hamilton County, Ohio, region, where there is a known high bladder cancer rate. Six controls were matched to each case on sex and residence in the county at the time of death, year of death, age of death and race. Death certificates and city directories for all residents over 18 were used to identify job history. The first two controls that were listed in the directory within at least five years of the first listing of the cases were selected. Of the 648 cases (89%) listed in the directories, all but 21 had two controls; the remaining 21 had one control. A comparable analysis of all 731 cases and two controls per case was carried out using usual lifetime occupation from the death certificate. A significant increase in the frequency of bladder cancer was found for men with more than 20 years' duration of employment, identified through the city directories as truck drivers (odds ratio, 12.0 [95% CI, 2.3–62.9]; six cases, one control) and railroad workers (odds ratio, 2.2 [95% CI, 1.2–4.0]). Notably, those workers identified as 'drivers not otherwise specified' for ⩽20 years had an odds ratio of 0.15 [95% CI, 0–0.8]. In contrast, on the basis of job ever held identified from either the death certificate or the city directory (without taking duration into account), none of the above findings was significant. [The Working Group noted that this study involved application of a new methodology for exposure ascertainment, which requires further validation.]

In a case-control study of bladder cancer incidence in Edmonton, Calgary and Toronto and Kingston, Canada (Risch *et al.*, 1988), 826 cases of histologically verified bladder cancer were compared with 792 population-based controls matched for age, sex and area of residence. Cases were aged 35–79 and had been ascertained between 1979 and 1982. Information was collected by questionnaire, administered by personal interview, covering family, medical, occupational, residential, smoking and dietary histories. Analysis of the occupational data included adjustment for lifetime smoking habits. Among other findings related to occupation and industry was that the 309 men who had had jobs with exposure to engine exhausts had an odds ratio of 1.5 (95% CI, 1.2–2.0) for 'ever' exposure and an odds ratio of 1.7 (1.2–2.3) for exposure during the period eight to 28 years prior to diagnosis. The authors also calculated that there was a significant increase in trend with duration of exposure for each ten years (1.2; 1.1–1.4). This relationship was not seen for women, but only 19 had been exposed. The relationship was also not seen when an analysis was undertaken by exposure to 18 categories of substances, including engine exhaust. [The Working Group found it difficult to interpret the differences in risk seen when exposure was defined in various ways.]

(iii) Other and multiple sites

In a hypothesis-generating, hospital-based case-control study in Sweden, Flodin *et al.* (1987) analysed the association between occupation and multiple myeloma. The cases were in persons diagnosed between 1973 and 1983 and still alive during 1981–83. From comparisons with cancer registry data, it was concluded that the cases represented one-third of all cases diagnosed in the area. Controls were drawn randomly from population registers. There were 131 cases and 431 controls for analysis. Information on occupational history, X-ray treatment and smoking habits were obtained by a mailed questionnaire. The crude odds ratio for occupational exposure to engine exhaust was 2.3 (95% CI, 1.4–3.7); this association remained significant after adjusting for confounding variables. In a study using the same set of controls (431) and source of cases, Flodin *et al.* (1988) investigated the association with occupational exposures for 111 cases of chronic lymphatic [lymphocytic] leukaemia. The crude odds ratio for occupational exposure to engine exhausts was 2.5 (95% CI, 1.5–4.0); the association remained significant after adjustment for confounding variables. [The Working Group noted that the study population and control of confounding were not clearly described, and that exposure to engine exhausts was self-reported and not further defined by the authors.]

In a large, hypothesis-generating, population-based case-control study in Canada (Siemiatycki *et al.*, 1988), the associations between ten types of engine exhaust and combustion products and cancers at 12 different sites were evaluated. The 3726 cancer patients diagnosed in any of the 19 participating hospitals in Montreal were interviewed (rate of response, 82%). The patients were all men aged 35–70 years. For each cancer site, patients with cancers at other sites comprised the control group. The interview elicited a detailed job history, and a team of chemists and industrial hygienists translated each job into a list of potential exposures (Gérin *et al.*, 1985). The probability of exposure ('possible', 'probable', 'definite'), the frequency of exposure (<5, 5–30, >30% working time) and the level of exposure (low, medium, high) were estimated. Separate analyses were performed for oat-cell, squamous-cell, adenocarcinoma and other carcinomas of the lungs. After stratifying for age, socioeconomic status, ethnic group, cigarette smoking and blue-/white-collar job history, an elevated odds ratio was observed for squamous-cell cancer of the lung and exposure to gasoline engine exhaust (OR, 1.2; 90% CI, 1.0–1.4). In a detailed analysis in which all covariables that changed the estimate of the disease-exposure odds ratio by more than 10% were included as confounders, further associations were revealed: long-term high-level exposure to gasoline engine exhaust (1.4; 1.1–1.8) and short-term high-level exposure to diesel engine exhaust (1.5; 0.9–2.7) were associated with squamous-cell cancer of the lung. The odds ratio for squamous-cell cancer of the lung (1.5; 0.9–2.5) was also elevated for bus, truck and taxi drivers (classified as exposed to gasoline engine exhaust) and for mining and quarrying (classified as exposed to diesel engine exhaust; 2.8, 1.4–5.8), but analyses by duration and intensity of exposure did not support a causal association. Marginally elevated odds ratios were also seen for colon cancer and exposure to diesel engine exhaust (1.3; 1.1–1.6); for cancer of the rectum (1.6; 1.1–2.3) and kidney (1.4; 1.0–2.0) with long-term high-level exposure to gasoline engine exhaust; for colon cancer (1.7; 1.2–2.5) with long-term high-level exposure to diesel engine exhaust; and for rectal cancer (1.5; 1.0–2.2) in bus, truck and taxi drivers. [The Working Group noted that 90% CI were used and that, at the 95% level, most of the intervals would have included unity.]

(e) Childhood cancer

Studies have been carried out to examine the hypothesis that exposure of adults to engine exhaust may result in mutations in germ cells, direct intrauterine exposure or early postnatal exposure.

In a case-control study in Québec, Canada (Fabia & Thuy, 1974), occupation of the father at time of birth was ascertained from the birth certificates of 386 children (out of 402 patients ascertained from death certificates, hospital insurance data and hospital records) who had died from malignant disease before the age of five years in 1965–70 and of 772 control children whose birth registration immediately preceded or followed that of the case in the official records. The occupation of the father was not known for 30 cases or for 56 controls. Father's occupation was recorded as motor vehicle mechanic or service station attendant for 29 (7.5%) cases and 29 (3.8%) controls [odds ratio, 2.1 (95% CI, 1.2–3.4)] and as driver for 19 (4.9%) cases and 49 (6.4%) controls [0.76 (0.4–1.3)].

In a case-control study in Finland (Hakulinen *et al.*, 1976), all 1409 incident cases of cancer in children under 15 years reported to the Cancer Registry in 1959–68 were ascertained. Paternal occupation was obtained from antenatal clinic records for the first trimester of pregnancy. After excluding twins and cases for which the father's occupation was unobtainable, 852 cases were available for analysis. For each case, a child with date of birth immediately before that of the case and who had been born in the same maternity welfare district was chosen as a control. Leukaemias and lymphomas (339 pairs; 158 under five years of age), brain tumours (219 pairs; 77 under five years of age) and other tumours (294 pairs; 160 under five years of age) were analysed separately; analyses were carried out separately for the whole group (children under 15 years of age) and for children under five years of age at the time of diagnosis. Paternal occupation as a motor vehicle driver was not more frequent in any group of cases than in controls: the odds ratio for leukaemia in children under five (based on 14 cases) was 0.74 (95% CI, 0.34–1.6); that for leukaemia and lymphoma in the whole group (35 cases), 1.1 (0.63–1.8); that for brain tumours in children under five (four cases), 0.17 (0.00–1.4); and that for brain tumours in the whole group (16 cases), 0.67 (0.29–1.5). [The Working Group noted that only 60% of cases were available for analysis.]

In a case-control study in Connecticut, USA (Kantor *et al.*, 1979), paternal occupation was ascertained from birth certificates for all 149 cases of Wilms' tumour (aged 0–19 years) reported to the Connecticut Tumor Registry in 1935–73 and for 149 controls selected from State Health

Department files and matched for sex, race and year of birth. The father's occupation was recorded as driver for eight cases and four controls [odds ratio, 2.1 (95% CI, 0.6–6.7)], as motor vehicle mechanic for six cases and one control [6.2 (0.8–49.8)] and as service station attendant for three cases and no control.

In a case-control study on the association between paternal occupation and childhood cancer (Kwa & Fine, 1980), 692 children born in 1947–57 or 1963–67 and who had died of cancer before the age of 15 in Massachusetts, USA, were identified from the National Center for Health Statistics. Two controls were selected from the registry of births for each case — one born immediately before the case and the other immediately after. Paternal occupation was taken from birth certificates and classified into one of nine categories on the basis of the type of chemical exposures involved. Mechanic/service station attendant was recorded as the father's occupation for 21 (4.9%) leukaemia/lymphoma cases [odds ratio, 1.1 (95% CI, 0.7–1.5)], six (4.5%) cases of neurological cancer[1.02 (0.4–2.4)], four (11.8%) cases of urinary tract cancer [2.9 (1.0–8.1); significant], four (4.2%) cases of all other cancers [0.93 (0.34–2.6)] and 61 (4.4%) controls. No excess of leukaemia/lymphoma, neurological cancer, urinary tract cancer or all other cancer was observed in the children of fathers who were motor vehicle drivers.

In a case-control study on associations between childhood cancer and parental occupation (Zack *et al.*, 1980), the parents of 296 children with cancer followed at a haematology clinic in Houston, TX, USA, from March 1976 to December 1977 and three sets of controls were interviewed for demographic information and job history in the year preceding the birth of the child until diagnosis of cancer. The first set of controls comprised 283 fathers and stepfathers and 283 mothers and stepmothers of children without cancer in the same clinic; the second set consisted of siblings of the parents of the case (413 uncles and 425 aunts), matched by age and number of children; and the third set was selected from among residents in the neighbourhood of the cases (228 fathers and 237 mothers). The proportion of cases with paternal occupation as motor vehicle mechanic, service station attendant or driver did not differ from that in any control group [crude odds ratio in comparison with the first control group, 0.59 (95% CI, 0.28–1.2); that in comparison with the second control group, 0.79 (0.38–1.6); and that in comparison with neighbourhood controls, 0.92 (0.40–2.1)]. [The Working Group noted that the selection criteria were not given for either cases or controls, that it was unclear whether information on exposure was obtained from mothers or fathers or both, and that confounding factors were not taken into consideration.]

Hemminki *et al.* (1981) obtained data from the Finnish Cancer Registry on children less than 15 years old with cancer diagnosed in 1959–75 and on parental occupation, as in the study of Hakulinen *et al.* (1976; see pp. 145–146). The odds ratio for the father of a child with leukaemia in 1969–75 being a professional driver was 1.9 [95% CI, 1.1–3.7].

In a proportionate mortality study in England and Wales (Sanders *et al.*, 1981), paternal occupations recorded on the death certificates of children under 15 years of age during the years 1959–63 and 1970–72 (167 646 deaths; 6920 deaths from neoplasms) were investigated. Proportionate mortality ratios for neoplasms were not elevated for children of fathers employed as ‘drivers of stationary engines, cranes, etc.’, as transport workers or as warehousemen.

Associations between paternal occupation and childhood leukaemia and brain tumours were investigated in a case-control study in Maryland, USA (Gold *et al.*, 1982). Children under the age of 20 with leukaemia (diagnosed in 1969–74) or brain tumours (diagnosed in 1965–74) were ascertained in the Baltimore Standard Metropolitan Statistical Area from hospital records, death certificates, hospital tumour registries and from the pathology, radiotherapy and clinical oncology records of 21 of 23 Baltimore hospitals. There were two control groups: one consisted of children with no malignant disease, selected from birth certificates at the Maryland State Health

Department and matched for sex, date of birth and race; the other group consisted of children with malignancies other than leukaemia or brain cancer, matched for sex, race, date of diagnosis and age at diagnosis. Information on occupational exposures of both parents before the birth of the child and between birth and diagnosis was collected by interviewing the mother. A total of 43 children had leukaemia and 70 had brain tumours. The paternal occupational category that included driver, motor vehicle mechanic, service station attendant or railroad worker was not more frequent for children with leukaemia or brain tumours than for the control children. [The Working Group noted the small numbers involved and found the results difficult to interpret.]

In a case-control study on childhood leukaemia and neuroblastoma (Vianna *et al.*, 1984), children born in 1949–78 who were diagnosed with acute leukaemia during the first year of life and reported to the Tumor Registry of the New York State Health Department or with neuroblastoma up to 12 years of age at diagnosis were identified. Using information from birth certificates, two sets of controls were selected: one was matched by year of birth, sex, race and county of residence; the other was additionally matched for age of the mother and birth order of the child. Information on parental age, race, education and occupation, and medical, obstetrical and therapeutic histories were obtained by telephone interview of the mothers. Of 65 eligible cases of leukaemia, 60, with two controls each, were finally included in the analysis. The odds ratio for acute leukaemia for children with ‘high’ presumed paternal exposure to motor exhaust fumes (service station attendants, automobile or truck repairmen, aircraft maintenance personnel) was 2.5 [1.2–5.3] in comparison with the first control group and 2.4 [1.1–3.7] in comparison with the second. For ‘lower’ presumed exposure (taxi drivers, travelling salesmen, truck or bus drivers, railroad workers, toll-booth attendants, highway workers, police officers), the odds ratio was 3.4 [1.4–10.2] in comparison with the first control group and 1.3 [0.8–2.1] in comparison with the second. For the 103 cases of neuroblastoma, there was no significant difference from controls in the number of fathers who had had ‘high’ exposure. [The Working Group questioned the categorization of exposures as ‘high’ and ‘lower’ on the basis of the jobs listed.]

In a case-control study on paternal occupation and Wilms' tumour (Wilkins & Sinks, 1984), 105 patients were identified through the Columbus, OH, USA, Children's Hospital Tumor Registry during the period 1950–81. For each case, two controls were selected from Ohio birth certificate files; the first control series was individually matched for sex, race and year of birth, and the second series was additionally matched for mother's county of residence when the child was born. Due to changes in birth certification, the study included only the 62 cases and their matched controls for which father's occupation was recorded. The crude odds ratio for Wilms' tumour in children with paternal occupation as motor vehicle mechanic, service station attendant or driver/heavy equipment operator was 1.1 [95% CI, 0.36–3.5 compared to both controls taken together].

4. Summary of Data Reported and Evaluation

4.1. Exhaust composition and exposure data

Internal combustion engines have been used in cars, trucks, locomotives and other motorized machinery for about 100 years. Engine exhausts contain thousands of gaseous and particulate substances. The major gaseous products of both diesel- and gasoline-fuelled engines are carbon dioxide and water, but lower percentages of carbon monoxide, sulfur dioxide and nitrogen oxides as well as low molecular weight hydrocarbons and their derivatives are also formed. Submicron-size particles are present in the exhaust emissions of internal combustion engines. The particles present in diesel engine exhaust are composed mainly of elemental carbon, adsorbed organic material and traces of metallic compounds. The particles emitted from gasoline engines are composed primarily of metallic compounds (especially lead, if present in the fuel), elemental carbon and adsorbed organic material. Soluble organic fractions of the particles contain primarily polycyclic aromatic hydrocarbons, heterocyclic compounds, phenols, nitroarenes and other oxygen- and nitrogen- containing derivatives.

The composition and quantity of the emissions from an engine depend mainly on the type and condition of the engine, fuel composition and additives, operating conditions and emission control devices. Particles emitted from engines operating with gasoline are different from diesel engine exhaust particles in terms of their size distribution and surface properties. Emissions of organic compounds from gasoline (leaded and unleaded) and diesel engines are qualitatively similar, but there are quantitative differences: diesel engines produce two to 40 times more particulate emissions and 20–30 times more nitroarenes than gasoline engines with a catalytic converter in the exhaust system when the engines have similar power output. Gasoline engines without catalytic converters and diesel engines of similar power output produce similar quantities of polycyclic aromatic hydrocarbons per kilometre; catalytic converters of the type used with gasoline vehicles reduce emissions of polycyclic aromatic hydrocarbons by more than ten times. Lead and halogenated compounds are also typically found in emissions from engines using leaded gasoline.

In urban areas, exposures to low levels and short-term peak levels of engine exhausts are ubiquitous. Higher exposures to engine exhausts may occur in some occupations, such as transportation and garage work, underground mining, vehicle maintenance and examination, traffic control, logging, firefighting and heavy equipment operation. The components of exhaust most often quantified in an occupational setting are particles, carbon monoxide and oxides of nitrogen; polycyclic aromatic compounds and aldehydes from engine exhausts have also been measured in work environments.

The exhausts of engines share similar physical and chemical characteristics with airborne materials from many sources. This makes it difficult to quantify the portion of an individual's exposure from the general environment that derives directly from engine exhausts and also complicates assessment of occupational exposures to engine exhausts.

4.2. Experimental data

Many studies have been carried out, using several animal species, to evaluate the potential carcinogenicity of exposure to whole exhaust and to components of exhaust from diesel- and gasoline-fuelled internal combustion engines. The studies are considered within six subgroupings: (i) whole diesel engine exhaust; (ii) gas-phase diesel engine exhaust (with particles removed); (iii) diesel engine exhaust particles or extracts of diesel engine exhaust particles; (iv) whole gasoline engine exhaust; (v) condensates/extracts of gasoline engine exhaust; and (vi) engine exhausts in combination with known carcinogens.

Whole diesel engine exhaust

Mice, rats, Syrian hamsters and monkeys (*Macaca fascicularis*) were exposed by inhalation to a range of concentrations of whole diesel engine exhaust, with observations in some studies extending to the lifespan of the animals. Five studies conducted using two different strains of rats showed an increased incidence of benign and malignant lung tumours that was related to the exposure concentration. Four of the studies involved exhaust from light-duty engines, and one the exhaust from a heavy-duty engine. One study of rats exposed to exhaust from a light-duty engine did not show a tumorigenic effect. Of three studies in Syrian hamsters, two did not show induction of lung tumours; the other was considered to be inadequate for an evaluation of carcinogenicity. In two studies in mice, the incidences of lung tumours, including adenocarcinomas, were increased over that in concurrent controls; however, in one study, the total incidence of lung tumours was not elevated over that in historical controls. Monkeys exposed for two years to diesel exhaust did not develop lung tumours, but the short duration of the experiment rendered it inadequate for an evaluation of carcinogenicity.

Gas-phase diesel engine exhaust (with particles removed)

Three studies in which rats and Syrian hamsters were exposed to diesel engine exhaust from which soot particles had been removed by filtration did not show induction of lung tumours. In one study, mice exposed to filtered diesel engine exhaust had an increased incidence of lung tumours, including adenocarcinomas, compared to concurrent controls, a result similar to that seen with exposure to whole exhaust. However, the total incidence of lung tumours in this study was similar to that of historical controls.

Diesel engine exhaust particles or extracts of diesel engine exhaust particles

In other studies, organic extracts of diesel engine exhaust particles were used to evaluate the effects of concentrates of the organic compounds associated with carbonaceous soot particles. These extracts were applied to the skin or administered by intratracheal instillation or intrapulmonary implantation to mice, rats or Syrian hamsters. An excess of skin tumours was observed in mice in one study by skin painting and in one series of studies on tumour initiation using extracts of particles from several different diesel engines. An excess of lung tumours was observed in one study in rats following intrapulmonary implantation of beeswax pellets containing extracts of diesel engine exhaust particles.

In one study, an excess of tumours at the injection site was observed following subcutaneous administration of diesel engine exhaust particles to mice.

Whole gasoline engine exhaust

In one study in which rats were exposed by inhalation to whole leaded gasoline engine exhaust for up to two years and observed for up to an additional six months, the incidence of lung tumours was not different from that in controls. A similar study in Syrian hamsters also showed no induction of lung tumours. In a third study, dogs exposed to whole leaded gasoline exhaust for 68 months and held for an additional 32–36 months did not develop lung tumours.

Condensates/extracts of gasoline engine exhaust

Condensates/extracts of gasoline engine exhaust have been tested by skin painting, subcutaneous injection, intratracheal instillation or implantation into the lung. An excess of skin tumours was produced in five studies in mice by skin painting and in one series of tumour-initiation studies. An excess of lung tumours was observed in one study in rats that were given intrapulmonary implants of beeswax pellets containing condensates/extracts of gasoline engine exhaust. In one study, an excess of lung adenomas was observed in Syrian hamsters given intratracheal instillations of condensates/extracts of gasoline engine exhaust. Subcutaneous injections of condensates/extracts of gasoline engine exhaust also produced an excess of tumours at the injection site in one study in mice.

Engine exhausts in combination with known carcinogens

In studies in which known carcinogens were given to animals exposed either to diesel or gasoline engine exhausts or administered organic compounds from gasoline engine exhaust, inconclusive and inconsistent results were obtained.

4.3. Human data

Studies of workers whose predominant engine exhaust exposure is that from diesel engines

In the two most informative cohort studies (of railroad workers), one in the USA and one in Canada, the risk for lung cancer in those exposed to diesel engine exhaust increased significantly with duration of exposure in the first study and with increased likelihood of exposure in the second (in which smoking was not considered). Three further studies of cohorts with less certain exposure to diesel engine exhaust were also considered; two studies of London bus company employees showed elevated lung cancer rates that were not statistically significant, but a third, of Swedish dockers, showed a significantly increased risk for lung cancer.

In only two case-control studies of lung cancer (one of US railroad workers and one in Canada) could exposure to diesel engine exhaust be distinguished satisfactorily from exposures to other exhausts; modest increases in risk for lung cancer were seen in both, and in the first the increase was significant. In three further case-control studies, in which exposure to diesel engine exhaust in professional drivers and lung cancer risks were addressed, the Working Group considered that the possibility of mixed exposure to engine exhausts could not be excluded. None of these studies showed a significant increase in risk for lung cancer, although the risk was elevated in two.

In the three cohort studies (on railroad workers, bus company workers and ‘dockers’, respectively) in which bladder cancer rates were reported, the risk was elevated, although not significantly so. Four of the case-control studies of bladder cancer were designed to examine groups whose predominant engine exhaust exposure was assumed to be to that from diesel engines. Three showed a significantly increased risk for bladder cancer. In one of these, the large US study, a significant trend was also seen with duration of exposure; and in an analysis of one subset of self-reported diesel truck drivers, a substantial, significant relative risk was seen for bladder cancer.

Studies of workers whose predominant engine exhaust exposure is that from gasoline engines

Only one cohort study addressed workers exposed predominantly to gasoline engine exhaust (vehicle examiners). The risk for cancer increased with latency; no particular site accounted for this increase. In one case-control study, exposure to gasoline engine exhaust was isolated from that to diesel engine exhaust, but no consistent increase in risk was observed.

Studies of workers whose predominant engine exhaust exposure cannot be defined

In a cohort of Swedish drivers, a statistically significantly elevated risk for lung cancer was reported. A second cohort study of heavy construction equipment drivers showed significant increasing trends in lung cancer risk with duration of exposure, but the trend in risk for other smoking-related diseases was also increased. Increased risks for lung cancer were seen in three case-control studies of persons with mixed occupational exposures to engine exhausts in the USA, Italy and France; in two of these, the increase was significant.

In the one cohort study that addressed risk for bladder cancer, the risk was elevated, although not significantly so. In three case-control studies of bladder cancer in the USA, Italy and Denmark, modest increases in risk were seen; two showed significant trends with duration of exposure. In two further studies using the same set of controls, significant associations were also seen with multiple myeloma and chronic lymphocytic leukaemia. Three occupational groups in the US Navy with presumed exposure to engine exhausts were found to have a significantly high incidence of testicular cancer, although the influence of other exposures could not be assessed.

Possible associations between parental exposure to engine exhausts and cancer in children were considered in ten studies. No clear pattern of risk emerged.

4.4. Other relevant data

No relevant data were available on the toxic effects or metabolism of engine exhausts in humans, and there was no adequate study to evaluate whether diesel and gasoline engine exhausts induce chromosomal effects in humans.

Prolonged exposure of experimental animals to diesel engine exhaust leads to a number of effects related to the concentration to which they are exposed, including particle accumulation in macrophages, changes in the lung cell population, fibrotic effects and squamous metaplasia, which appear to be correlated with impaired pulmonary clearance. It has also caused exposure-related pathological changes in regional lymph nodes in mice and rats and an apparent increase in immunoglobulin M antibody response.

Prolonged exposure to diesel engine exhaust resulted in DNA adduct formation in rats and protein adduct formation in rats and hamsters.

Exposure of rodents to whole diesel engine exhaust induced sister chromatid exchange but not germ-cell mutations, micronuclei or dominant lethal mutations. Whole diesel engine exhaust induced sister chromatid exchange in cultured human cells. It did not induce sex-linked recessive lethal mutations in *Drosophila melanogaster* and gave inconclusive results in an assay for recombination in yeast. Particles or their extracts induced somatic gene mutations and sister chromatid exchange in rodents *in vivo* but did not induce micronuclei. They induced chromosomal aberrations, sister chromatid exchange and gene mutations in cultured human cells and cell transformation, sister chromatid exchange, gene mutations and DNA damage in rodent cells *in vitro* and inhibited intercellular communication. Particles or their extracts were weakly recombinogenic in yeast and induced mutations and DNA damage in bacteria. The gaseous phase was also mutagenic to bacteria.

Prolonged exposure to gasoline engine exhaust caused protein adduct formation in rats and hamsters.

Whole gasoline engine exhaust induced micronuclei in mice. Gasoline engine exhaust particle extracts induced cell transformation, aneuploidy, chromosomal aberrations, sister chromatid exchange, gene mutations and DNA damage in cultured animal cells but were not recombinogenic in yeast. Whole gasoline engine exhaust, particle extracts and the gaseous phase were mutagenic to bacteria.

4.5. Evaluation[1]

There is *sufficient evidence* for the carcinogenicity in experimental animals of whole diesel engine exhaust.

There is *inadequate evidence* for the carcinogenicity in experimental animals of gas-phase diesel engine exhaust (with particles removed).

There is *sufficient evidence* for the carcinogenicity in experimental animals of extracts of diesel engine exhaust particles.

There is *inadequate evidence* for the carcinogenicity in experimental animals of whole gasoline engine exhaust.

There is *sufficient evidence* for the carcinogenicity in experimental animals of condensates/extracts of gasoline engine exhaust.

There is *limited evidence* for the carcinogenicity in humans of diesel engine exhaust.

There is *inadequate evidence* for the carcinogenicity in humans of gasoline engine exhaust.

There is *limited evidence* for the carcinogenicity in humans of engine exhausts (unspecified as from diesel or gasoline engines).

Overall evaluation

Diesel engine exhaust *is probably carcinogenic to humans (Group 2A)*. Gasoline engine exhaust *is possibly carcinogenic to humans (Group 2B)*.

Summary table of genetic and related effects of diesel and gasoline engine exhausts

View in own window

Nonmammalian systems													**Mammalian systems**												
Prokaryotes		**Lower eukaryotes**				**Plants**			**Insects**				***In vitro***												
													Animal cells								**Human cells**				
D	**G**	**D**	**R**	**G**	**A**	**D**	**G**	**C**	**R**	**G**	**C**	**A**	**D**	**G**	**S**	**M**	**C**	**A**	**T**	**I**	**D**	**G**	**S**	**M**	**C**
Diesel engine exhaust																									
$+^{1b}$	$+^{ab}$		$?^{bc}$							$-^{1c}$			$+^{b}$	$+^{b}$	$+^{b}$		$?^{b}$		$+^{b}$	$+^{1b}$		$+^{b}$	$+^{b1c}$		+
Gasoline engine exhaust																									
	$+^{abc}$		$-^{1b}$										$+^{1b}$	a	$+^{b}$		$+^{1b}$	$+^{1b}$	$+^{b}$						

A, aneuploidy; C, chromosomal aberrations; D, DNA damage; DL, dominant lethal mutation; G, gene mutation; I, inhibition of intercellular communication; M, micronuclei; R, mitotic recombination and gene conversion; S, sister chromatid exchange; T, cell transformation

In completing the tables, the following symbols indicate the consensus of the Working Group with regard to the results for each endpoint:

+ considered to be positive for the specific endpoint and level of biological complexity

+1 considered to be positive, but only one valid study was available to the Working Group

− considered to be negative

−1 considered to be negative, but only one valid study was available to the Working Group

? considered to be equivocal or inconclusive (e.g., there were contradictory results from different laboratories; there were confounding exposures; the results were equivocal)

a gas

b particles or extracts thereof

c whole exhaust

* positive in somatic cells^{1b}, negative in germ cells^{1c}

5. References

Abraham W.M., Kim C.S., Januszkiewicz A.J., Welker M., Mingle M.A., Schreck R. Effects of a brief low-level exposure to the particulate fraction of diesel exhaust on pulmonary function of conscious sheep. Arch. environ. Health. 1980;35:77–80. [PubMed:

6154444]

Ahlberg J., Ahlbom A., Lipping H., Norell S., Österblom L. Cancer among professional drivers — a problem-oriented register-based study (Swed.). Lakartidningen. 1981;78:1545–1546. [PubMed: 6166819]

Al-Mutaz I.S. Automotive emission problem in Saudi Arabia. Environ. int. 1987;13:335–338.

Alsberg, T., Westerholm, R., Stenberg, U., Strandell, M. & Jansson, B. (1984) Particle associated organic halides in exhausts from gasoline and diesel fueled vehicles. In: Cooke, M. & Dennis, A.J., eds, *Polynuclear Aromatic Hydrocarbons, 8th International Symposium: Mechanisms, Methods and Metabolism*, Columbus, OH, Battelle, pp. 87–97.

Alsberg T., Stenberg U., Westerholm R., Strandell M., Rannug U., Sundvall A., Romert L., Bernson V., Pettersson B., Toftgård R., Franzén B., Jansson M., Gustafsson J.A., Egebäck K.E., Tejle G. Chemical and biological characterization of organic material from gasoline exhaust materials. Environ. Sci. Technol. 1985;19:43–50.

Ames R.G., Attfield M.D., Hankinson J.L., Hearl F.J., Reger R.B. Acute respiratory effects of exposure to diesel emissions in coal miners. Am. Rev. respir. Dis. 1982;125:39–42. [PubMed: 7065507]

Ames R.G., Hall D.S., Reger R.B. Chronic respiratory effects of exposure to diesel emissions in coal mines. Arch. environ. Health. 1984;39:389–394. [PubMed: 6524958]

Anon. (1984) Report on the consensus workshop on formaldehyde. *Environ. Health Perspect., 58*, 323–381. [PMC free article: PMC1569424] [PubMed: 6525992]

Apol, A.G. (1983) *Health Hazard Evaluation Report No. HETA-82-137-1264, Regional Transportation District, Denver, CO*, Cincinnati, OH, National Institute for Occupational Safety and Health.

Aronow W.S., Harris C.N., Isbell M.W., Rokaw S.N., Imparato B. Effect of freeway travel on angina pectoris. Ann. intern. Med. 1972;77:669–676. [PubMed: 4117097]

Attfield M.D., Trabant G.D., Wheeler R.W. Exposure to diesel fumes and dust at six potash mines. Ann. occup. Hyg. 1982;26:817–831. [PubMed: 7181309]

Austin A.C., Claxton L.D., Lewtas J. Mutagenicity of the fractionated organic emissions from diesel, cigarette smoke condensate, coke oven, and roofing tar in the Ames assay. Environ. Mutagenesis. 1985;7:471–487. [PubMed: 2414094]

Ayres S.M., Evans R., Licht D., Griesbach J., Reimold F., Ferrand E.F., Criscitiello A. Health effects of exposure to high concentrations of automotive emissions. Studies in bridge and tunnel workers in New York City. Arch. environ. Health. 1973;27:168–178. [PubMed: 4124690]

Ball, D.J. (1987) Particulate carbon emissions and diesel vehicles. In: *Proceedings of the Institution of Mechanical Engineers: Vehicle Emissions and their Impact in European Air Quality, March 1987 (C337/87)*, Edmonds, Surrey, Automobile Division of the Institution of Mechanical Engineers, pp. 83–87.

Ball D.J., Hume R. The relative importance of vehicular and domestic emissions of dark smoke in greater London in the mid-1970s, the significance of smoke shade measurements, and an explanation of the relationship of smoke shade to gravimetric measurements of particulate. Atmos. Environ. 1977;11:1065–1073.

Barfknecht, T.R., Andon, B.M., Thilly, W.G. & Hites, R.A. (1981) Soot and mutation in bacteria and human cells. In: Cooke, M. & Dennis, A.J., eds, *Polynuclear Aromatic Hydrocarbons, 5th International Symposium: Chemical Analysis and Biological Fate*, Columbus, OH, Battelle, pp. 231–242.

Barnhart M.I., Chen S.-T., Salley S.O., Puro H. Ultrastructure and morphometry of the alveolar lung of guinea pigs chronically exposed to diesel engine exhaust; six months' experience. J. appl. Toxicol. 1981;1:88–103. [PubMed: 6206119]

Barnhart, M.I., Salley, S.O., Chen, S.-T. & Puro, H. (1982) Morphometric ultrastructural analysis of alveolar lungs of guinea pigs chronically exposed by inhalation to diesel exhaust (DE). In: Lewtas, J., ed., *Toxicological Effects of Emissions from Diesel Engines*, Amsterdam, Elsevier, pp. 183–200. [PubMed: 6176422]

Battigelli M.C. Effects of diesel exhaust. Arch. environ. Health. 1965;10:165–167. [PubMed: 14232896]

Battigelli M.C., Mannella R.J., Hatch T.F. Environmental and clinical investigation of workmen exposed to diesel exhaust in railroad engine houses. Ind. Med. Surg. 1964;33:121–124. [PubMed: 14126828]

Battigelli M.C., Hengstenberg F., Mannella R.J., Thomas A.P. Mucociliary activity. Arch. environ. Health. 1966;12:460–466. [PubMed: 4159747]

Baxter P. J., McDowall M.E. Occupation and cancer in London: an investigation into nasal and bladder cancer using the Cancer Atlas. Br. J. ind. Med. 1986;43:44–49. [PMC free article: PMC1007599] [PubMed: 3947560]

Begeman C.R., Colucci J.M. Apparatus for determinating the contribution of the automobile to the benzene-soluble organic matter in air. Natl Cancer Inst. Monogr. 1962;9:17–57. [PubMed: 13866550]

Belisario M. A., Buonocore V., De Marinis E., De Lorenzo F. Biological availability of mutagenic compounds adsorbed onto diesel exhaust particulate. Mutat. Res. 1984;135:1–9. [PubMed: 6198585]

Belisario M.A., Farina C., Buonocore V. Evaluation of concentration procedures of mutagenic metabolites from urine of diesel particulate-treated rats. Toxicol. Lett. 1985;25:81–88. [PubMed: 2581335]

Bellmann B., Muhle H., Heinrich U. Lung clearance after long time exposure of rats to airborne pollutants. J. Aerosol Sci. 1983;14:194–196.

Benhamou S., Benhamou E., Flamant R. Occupational risk factors of lung cancer in a French case-control study. Br. J. ind. Med. 1988;45:231–233. [PMC free article: PMC1007981] [PubMed: 3377999]

Bhatnagar, R.S. (1980) Collagen and prolyl hydroxylase levels in lungs in dogs exposed to automobile exhaust and other noxious gas mixtures. In: Stara, J.F., Dungworth, D.L., Orthoefer, J.G. & Tyler, W.S., eds, *Long-term Effects of Air Pollutants: in Canine Species (EPA-600/8-80-014)*, Washington DC, US Environmental Protection Agency, pp. 71–77.

Bice D.E., Mauderly J.L., Jones R.K., McClellan R.O. Effects of inhaled diesel exhaust on immune responses after lung immunization. Fundam. appl. Toxicol. 1985;5:1075–1086. [PubMed: 2419196]

Bini G. Lead in the urban environment. 2. Int. J. environ. Stud. 1973;5:131–135.

Bjørseth, A. (1983) *Handbook of Polycyclic Aromatic Hydrocarbons*, New York, Marcel Dekker.

Bond J.A., Butler M.M., Medinsky M.A., Muggenburg B.A., McClellan R.O. Dog pulmonary macrophage metabolism of free and particle-associated [^{14}C]benzo[*a*]pyrene. J. Toxicol., environ. Health. 1984;14:181–189. [PubMed: 6209409]

Bond J.A., Mauderly J.L., Henderson R.F., McClellan R.O. Metabolism of 1-[^{14}C]nitropyrene in respiratory tract tissue of rats exposed to diesel exhaust. Toxicol appl. Pharmacol. 1985;79:461–470. [PubMed: 2412308]

Bond J. A., Sun J.D., Medinsky M.A., Jones R.K., Yeh H.C. Deposition, metabolism, and excretion of 1-[^{14}C]nitropyrene and 1-[^{14}C]nitropyrene coated on diesel exhaust particles as influenced by exposure concentration. Toxicol. appl. Pharmacol. 1986;85:102–117. [PubMed: 2425457]

Bradow R.L. Diesel particle emissions. Bull. N. Y. Acad. Med. 1980;56:797–811. [PMC free article: PMC1808362] [PubMed: 6161659]

Brightwell, J., Fouillet, X., Cassano-Zoppi, A.-L., Bernstein, D., Gatz, R. & Duchosal, F. (1986) Neoplastic and functional changes in rodents after chronic inhalation of engine exhaust emissions. In: Ishinishi, N., Koizumi, A., McClellan, R.O. & Stöber, W., eds, *Carcinogenic and Mutagenic Effects of Diesel Engine Exhaust*, Amsterdam, Elsevier, pp. 471–485.

Brightwell J., Fouillet X., Cassano-Zoppi A.-L., Bernstein D., Crawley F., Duchosal F., Gatz R., Perczel S., Pfeifer H. Tumours of the respiratory tract in rats and hamsters following chronic inhalation of engine exhaust emissions. J. appl. Toxicol. 1989;9:23–31. [PubMed: 2466883]

Brooks, A.L., Wolff, R.K., Royer, R.E., Clark, C.R., Sanchez, A. & McClellan, R.O. (1980) Biological availability of mutagenic chemicals associated with diesel exhaust particles. In: Pepelko, W.E., Danner, R.M. & Clarke, N.A., eds, *Health Effects of Diesel Engine Emissions (EPA-600/9-80-057a)*, Cincinnati, OH, US Environmental Protection Agency, pp. 345–358.

Brooks A.L., Li A.P., Dutcher J.S., Clark C.R., Rothenberg S.J., Kiyoura R., Bechtold W.E., McClellan R.O. A comparison of genotoxicity of automotive exhaust particles from laboratory and environmental sources. Environ. Mutagenesis. 1984;6:651–668. [PubMed: 6207015]

Brorström, E., Grennfelt, P., Lindskog, A., Sjödin, A. & Nielsen, T. (1983) Transformation of polycyclic aromatic hydrocarbons during sampling in ambient air by exposure to different oxidized nitrogen compounds and ozone. In: Cooke, M. & Dennis, A.J., eds, *Polynuclear Aromatic Hydrocarbons, 7th International Symposium: Formation, Metabolism and Measurement*, Colombus, OH, Battelle, pp. 201–210.

deBruin A. Carboxyhemoglobin levels due to traffic exhaust. Arch. environ. Health. 1967;15:384–389. [PubMed: 4166539]

Brune H., Habs M., Schmähl D. The tumor-producing effect of automobile exhaust condensate and fractions thereof. Part II: Animal studies. J. environ. Pathol. Toxicol. 1978;1:737–746. [PubMed: 83348]

Buiatti E., Kriebel D., Geddes M., Santucci M., Pucci N. A case control study of lung cancer in Florence, Italy. I. Occupational risk factors. J. Epidemiol. Commun. Health.

1985;39:244–250. [PMC free article: PMC1052443] [PubMed: 4045367]

Burgess W.A., DiBerardinis L., Speizer F.E. Exposure to automobile exhaust. III. An environmental assessment. Arch. environ. Health. 1973;26:325–329. [PubMed: 4122091]

Burgess W.A., DiBerardinis L., Speizer F.E. Health effects of exposure to automobile exhaust — V. Exposure of toll booth operators to automobile exhaust. Am. ind. Hyg. Assoc. J. 1977;38:184–191. [PubMed: 68672]

Cadle S.H., Mulawa P. A. Low molecular weight aliphatic amines in exhaust from catalyst-equipped cars. Environ. Sci. Technol. 1980;14:718–723. [PubMed: 22296480]

Calabrese E.J., Moore G.S., Guisti R.A., Rowan C.A., Schulz E.N. A review of human health effects associated with exposure to diesel fuel exhaust. Environ. int. 1981;5:473–477.

Campbell J.A. The effects of exhaust gases from internal combustion engines and of tobacco smoke upon mice, with special reference to incidence of tumours of the lung. Br. J. exp. Pathol. 1936;17:146–158.

Campbell K.I., George E.L., Washington I.S. Jr. Enhanced susceptibility to infection in mice after exposure to dilute exhaust from light duty diesel engines. Environ. int. 1981;5:377–382.

Cantrell E.T., Tyrer H.W., Peirano W.B., Danner R.M. Benzo(a)pyrene metabolism in mice exposed to diesel exhaust: II. Metabolism and excretion. Environ. int. 1981;5:313–316.

Cantrell, B.K., Zeller, H.W., Williams, K.L. & Cocalis, J. (1986) Monitoring and measurement of in-mine aerosol: diesel emissions. In: *Diesels in Underground Mines, Proceedings of the Bureau of Mines Technology Transfer Seminar, Louisville KY, 21 April 1987 and Denver CO, 23 April 1987 (BOM Information Circular 9141)*, Washington DC, US Department of the Interior, Bureau of Mines, pp. 18–40.

Carey, P.M. (1987) *Air Toxics Emissions from Motor Vehicles* (*Technical Report*) (*EPA-AA-TSS-PA-86-5*), Washington DC, US Environmental Protection Agency.

Casto B.C., Hatch G.G., Huang S.L., Lewtas J., Nesnow S., Waters M.D. Mutagenic and carcinogenic potency of extracts of diesel and related environmental emissions: in vitro mutagenesis and oncogenic transformation. Environ. int. 1981;5:403–409.

Castranova V., Bowman L., Reasor M.J., Lewis T., Tucker J., Miles P.R. The response of rat alveolar macrophages to chronic inhalation of coal dust and/or diesel exhaust. Environ. Res. 1985;36:405–419. [PubMed: 2579806]

Chamberlain A.C. Prediction of response of blood lead to airborne and dietary lead from volunteer experiments with lead isotopes. Proc. R. Soc. Lond. B. 1985;224:149–182. [PubMed: 2860671]

Chamberlain A.C., Clough W.S., Heard M.J., Newton D., Stott A.N.B., Wells A.C. Uptake of lead by inhalation of motor exhaust. Proc. R. Soc. Lond. B. 1975;192:77–110. [PubMed: 54924]

Chamberlain, A.C., Heard, Ml, Little, P., Newton, D., Wells, A.C. & Wiffen, R.D. (1978) *Investigations into Lead from Motor Vehicles* (*Harwell Laboratory Report A ERE-R9198*), London, Her Majesty's Stationery Office.

Chambers D., Farrant G.B., Mendham J. Lead levels in exhaust replacement centres. Sci.

total Environ. 1984;33:31–36.

Chan T.L., Lee P.S., Hering W.E. Deposition and clearance of inhaled diesel exhaust particles in the respiratory tract of Fischer rats. J. appl. Toxicol. 1981;1:77–82. [PubMed: 6206117]

Chan T.L., Lee P.S., Hering W.E. Pulmonary retention of inhaled diesel particles after prolonged exposures to diesel exhaust. Fundam. appl. Toxicol. 1984;4:624–631. [PubMed: 6207068]

Chen K.C. Induction of aryl hydrocarbon hydroxylase in rat tissue following intratracheal instillation of diesel particulate extract and benzo[*a*]pyrene. J. appl. Toxicol. 1986;6:259–262. [PubMed: 2428858]

Chen K.C., Vostal J.J. Aryl hydrocarbon hydroxylase activity induced by injected diesel particulate extract vs inhalation of diluted diesel exhaust. J. appl. Toxicol. 1981;1:127–131. [PubMed: 6206112]

Chen S., Weller M.A., Barnhart M.I. Effects of diesel engine exhaust on pulmonary alveolar macrophages. Scanning Electron Microsc. 1980;3:327–338. [PubMed: 6158086]

Cheng Y.S., Yeh H.C., Mauderly J.L., Mokler B.V. Characterization of diesel exhaust in a chronic inhalation study. Am. ind. Hyg. Assoc. J. 1984;45:547–555. [PubMed: 6206709]

Chescheir, G.M., III, Garrett, N.E., Shelburne, J.D., Lewtas Huisingh, J. & Waters, M.D. (1981) Mutagenic effects of environmental particulates in the CHO/HGPRT system. In: Waters, M.D., Sandhu, S.S., Lewtas Huisingh, J., Claxton, L. & Nesnow, S., eds, *Short-term Bioassays in the Analysis of Complex Environmental Mixtures, II*, New York, Plenum, pp. 337–350.

Chuang, C.C. & Petersen, B.A. (1985) *Review of Sampling and Analysis Methodology for Polynuclear Aromatic Compounds in Air from Mobile Sources (EPA 600/4-85-045; US NTIS PB85-227759)*, Research Triangle Park, NC, US Environmental Protection Agency.

Clark C.R., Vigil C.L. Influence of rat lung and liver homogenates on the mutagenicity of diesel exhaust particulate extracts. Toxicol. appl. Pharmacol. 1980;56:110–115. [PubMed: 6160647]

Clark C.R., Royer R.E., Brooks A.L., McClellan R.O., Marshal W.F., Naman T.M., Seizinger D.E. Mutagenicity of diesel exhaust particle extracts: influence of car type. Fundam. appl. Toxicol. 1981;1:260–265. [PubMed: 6192031]

Clark C.R., Henderson T.R., Royer R.E., Brooks A.L., McClellan R.O., Marshall W.F., Naman T.M. Mutagenicity of diesel exhaust particle extracts: influence of fuel composition in two diesel engines. Fundam. appl. Toxicol. 1982a;2:38–43. [PubMed: 6193020]

Clark C.R., Dutcher J.S., Brooks A.L., McClellan R.O., Marshall W.F., Naman T.M. Mutagenicity of diesel exhaust particle extracts: influence of driving cycle and environmental temperature. Fundam. appl. Toxicol. 1982b;2:153–157. [PubMed: 6193022]

Clark C.R., McClellan R.O., Marshall W.F., Naman T.M., Seizinger D.E. Mutagenicity of diesel exhaust particle extracts: influence of non-petroleum fuel extenders. Arch environ. Contam. Toxicol. 1982c;11:749–752. [PubMed: 6187304]

Clark C.R., Dutcher J.S., McClellan R.O., Naman T.M., Seizinger D.E. Influence of ethanol and methanol gasoline blends on the mutagenicity of particulate exhaust extracts. Arch. environ. Contam. Toxicol. 1983;12:311–317. [PubMed: 6192773]

Clark C.R., Dutcher J.S., Henderson T.R., McClellan R.O., Marshall W.F., Naman T.M., Seizinger D.E. Mutagenicity of automotive particulate exhaust: influence of fuel extenders, additives and aromatic content. Adv. mod. environ. Toxicol. 1984;6:109–122.

Claxton L.D. Mutagenic and carcinogenic potency of diesel and related environmental emissions: *Salmonella* bioassay. Environ. int. 1981;5:389–391.

Claxton L.D. Characterization of automotive emissions by bacterial mutagenesis bioassay: a review. Environ. Mutagenesis. 1983;5:609–631. [PubMed: 6191975]

Claxton L.D., Barnes H.M. The mutagenicity of diesel-exhaust particle extracts collected under smog-chamber conditions using the *Salmonella typhimurium* test system. Mutat. Res. 1981;88:255–272. [PubMed: 7019687]

Claxton, L.D. & Kohan, M. (1981) Bacterial mutagenesis and the evaluation of mobile-source emissions. In: Waters, M.D., Sandhu, S.S., Lewtas Huisingh, J., Claxton, L. & Nesnow, S., eds, *Short-term Bioassays in the Analysis of Complex Environmental Mixtures, II*, New York, Plenum, pp. 299–317.

Coggon D., Pannett B., Acheson E.D. Use of job-exposure matrix in an occupational analysis of lung and bladder cancers on the basis of death certificates. J. natl Cancer Inst. 1984;72:61–65. [PubMed: 6363790]

Cohen S.I., Dorion G., Goldsmith J.R., Permutt S. Carbon monoxide uptake by inspectors at a United States-Mexico border station. Arch. environ. Health. 1971;22:47–54. [PubMed: 4099772]

Commission of the European Communities. Council Directive of 20 March 1970 concerning the approximation of the laws of the Member States relating to measures to take against air pollution by gases from ignition engines of motor vehicles (70/220/CEE). Off. J. Eur. Communities. 1970;L76:1–23.

Commission of the European Communities. Council Directive of 3 December 1987 amending Directive 70/220/EEC on the approximation of the laws of the Member States relating to measures to be taken against air pollution by gases from the engines of motor vehicles (88/76/EEC). Off J. Eur. Communities. 1988;L36:1–61.

Cooper G.P., Lewkowski J.P., Hastings L., Malanchuk M. Catalytically and noncatalytically treated automobile exhaust: biological effects in rats. J. Toxicol environ. Health. 1977;3:923–934. [PubMed: 74417]

Cornwell, R.J. (1982) *Health Hazard Evaluation Determination Report No. MHETA-81-108-9004; Climax Molybdenum Company, Climax, CO* (*PB84-14850 1*), Morgantown, WV, National Institute for Occupational Safety and Health.

Cuddihy, R.G., Seiler, F. A., Griffith, W.C., Scott, B.R. & McClellan, R.O. (1980) *Potential Health and Environmental Effects of Diesel Light Duty Vehicles* (*LME-82*), Springfield, VA, National Technical Information Service, US Department of Commerce.

Cuddihy, R.G., Griffith, W.C., Clark, C.R. & McClellan, R.O. (1981) *Potential Health and Environmental Effects of Light Duty Diesel Vehicles. II* (*LMF-89*), Springfield, VA, National Technical Information Service, US Department of Commerce.

Cuddihy R.G., Griffith W.C., McClellan R.O. Health risks from light-duty diesel vehicles. Environ. Sci. Technol. 1984;18:14A–21A. [PubMed: 22657122]

Curren R.D., Kouri R.E., Kim C.M., Schechtman L.M. Mutagenic and carcinogenic potency of extracts from diesel related environmental emissions: simultaneous morphological transformation and mutagenesis in BALB/c 3T3 cells. Environ. int. 1981;5:411–415.

Currie, L.A. & Klouda, G.A. (1982) Counters, accelerators, and chemistry. In: Currie, L.A., ed., *Nuclear and Chemical Dating Techniques, Interpreting the Environmental Record* (*ACS Symposium Series 176*), Washington DC, American Chemical Society, pp. 159–166.

Daisey, J.M. (1983) Analysis of polycyclic aromatic hydrocarbons by thin-layer chromatography. In: Bjørseth, A., ed., *Handbook of Polycyclic Aromatic Hydrocarbons*, New York, Marcel Dekker, pp. 397–437.

Damber L.A., Larsson L.G. Occupation and male lung cancer: a case-control study in northern Sweden. Br. J. ind. Med. 1987;44:446–453. [PMC free article: PMC1007858] [PubMed: 3620367]

Daniel, J.H., Jr (1984) *Diesels in Underground Mining: a Review and an Evaluation of an Air Quality Monitoring Methodology (RI-8884; US NTIS PB84-214444)*, Washington DC, US Department of the Interior, Bureau of Mines.

Davies C.N. Absorption of gases in the respiratory tract. Ann. occup. Hyg. 1985;29:13–25. [PubMed: 4026114]

Decouflé, P., Stanislawczyk, K., Houten, L., Bross, J.D.J. & Viadana, E. (1977) *A Retrospective Survey of Cancer in Relation to Occupation* (*DHEW(NIOSH) Publ. No. 77-178*), Cincinnati, OH, US Department of Health, Education, and Welfare.

Dehnen W., Tomingas R., Kouros M., Mönch W. Comparative study on the behaviour of particles from diesel and gasoline engines in the lungs of rodents: elimination rate and induction of benzo[a]pyrene hydroxylase and ethoxycoumarin deethylase (Ger.). Zbl. Bakt. Hyg., I. Abt. Orig. B. 1985;180:351–358. [PubMed: 2408402]

Depass, L.R., Chen, K.C. & Peterson, L.G. (1982) Dermal carcinogenesis bioassays of diesel particulates and dichloromethane extract of diesel particulates in C3H mice. In: Lewtas, J., ed., *Toxicological Effects of Emissions from Diesel Engines*, Amsterdam, Elsevier, pp. 321–327. [PubMed: 6176430]

Deutsche Forschungsgemeinschaft (German Research Association) (1985) *Air Analysis* (Ger.), Weinheim, VCH Verlagsgesellschaft mbH.

Doran T., McTaggart N.G. The combined use of high efficiency liquid and capillary gas chromatography for the determination of polycyclic aromatic hydrocarbons in automotive exhaust condensates and other hydrocarbon mixtures. J. chromatogr. Sci. 1974;12:715–721. [PubMed: 4138169]

Draper W.M. Quantitation of nitro- and dinitropolycyclic aromatic hydrocarbons in diesel exhaust particulate matter. Chemosphere. 1986;15:437–447.

Dubrow R., Wegman D.H. Cancer and occupation in Massachusetts: a death certificate study. Am. J. ind. Med. 1984;6:207–230. [PubMed: 6475966]

Dukovich M., Yasbin R.E., Lestz S.S., Risby T.H., Zweidinger R.B. The mutagenic and SOS-inducing potential of the soluble organic fraction collected from diesel particulate emissions. Environ. Mutagenesis. 1981;3:253–264. [PubMed: 6168464]

Duleep, K.G. & Dulla, R.G. (1980) Survey and analysis of automotive particulate sampling. In: Pepelko, W.E., Danner, R.M. & Clarke, N.A., eds, *Health Effects of Diesel*

Engine Emissions: Proceedings of an International Symposium, December 3–5, 1979 (*EPA-60019-80-057A*), Springfield, VA, US Environmental Protection Agency, pp. 93–112.

Dünges, W. (1979) Prä-chromatographische Mikromethoden. µl-Techniken für die Biomedizinische Spureanalytik [Pre-chromatographic Micromethods. µl-Techniques for Biomedical Trace Analysis], Heidelberg, A. Hüthig Verlag.

Dutcher J.S., Sun J.D., Lopez J. A., Wolf I., Wolff R.K., McClellan R.O. Generation and characterization of radiolabelled diesel exhaust. Am. ind. Hyg. Assoc. J. 1984;45:491–498. [PubMed: 6205579]

Dziedzic D. Differential counts of B and T lymphocytes in the lymph nodes, circulating blood and spleen after inhalation of high concentrations of diesel exhaust. J. appl. Toxicol. 1981;1:111–115. [PubMed: 6206109]

Edling C., Anjou C.-G., Axelson O., Kling H. Mortality among personnel exposed to diesel exhaust. Int. Arch. occup. environ. Health. 1987;59:559–565. [PubMed: 2445695]

Edwards N.T. Polycyclic aromatic hydrocarbons (PAH's) in the terrestrial environment. A review. J. environ. Qual. 1983;12:427–441.

Egan, H., Castegnaro, M., Bogovski, P., Kunte, H. & Walker, E.A., eds (1979) *Environmental Carcinogens. Selected Methods of Analysis*, Vol. 3, *Analysis of Polycyclic Aromatic Hydrocarbons in Environmental Samples* (*IARC Scientific Publications No. 29*), Lyon, International Agency for Research on Cancer.

Eisenberg, W.C. & Cunningham, D.L.B. (1984) Analysis of polycyclic aromatic hydrocarbons in diesel emissions using high performance liquid chromatography: a method development study. In: Cooke, M. & Dennis, A.J., eds, *Polynuclear Aromatic Hydrocarbons. 8th International Symposium: Mechanisms, Methods and Metabolism*, Columbus, OH, Battelle, pp. 379–393.

El Batawi M.A., Noweir M.H. Health problems resulting from prolonged exposure to air pollution in diesel bus garages. Ind. Health. 1966;4:1–10.

El-Shobokshy, M.S. (1985) Atmospheric lead pollution in areas of children's schools in the city of Riyadh. In: *Proceedings of the 78th Annual Meeting of the Air Pollution Control Association, Detroit, MI June 16–21*, 1985, Vol. 5, paper (85-59B.3), Pittsburg, PA, Air Pollution Control Association.

Fabia J., Thuy T.D. Occupation of father at time of birth of children dying of malignant dieseases. Br. J. prev. soc. Med. 1974;28:98–100. [PMC free article: PMC478845] [PubMed: 4853418]

Falk H.L. Conclusions of the Committee on Human Health: consequences of lead exposure from automobile emissions. Environ. Health Perspect. 1977;19:243–246. [PMC free article: PMC1637410] [PubMed: 71233]

Fishbein L. Environmental metallic carcinogens: an overview of exposure levels. J. Toxicol. environ. Health. 1976;2:77–109. [PubMed: 792462]

Fisher, A. & LeRoy, P. (1975) Particulate lead concentrations in Melbourne air. *Clean Air, August*, 56–57.

Flodin U., Fredriksson M., Persson B. Multiple myeloma and engine exhausts, fresh wood, and creosote: a case-referent study. Am. J. ind. Med. 1987;12:519–529. [PubMed: 2446496]

Flodin U., Fredriksson M., Persson B., Axelson O. Chronic lymphatic leukaemia and engine exhausts, fresh wood, and DDT: a case-referent study. Br. J. ind. Med. 1988;45:33–38. [PMC free article: PMC1007942] [PubMed: 2449239]

Fredga K., Dävring L., Sunner M., Bengtsson B.O., Elinder C.-G., Sigtryggsson P., Berlin M. Chromosome changes in workers (smokers and nonsmokers) exposed to automobile fuels and exhaust gases. Scand. J. Work Environ. Health. 1982;8:209–221. [PubMed: 6186020]

Froines J.R., Hinds W.C., Duffy R.M., Lafuente E.J., Liu W.-C.V. Exposure of firefighters to diesel emissions in fire stations. Am. ind. Hyg. Assoc. J. 1987;48:202–207. [PubMed: 2437785]

Fulford, J.E., Sakuma, T. & Lane, D.A. (1982) Real-time analysis of exhaust gases using triple quadrupole mass spectrometry. In: Cooke, M., Dennis, A.J. & Fisher, G.L., eds, *Polynuclear Aromatic Hydrocarbons, 6th International Symposium: Physical and Biological Chemistry*, Columbus, OH, Battelle, pp. 297–303.

Gaddo, P., Settis, M. & Giacomelli, L. (1984) *Artifact formation during diesel particulate collection*. In: Cooke, M. & Dennis, A.J., eds, *Polynuclear Aromatic Hydrocarbons, 8th International Symposium: Mechanisms, Methods and Metabolism*, Columbus, OH, Battelle, pp. 437–449.

Gamble J., Jones W., Hudak J. An epidemiological study of salt miners in diesel and nondiesel mines. Am. J. ind. Med. 1983;4:435–458. [PubMed: 6601909]

Gamble J., Jones W., Minshall S. Epidemiological-environmental study of diesel bus garage workers: acute effects of NO_2 and respirable particulate on the respiratory system. Environ. Res. 1987a;42:201–214. [PubMed: 2433131]

Gamble J., Jones W., Minshall S. Epidemiological-environmental study of diesel bus garage workers: chronic effects of diesel exhaust on the respiratory system. Environ. Res. 1987b;44:6–17. [PubMed: 2443345]

Garg B.D. Histologic quantitation of macrophage aggregates in the lungs of diesel exhaust exposed rats. Acta stereol. 1983;2(I):235–238.

Garland F.C., Gorham E.D., Garland C.F., Ducatman A.M. Testicular cancer in US Navy personnel. Am. J. Epidemiol. 1988;127:411–414. [PubMed: 3337092]

Garshick E., Schenker M.B., Muñoz A., Segal M., Smith T.J., Woskie S.R., Hammond K.S., Speizer F.E. A case-control study of lung cancer and diesel exhaust exposure in railroad workers. Am. Rev. respir. Dis. 1987;135:1242–1248. [PubMed: 3592400]

Garshick E., Schenker M.B., Muñoz A., Segal M., Smith T.J., Woskie S.R., Hammond S.K., Speizer F.E. A retrospective cohort study of lung cancer and diesel exhaust exposure in railroad workers. Am. Rev. respir. Dis. 1988;137:820–825. [PubMed: 3354987]

Gérin M., Siemiatycki J., Kemper H., Bégin D. Obtaining occupational exposure histories in epidemiologic case-control studies. J. occup. Med. 1985;27:420–426. [PubMed: 4020500]

Gibson, T.L., Ricci, A.I. & Williams, R.L. (1981) Measurement of polynuclear aromatic hydrocarbons, their derivatives, and their reactivity in diesel automobile exhaust. In: Cooke, M. & Dennis, A.J., eds, *Polynuclear Aromatic Hydrocarbons, 5th International Symposium: Chemical Analysis and Biological Fate*, Columbus, OH, Battelle, pp.

707–717.

Gillespie, J.R. (1980) Review of the cardiovascular and pulmonary function studies on beagles exposed for 68 months to auto exhaust and other air pollutants. In: Stara, J.F., Dungworth, D.L., Orthoefer, J.G. & Tyler, W.S., eds, *Long-term Effects of Air Pollutants: in Canine Species* (*EPA-600/8-80-014*), Washington DC, US Environmental Protection Agency, pp. 115–148.

Goff E.U., Coombs J.R., Fine D.H., Baines T.M. Determination of *N*-nitrosamines from diesel engine crankcase emissions. Anal. Chem. 1980;52:1833–1836.

Gold E.B., Diener M.D., Szklo M. Parental occupations and cancer in children. A case-control study and review of the methodologic issues. J. occup. Med. 1982;24:578–584. [PubMed: 6750059]

Gordon R.J. Distribution of airborne polycyclic aromatic hydrocarbons throughout Los Angeles. Environ. Sci. Technol. 1976;10:370–373.

Göthe C.-J., Fristedt B., Sundell L., Kolmodin B., Ehrner-Samuel H., Göthe K. Carbon monoxide hazard in city traffic. An examination of traffic policemen in three Swedish towns. Arch. environ. Health. 1969;19:310–314. [PubMed: 4185330]

Green F.H.Y., Boyd R.L., Danner-Rabovsky J., Fisher M.J., Moorman W.J., Ong T.-M., Tucker J., Vallyathan V., Whong W.-Z., Zoldak J., Lewis T. Inhalation studies of diesel exhaust and coal dust in rats. Scand. J. Work Environ. Health. 1983;9:181–188. [PubMed: 6196842]

Griest, W.H. & Caton, J.E. (1983) Extraction of polycyclic aromatic hydrocarbons for quantitative analysis. In: Björseth, A., ed., *Handbook of Polycyclic Aromatic Hydrocarbons*, New York, Marcel Dekker, pp. 95–148.

Griffis L.C., Wolff R.K., Henderson R.F., Griffith W.C., Mokler B.V., McClellan R.O. Clearance of diesel soot particles from rat lung after a subchronic diesel exhaust exposure. Fundam. appl. Toxicol. 1983;3:99–103. [PubMed: 6192034]

Grimmer G., Böhnke H. Determination of polycyclic aromatic hydrocarbons in automobile exhaust and air dust by capillary-gas-chromatography (Gen). Z. anal Chem. 1972;261:310–314.

Grimmer C., Jacob J. Recommended method for a thin-layer chromatographic screening method for the determination of benzo(a)pyrene in smoked food. Pure appl. Chem. 1987;59:1735–1738.

Grimmer G., Hildebrandt A., Böhnke H. Investigations on the carcinogenic burden by air pollution in man. II. Sampling and analysis of polycyclic aromatic hydrocarbons in automobile exhaust gas. 1. Optimization of the collecting arrangement. Zbl Bakt. Hyg., I. Abt. Orig. B. 1973a;158:22–34. [PubMed: 4130670]

Grimmer G., Hildebrandt A., Böhnke H. Investigations on the carcinogenic burden by air pollution in man. III. Sampling and analytics of polycyclic aromatic hydrocarbons in automobile exhaust gas. 2. Enrichment of the PNA and separation of the mixture of all PNA. Zbl. Bakt. Hyg., I. Abt. Orig. B. 1973b;158:35–49. [PubMed: 4130671]

Grimmer G., Böhnke H., Glaser A. Investigation on the carcinogenic burden by air pollution in man. XV. Polycyclic aromatic hydrocarbons in automobile exhaust gas — an inventory. Zbl. Bakt. Hyg., I. Abt. Orig. B. 1977;164:218–234. [PubMed: 70130]

Grimmer G., Naujack K.-W., Schneider D. Comparison of the profiles of polycyclic aromatic hydrocarbons in different areas of a city by glass-capillary-gas-chromatography in the nanogram-range. Int. J. environ. anal. Chem. 1981;10:265–276.

Grimmer G., Naujack K.-W., Schneider D. Profile analysis of polycyclic aromatic hydrocarbons by glass capillary gas chromatography in atmospheric suspended particulate matter in the nanogram range collecting 10 m^3 of air. Fresenius Z. anal Chem. 1982;311:475–484.

Grimmer G., Brune H., Deutsch-Wenzel R., Naujack K.-W., Misfeld J., Timm J. On the contribution of polycyclic aromatic hydrocarbons to the carcinogenic impact of automobile exhaust condensate evaluated by local application onto mouse skin. Cancer Lett. 1983a;21:105–113. [PubMed: 6196104]

Grimmer G., Naujack K.-W., Dettbarn G., Brune H., Deutsch-Wenzel R., Misfeld J. Characterization of polycyclic aromatic hydrocarbons as essential carcinogenic constituents of coal combustion and automobile exhaust using mouse-skin painting as a carcinogen-specific detector. Toxicol environ. Chem. 1983b;6:97–107.

Grimmer G., Brune H., Deutsch-Wenzel R., Dettbarn G., Misfeld J. Contribution of polycyclic aromatic hydrocarbons to the carcinogenic impact of gasoline engine exhaust condensate evaluated by implantation into the lungs of rats. J. natl Cancer Inst. 1984;72:733–739. [PubMed: 6199545]

Grimmer G., Brune H., Deutsch-Wenzel R., Dettbarn G., Jacob J., Naujack K.-W., Mohr U., Ernst H. Contribution of polycyclic aromatic hydrocarbons and nitro-derivatives to the carcinogenic impact of diesel engine exhaust condensate evaluated by implantation into the lungs of rats. Cancer Lett. 1987;37:173–180. [PubMed: 2445467]

Grimmer, G., Jacob, J., Dettbarn, G. & Naujack, K.-W. (1988) Effect of the pH-value of diesel exhaust on the amount of filter-collected nitro-PAH. In: Cooke, M. & Dennis, A.J., eds, *Polynuclear Aromatic Hydrocarbons, 10th International Symposium: A Decade of Progress*, Columbus, OH, Battelle, pp. 341–351.

Grosjean D. Formaldehyde and other carbonyls in Los Angeles ambient air. Environ. Sci. Technol. 1982;16:254–262. [PubMed: 22257249]

Gross K.B. Pulmonary function testing of animals chronically exposed to diluted diesel exhaust. J. appl. Toxicol. 1981;1:116–123. [PubMed: 6206110]

Guerrero R.R., Rounds D.E., Orthoefer J. Genotoxicity of Syrian hamster lung cells treated *in vivo* with diesel exhaust particulates. Environ. int. 1981;5:445–454.

Gustafsson L., Wall S., Larsson L.-G., Skog B. Mortality and cancer incidence among Swedish dock workers — a retrospective cohort study. Scand. J. Work Environ. Health. 1986;12:22–26. [PubMed: 3961438]

Gutwein E.E., Landolt R.R., Brenchley D.L. Barium retention in rats exposed to combustion products from diesel fuel containing a barium-based antismoke additive. J. Air Pollut. Control Assoc. 1974;24:40–43. [PubMed: 4131576]

Hadnagy W., Seemayer N.H. Induction of C-type metaphases and aneuploidy incultures of V79 cells exposed to extract of automobile exhaust particulates. Mutagenesis. 1986;1:445–448. [PubMed: 2457784]

Hagberg, M., Kolmodin-Hedman, B., Lindahl, R., Nilsson, C.-A. & Norström, Å. (1983)

Sampling and Analysis of Chain Saw Exhaust. III. Lung Function, Carboxyhaemoglobin and Complaints among Chain Saw Operators after Exposure to Exhaust (Swed.) (*Arbete och Hälsa 1983:7*), Solna, Arbetarskyddsstyrelsen, pp. 75–104.

Hahon N., Booth J.A., Green F., Lewis T.R. Influenza virus infection in mice after exposure to coal dust and diesel engine emissions. Environ. Res. 1985;37:44–60. [PubMed: 2581774]

Hakulinen T., Salonen T., Teppo L. Cancer in the offspring of fathers in hydrocarbon-related occupations. Br. J. prev. soc. Med. 1976;30:138–140. [PMC free article: PMC478952] [PubMed: 953378]

Hall N.E.L., Wynder E.L. Diesel exhaust exposure and lung cancer: a case-control study. Environ. Res. 1984;34:77–86. [PubMed: 6202502]

Hallock M., Smith T.S., Hammond K., Beck B., Brain J.D. A new technique for collecting ambient diesel particles for bioassays. Am. ind. Hyg. Assoc. J. 1987;48:487–493. [PubMed: 2438921]

Hamming W.J., MacPhee R.D. Relationship of nitrogen oxides in auto exhaust to eye irritation — further results of chamber studies. Atmos. Environ. 1967;1:577–584. [PubMed: 4168649]

Hammond, S.K., Smith, T.J., Woskie, S., Schenker, M.B. & Speizer, F.E. (1984) Characterization of diesel exhaust exposures for a mortality study. In: Cooke, M. & Dennis, A.J., eds, *Polynuclear Aromatic Hydrocarbons, 8th International Symposium: Mechanisms, Methods and Metabolism*, Columbus, OH, Battelle, pp. 533–541.

Hampton C.V., Pierson W.R., Schuetzle D., Harvey T.M. Hydrocarbon gases emitted from vehicles on the road. 2. Determination of emission rates from diesel and spark-ignition vehicles. Environ. Sci. Technol. 1983;17:699–708. [PubMed: 22283124]

Handa T., Yamauchi T., Ohnishi M., Hisamatsu Y., Ishii T. Detection and average content levels of carcinogenic and mutagenic compounds from the particulates on diesel and gasoline engine mufflers. Environ. int. 1983;9:335–341.

Hare, C.T. & Baines, T.M. (1979) *Characterization of Particulate and Gaseous Emissions from Two Diesel Automobiles as Functions of Fuel and Driving Cycle* (*Technical Paper Series 790424*), Warrendale, PA, Society of Automotive Engineers.

Hare, C.T., Springer, K.J. & Bradow, R.L. (1979) *Fuel and Additive Effects on Diesel Particulate — Development and Demonstration of Methodology* (*SAE-paper No. 760130*), Warrendale, PA, Society of Automotive Engineers.

Harris G. W., Mackay G.I., Iguchi T., Schiff H.I., Schuetzle D. Measurement of NO_2 and HNO_3 in diesel exhaust gas by tunable diode laser absorption spectrometry. Environ. Sci. Technol. 1987;21:299–304. [PubMed: 22185110]

Harsch D.E., Rasmussen R. A. Identification of methyl bromide in urban air. Anal. Lett. 1977;10:1041–1047.

Häsänen E., Karlsson V., Leppämaki E., Juhula M. Benzene, toluene and xylene concentrations in car exhausts and in city air. Atmos. Environ. 1981;15:1755–1757.

Heidemann A., Miltenburger H.G. Investigations on the mutagenic activity of fractions from diesel exhaust particulate matter in mammalian cells *in vivo* and *in vitro* (Abstract No. 15). Mutat. Res. 1983;113:339.

Heino M., Ketola R., Mäkelä P., Mäkinen R., Niemelä R., Starck J., Partanen T. Work conditions and health of locomotive engineers. I. Noise, vibration, thermal climate, diesel exhaust constituents, ergonomics. Scand. J. Work Environ. Health. 1978;4(3):3–14. [PubMed: 734424]

Heinrich, U., Peters, L., Funcke, W., Pott, F., Mohr, U. & Stöber, W. (1982) Investigations of toxic and carcinogenic effects of diesel exhaust in long-term inhalation exposure of rodents. In: Lewtas, J., ed., *Toxico logical Effects of Emissions from Diesel Engines*, Amsterdam, Elsevier, pp. 225–242. [PubMed: 6176424]

Heinrich U., Muhle H., Takenaka S., Ernst E., Fuhst R., Mohr U., Pott F., Stöber W. Chronic effects on the respiratory tract of hamsters, mice and rats after long-term inhalation of high concentrations of filtered and unfiltered diesel engine emissions. J. appl. Toxicol. 1986a;6:383–395. [PubMed: 2433325]

Heinrich U., Pott F., Mohr U., Fuhst R., König J. Lung tumours in rats and mice after inhalation of PAH-rich emissions. Exp. Pathol. 1986b;29:29–34. [PubMed: 3699126]

Heinrich, U., Peters, L., Mohr, U., Bellmann, B., Fuhst, R., Ketkar, M.B., König, J., König, H. & Pott, F. (1986c) *Investigation of Subacute and Chronic Effects of Gasoline Engine Exhaust on Rodents* (Ger.) (*FAT Series No. 55*), Frankfurt/Maine, Forschungsvereinigung Automobiltechnik e.V.

Hemminki K., Saloniemi L., Salonen T., Partanen T., Vainio H. Childhood cancer and parental occupation in Finland. J. Epidemiol. Commun. Health. 1981;35:11–15. [PMC free article: PMC1052112] [PubMed: 7264527]

Henderson Y., Haggard H.W., Teague M.C., Prince A.L., Wunderlich R.M. Physiological effects of automobile exhaust gas and standards of ventilation for brief exposures. J. ind. Hyg. 1921;3:79–92. 137–146.

Henderson T.R., Sun J.D., Royer R.E., Clark C.R., Li A.P., Harvey T.M., Hunt D.H., Fulford J.E., Lovette A.M., Davidson W.R. Triple-quadrupole mass spectrometry studies of nitroaromatic emissions from different diesel engines. Environ. Sci. Technol. 1983;17:443–449. [PubMed: 22283161]

Henderson T.R., Sun J.D., Li A.P., Hanson R.L., Bechtold W.E., Harvey T.M., Shabanowitz J., Hunt D.F. GC/MS and MS/MS studies of diesel exhaust mutagenicity and emissions from chemically defined fuels. Environ. Sci. Technol. 1984;18:428–434. [PubMed: 22247944]

Heyder J., Gebhart J., Roth C., Scheuch G., Stahlhofen W. Diffusional transport of aerosol particles. J. Aerosol Sci. 1983;14:279–280.

Hinkle L.E. Jr. Automobile emissions in the perspective of human health: health benefits and social costs of pollution control. Bull. N. Y. Acad. Med. 1980;56:948–979. [PMC free article: PMC1808378] [PubMed: 6161666]

Hites, R.A., Yu, M.-L. & Thilly, W.G. (1981) Compounds associated with diesel exhaust particulates. In: Cooke, M. & Dennis, J.D., eds, *Polynuclear Aromatic Hydrocarbons, 5th International Symposium: Chemical Analysis and Biological Fate*, Columbus, OH, Battelle, pp. 455–466.

Hoar S.K., Hoover R. Truck driving and bladder cancer mortality in rural New England. J. natl Cancer Inst. 1985;74:771–774. [PubMed: 3857373]

Hobbs, J.R., Walter, R.A., Hard, T. & Devoe, D. (1977) *Train Generated Air Contaminants in the Train Crew's Working Environment* (*FRA/ORD-77/08: US NTIS PB265-355*), Springfield, VA, National Technical Information Service, US Department of Commerce.

Hoffman D.J., Campbell K.I. Embryotoxicity of irradiated and nonirradiated catalytic converter-treated automotive exhaust. J. Toxicol environ. Health. 1977;3:705–712. [PubMed: 73596]

Hoffman D.J., Campbell K.I. Embryotoxicity of irradiated and nonirradiated automotive exhaust and carbon monoxide. Environ. Res. 1978;15:100–107. [PubMed: 74331]

Hoffmann D., Wynder E.L. A study of air pollution carcinogenesis. II. The isolation and identification of polynuclear aromatic hydrocarbons from gasoline engine exhaust condensate. Cancer. 1962a;15:93–102. [PubMed: 13908122]

Hoffmann D., Wynder E.L. Analytical and biological studies on gasoline engine exhaust. Natl Cancer Inst. Monogr. 1962b;9:91–112. [PubMed: 13908123]

Hoffmann D., Theisz E., Wynder E.L. Studies on the carcinogenicity of gasoline exhaust. J. Air Pollut. Control Assoc. 1965;15:162–165. [PubMed: 14273615]

Holland, W.D. (1978) *Determination of Breathing Zone Concentrations of Contaminants from Emissions from Diesel Powered Vehicles in Underground Mines* (*BuMines OFR 24-80; US NTIS PB80-150766*), Washington DC, US Department of the Interior, Bureau of Mines.

Holmberg B., Ahlborg U. Consensus report: mutagenicity and carcinogenicity of car exhausts and coal combustion emissions. Environ. Health Perspect. 1983;47:1–30. [PMC free article: PMC1569414] [PubMed: 6186474]

Howard, P.H. & Durkin, P.R. (1974) *Benzene, Environmental Sources of Contamination, Ambient Levels, and Fate* (*EPA 560/5-75-005; US NTIS PB-244-139*), Washington DC, US Environmental Protection Agency.

Howe G.R., Lindsay J.P. A follow-up study of a ten-percent sample of the Canadian labor force. I. Cancer mortality in males, 1965–73. J. natl Cancer Inst. 1983;70:37–44. [PubMed: 6571919]

Howe G.R., Burch J.D., Miller A.B., Cook G.M., Estève J., Morrison B., Gordon P., Chambers L.W., Fodor G., Winsor G.M. Tobacco use, occupation, coffee, various nutrients, and bladder cancer. J. natl Cancer Inst. 1980;64:701–713. [PubMed: 6928984]

Howe G.R., Fraser D., Lindsay J., Presnal B., Yu S.Z. Cancer mortality (1965–77) in relation to diesel fume and coal exposure in a cohort of retired railway workers. J. natl Cancer Inst. 1983;70:1015–1019. [PubMed: 6574269]

Hueter F.G., Contner G.L., Busch K.A., Hinners R.G. Biological effects of atmospheres contaminated by auto exhaust. Arch. environ. Health. 1966;12:553–560. [PubMed: 4160294]

Huisingh, J.L., Bradow, R., Jungers, R., Claxton, L., Zweidinger, R., Tejada, S., Bumgarner, J., Duffield, F., Waters, M., Simmon, V.F., Hare, C., Rodriguez, C. &Snow, L. (1978) Application of bioassay to the characterization of diesel particle emissions. In: Waters, M.D., Nesnow, S., Huisingh, J.L., Sandhu, S.S. & Claxton, L., eds, *Application of Short-term Bioassays in the Fractionation and Analysis of Complex Environmental Mixtures*, New York, Plenum, pp. 381–418.

Huisingh, J.L., Coffin, D.L., Bradow, R., Claxton, L., Austin, A., Zweidinger, R., Walter, R., Sturm, J. & Jungers, R.J. (1981) Comparative mutagenicity of combustion emissions of a high quality no. 2 diesel fuel derived from shale oil and a petroleum derived no. 2 diesel fuel. In: Griest, W.H., Guerin, M.R. & Coffin, D.L., eds, *Health Effects Investigations of Oil Shale Development*, Ann Arbor, MI, Ann Arbor Science, pp. 201–207.

Hyde, D., Orthoefer, J.G., Dungworth, D., Tyler, W., Carter, R. & Lum, H. (1980) Morphometric and morphologic evaluation of pulmonary lesions in beagle dogs chronically exposed to high ambient levels of air pollutants. In: Stara, J.F., Dungworth, D.L., Orthoefer, J.G. &Tyler, W.S., eds, *Long-term Effects of Air Pollutants: in Canine Species* (*EPA-600/8-80-014*), Washington DC, US Environmental Protection Agency, pp. 195–227.

Hyde D.M., Plopper C.G., Weir A.J., Murnane R.D., Warren D.L., Last J.A., Pepelko W.E. Peribronchiolar fibrosis in lungs of cats chronically exposed to diesel exhaust. Lab. Invest. 1985;52:195–206. [PubMed: 2578585]

IARC (1980) *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*, Vol. 23, *Some Metals and Metallic Compounds*, Lyon, pp. 325–415. [PubMed: 7000667]

IARC (1982a) *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*, Vol. 29, *Some Industrial Chemicals and Dyestuffs*, Lyon, pp. 345–389. [PubMed: 6957387]

IARC (1982b) *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*, Vol. 29, *Some Industrial Chemicals and Dyestuffs*, Lyon, pp. 93–148. [PubMed: 6957390]

IARC (1983) *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*, Vol 32, *Polynuclear Aromatic Compounds, Part 1, Chemical, Environmental and Experimental Data*, Lyon. [PubMed: 6586639]

IARC (1984) *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*, Vol. 33, *Polynuclear Aromatic Compounds, Part 2, Carbon Blacks, Mineral Oils and Some Nitroarenes*, Lyon, pp. 171–222. [PubMed: 6590450]

IARC (1987a) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Suppl. 7, *Overall Evaluations of Carcinogenicity: An Updating of* IARC Monographs *Volumes 1 to 42*, Lyon. [PubMed: 3482203]

IARC (1987b) *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*, Vol. 42, *Silica and Some Silicates*, Lyon, pp. 39–143. [PubMed: 2824340]

IARC (1988) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Vol. 43, *Man-made Mineral Fibres and Radon*, Lyon, pp. 173–259. [PubMed: 3065210]

IARC (1989) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Vol. 45, *Occupational Exposures in Petroleum Refining; Crude Oil and Major Petroleum Fuels*, Lyon, pp. 159–201, 219–237. [PubMed: 2664246]

Iscovich J., Castelletto R., Estève J., Mu<oz N., Colanzi R., Coronel A., Deamezola I., Tassi V., Arslan A. Tobacco smoking, occupational exposure and bladder cancer in Argentina. Int. J. Cancer. 1987;40:734–740. [PubMed: 3692621]

Ishinishi, N., Kuwabara, N., Nagase, S., Suzuki, T., Ishiwata, S. & Kohno, T. (1986a) Long-term inhalation studies on effects of exhaust from heavy and light duty diesel engines on F344 rats. In: Ishinishi, N., Koizumi, A., McClellan, R.O. & Stöber, W., eds, *Carcinogenic and Mutagenic Effects of Diesel Engine Exhaust*, Amsterdam, Elsevier, pp. 329–348. [PubMed: 2435494]

Ishinishi, N., Koizumi, A., McClellan, R.O. & Stöber, W., eds (1986b) *Carcinogenic and Mutagenic Effects of Diesel Engine Exhaust*, Amsterdam, Elsevier.

Iwai, K., Udagawa, T., Yamagishi, M. & Yamada, H. (1986) Long-term inhalation studies of diesel exhaust on F344 SPF rats. Incidence of lung cancer and lymphoma. In: Ishinishi, N., Koizumi, A., McClellan, R.O. & Stöber, W., eds, *Carcinogenic and Mutagenic Effects of Diesel Engine Exhaust*, Amsterdam, Elsevier, pp. 349–360. [PubMed: 2435495]

Jacob, J. & Grimmer, G. (1979) Extraction and enrichment of polycyclic aromatic hydrocarbons (PAH) from environmental matter. In: Egan, H., Castegnaro, M., Bogovski, P., Kunte, H. & Walker, E.A., eds, *Environmental Carcinogens. Selected Methods of Analysis*, Vol. 3, *Analysis of Polycyclic Aromatic Hydrocarbons in Environmental Samples* (*IARC Scientific Publications No. 29*), Lyon, International Agency for Research on Cancer, pp. 79–89.

Janssen, O. (1976) *Experiences of Collaborative Studies for Analysis of PAH* (Ger.) (*Erdöl & Kohle, Erdgas, Petrochemie Compendium 1975/1976*), Leinfelden, Hernhaussen KG, pp. 624–638.

Jensen O.M., Wahrendorf J., Knudsen J.B., Sørensen B.L. The Copenhagen case-referent study on bladder cancer. Risks among drivers, painters and certain other occupations. Scand. J. Work Environ. Health. 1987;13:129–134. [PubMed: 3602967]

John W., Reischl G. Measurements of the filtration efficiencies of selected filter types. Atmos. Environ. 1978;12:2015–2019.

Johnson, B.L., Cohen, H.H., Struble, R., Setzer, J.V., Anger, W.K., Gutnik, B.D., McDonough, T. & Häuser, P. (1974) Field evaluation of carbon monoxide exposed toll collectors. In: *Behavioral Toxicology, Early Detection of Occupational Hazards* (*DHEW (NIOSH) Publ No. 74-126*), Cincinnati, OH, National Institute for Occupational Safety and Health, pp. 306–328.

Johnson, J. (1988) Automotive emissions. In: Watson, A.Y., Bates, R.R. & Kennedy, D., eds, *Air Pollution, the Automobile, and Public Health*, Washington DC, National Academy Press.

Johnson, R.L., Shah, J.J., Cary, R.A. & Huntzicker, J.J. (1981) An automated thermal-optical method for the analysis of carbonaceous aerosol. In: Macias, E.S. & Hopke, P.K., eds, *Atmospheric Aerosol: Source/Air Quality Relationships* (*ACS Symposium Series No. 167*), Washington CD, American Chemical Society, pp. 223–233.

Jones E., Richold M., May J.H., Saje A. The assessment of the mutagenic potential of vehicle engine exhaust in the Ames *Salmonella* assay using a direct exposure method. Mutat. Res. 1985;155:35–40. [PubMed: 2578608]

Jones P.W., Giammar R.D., Strup P.E., Stanford T.B. Efficient collection of polycyclic organic compounds from combustion effluents. Environ. Sci. Technol. 1976;10:806–810. [PubMed: 22217057]

Jörgensen H., Svensson Å. Studies on pulmonary function and respiratory tract symptoms of workers in an iron ore mine where diesel trucks are used underground. J. occup. Med. 1970;12:348–354. [PubMed: 5482050]

Kantor A.F., McCrea Curnen M.G., Meigs J.W., Flannery J.T. Occupations of fathers of patients with Wilms's tumour. J. Epidemiol Commun. Health. 1979;33:253–256. [PMC free article: PMC1051966] [PubMed: 231629]

Kaplan I. Relationship of noxious gases to carcinoma of the lung in railroad workers. J. Am. med. Assoc. 1959;171:97–101. [PubMed: 14404393]

Kaplan, H.L., MacKenzie, W.F., Springer, K.J., Schreck, R.M. & Vostal, J.J. (1982) A subchronic study of the effects of exposure of three species of rodents to diesel exhaust. In: Lewtas, J., ed., *Toxicological Effects of Emissions from Diesel Engines*, Amsterdam, Elsevier, pp. 161–182. [PubMed: 6176421]

Karagianes M.T., Palmer R.F., Busch R.H. Effects of inhaled diesel emissions and coal dust in rats. Am. ind. Hyg. Assoc. J. 1981;42:382–391. [PubMed: 6164283]

Kawabata, Y., Iwai, K., Udagawa, T., Tukagoshi, K. & Higuchi, K. (1986) Effects of diesel soot on unscheduled DNA synthesis of tracheal epithelium and lung tumor formation. In: Ishinishi, N., Koizumi, A., McClellan, R.O. & Stöber, W., eds, *Carcinogenic and Mutagenic Effects of Diesel Engine Exhaust*, Amsterdam, Elsevier, pp. 213–222.

King L.C., Kohan M.J., Austin A.C., Claxton L.D., Lewtas Huisingh J. Evaluation of the release of mutagens from diesel particles in the presence of physiological fluids. Environ. Mutagenesis. 1981;3:109–121. [PubMed: 6165576]

King L.C., Loud K., Tejada S.B., Kohan M.J., Lewtas J. Evaluation of the release of mutagens and 1-nitropyrene from diesel particles in the presence of lung macrophages in culture. Environ. Mutagenesis. 1983;5:577–588. [PubMed: 6347680]

Köhler M., Eichhoff H.-J. Quick method for determination of aromatic hydrocarbons in air dust (Ger.). Z. anal. Chem. 1967;232:401–409.

Kotin P., Falk H.I., Thomas M. Aromatic hydrocarbons. II. Presence in the particulate phase of gasoline-engine exhausts and the carcinogenicity of exhaust extracts. Arch. ind. Hyg. occup. Med. 1954;9:164–177. [PubMed: 13113749]

Kotin P., Falk H.L., Thomas M. Aromatic hydrocarbons. III. Presence in the particulate phase of diesel-engine exhausts and the carcinogenicity of exhaust extracts. Arch. ind. Health. 1955;11:113–120. [PubMed: 13227636]

Kraft, J. & Lies, K.-H. (1981) *Polycyclic Aromatic Hydrocarbons in the Exhaust of Gasoline and Diesel Vehicles* (*Technical Paper Series No. 810082*), Warrendale, PA, Society of Automotive Engineers.

Kronoveter, K.J. (1976) *Industrial Hygiene Surveys at US Border Crossing Stations During August 1973–June 1974* (*DHEW(NIOSH) Publ No*. 75–135), Cincinnati, OH, National Institute for Occupational Safety and Health.

Kunitake, E., Shimamura, K., Katayama, H., Takemoto, K., Yamamoto, A., Hisanaga, A., Ohyama, S. & Ishinishi, N. (1986) Studies concerning carcinogenesis of diesel particulate extracts following intratracheal instillation, subcutaneous injection, or skin application. In: Ishinishi, N., Koizumi, A., McClellan, R.O. & Stöber, W., eds, *Carcinogenic and Mutagenic Effects of Diesel Engine Exhaust*, Amsterdam, Elsevier, pp. 235–252. [PubMed: 2435490]

Künstler K. Failure to induce tumors by intratracheal instillation of automobile exhaust condensate and fractions thereof in Syrian golden hamsters. Cancer Lett. 1983;18:105–108.

[PubMed: 6186363]

Kunte, H. (1979) Separation, detection and identification of polycyclic aromatic hydrocarbons. In: Egan, H., Castegnaro, M., Bogovski, P., Kunte, H. & Walker, E.A., eds, *Environmental Carcinogens. Selected Methods of Analysis*, Vol. 3, *Analysis of Polycyclic Aromatic Hydrocarbons in Environmental Samples* (*IARC Scientific Publications No. 29*), Lyon, International Agency for Research on Cancer, pp. 91–99.

Kwa S.-L., Fine L.J. The association between parental occupation and childhood malignancy. J. occup. Med. 1980;22:792–794. [PubMed: 7218055]

Lahmann, E. (1969) *Untersuchungen über Luftverunreinigungen durch den Kraftverkehr* [Air Pollution by Automobiles] (*Schriftenreihe des Vereins für Wasser-, Boden- und Luft hygiene No. 28*), Stuttgart, Gustav Fischer Verlag.

Lang, J.M., Snow, L., Carlson, R., Black, F., Zweidinger, R. &Tejada, S. (1981) *Characterization of Particulate Emissions from In-use Gasoline-fuelled Motor Vehicles* (*Technical Paper Series No. 811186*), Warrendale, PA, Society of Automotive Engineers.

Larsen R.I., Konopinski V.J. Sumner Tunnel air quality. Arch. environ. Health. 1962;5:597–608.

Lassiter, D.V. & Milby, T.H. (1978) *Health Effects of Diesel Exhaust Emissions: A Comprehensive Literature Review, Evaluation and Research Gaps Analysis* (*US NTIS PB-282-795*), Washington DC, American Mining Congress.

Lawter, J.R. & Kendall, D.A. (1977) *Effects of Diesel Engine Emissions on Coal Mine Air Quality* (*BuMines OFR 46–78; US NTIS PB-282-377*), Washington DC, US Department of the Interior, Bureau of Mines.

Laxen D.P.H., Noordally E. Nitrogen dioxide distribution in street canyons. Atmos. Environ. 1987;21:1899–1903.

Lee, F.S.-C. & Schuetzle, D. (1983) Sampling, extraction and analysis of polycyclic aromatic hydrocarbons from internal combustion engines. In: Bjørseth, A., ed., *Handbook of Polycyclic Aromatic Hydrocarbons*, New York, Marcel Dekker, pp. 27–94.

Lee S.D., Malanchuk M., Finelli V.N. Biological effects of auto emissions. I. Exhaust from engine with and without catalytic converter. J. Toxicol., environ. Health. 1976;1:705–712. [PubMed: 58066]

Lee, F.S.-C., Prater, T.J. & Ferris, F. (1979) PAH emissions from a stratified-charge vehicle with and without oxidation catalyst: sampling and analysis evaluation. In: Jones, P.W. & Leber, P., eds, *Polynuclear Aromatic Hydrocarbons, 3rd International Symposium: Chemistry and Biology. Carcinogenesis and Mutagenesis*, Ann Arbor, MI, Ann Arbor Science, pp. 83–110.

Lee, F.S.-C., Pierson, W.R. & Ezike, J. (1980) The problem of PAH degradation during filter collection of airborne particulates. An evaluation of several commonly used filter media. In: Björseth, A. & Dennis, A.J., eds, *Polynuclear Aromatic Hydrocarbons, 4th International Symposium: Chemistry and Biological Effects*, Columbus, OH, Battelle, pp. 543–563.

Lee I.P., Suzuki K., Lee S.D., Dixon R.L. Aryl hydrocarbon hydroxylase induction in rat lung, liver and male reproductive organs following inhalation exposure to diesel emission. Toxicol. appl. Pharmacol. 1980;52:181–184. [PubMed: 6153820]

Lee P.S., Chan T.L., Hering W.E. Long-term clearance of inhaled diesel exhaust particles in rodents. J. Toxicol. environ. Health. 1983;12:801–813. [PubMed: 6199508]

Lee P.S., Gorski R.A., Hering W.E., Chan T.L. Lung clearance of inhaled particles after exposure to carbon black generated from a resuspension system. Environ. Res. 1987;43:364–373. [PubMed: 2440669]

Leichnitz, K. (1986) *Gefahrstoff-Analytik* [Dangerous Substances Analysis], Landsberg, Ecomed Verlagsgesellschaft mbH.

Lerchen M.L., Wiggins C.L., Samet J.M. Lung cancer and occupation in New Mexico. J. natl Cancer Inst. 1987;79:639–645. [PubMed: 3477658]

Levine, S.P., Skewes, L.M., Abrams, L.D. & Palmer, A.G., III (1982) High performance semi-preparative liquid chromatography and liquid chromatography-mass spectrometry of diesel engine emission particulate extracts. In: Cooke, M., Dennis, A.J. & Fisher, G.L., eds, *Polynuclear Aromatic Hydrocarbons, 6th International Symposium: Physical and Biological Chemistry*, Columbus, OH, Battelle, pp. 439–448.

Lewis, T.R. & Moorman, W.J. (1980) Pulmonary and cardiovascular physiology studies during exposure. In: Stara, J.F., Dungworth, D.L., Orthoefer, J.G. & Tyler, W.S., eds, *Long-term Effects of Air Pollutants: in Canine Species* (*EPA-600/8-80-014*), Washington DC, US Environmental Protection Agency, pp. 97–108.

Lewis T.R., Hueter F.G., Busch K.A. Irradiated automobile exhaust. Its effects on the reproduction in mice. Arch. environ. Health. 1967;15:26–35. [PubMed: 4143658]

Lewis T.R., Moorman W.J., Yang Y.-Y., Stara J.F. Long-term exposure to auto exhaust and other pollutant mixtures. Effects on pulmonary funciton in the beagle. Arch. environ. Health. 1974;29:102–106. [PubMed: 4134859]

Lewis, T.R., Green, F.H.Y., Moorman, W.J., Burg, J.A.R. & Lynch, D.W. (1986) A chronic inhalation toxicity study of diesel engine emissions and coal dust, alone and combined. In: Ishinishi, N., Koizumi, A., McClellan, R.O. & Stöber, W., eds, *Carcinogenic and Mutagenic Effects of Diesel Engine Exhaust*, Amsterdam, Elsevier, pp. 361–380.

Lewis T.R., Green F.H.Y., Moorman W.J., Burg J.R., Lynch D.W. A chronic inhalation toxicity study of diesel engine emissions and coal dust, alone and combined. J. Am. Coll. Toxicol. 1989;8:345–375. [PubMed: 2435496]

Lewtas, J. (1982) *Mutagenic activity of diesel emissions*. In: Lewtas, J., ed., *Toxicological Effects of Emissions from Diesel Engines*, Amsterdam, Elsevier, pp. 243–264.

Lewtas J. Evaluation of the mutagenicity and carcinogenicity of motor vehicle emissions in short-term bioassays. Environ. Health Perspect. 1983;47:141–152. [PMC free article: PMC1569411] [PubMed: 6186475]

Lewtas, J. (1985) Combustion emissions: characterization and comparison of their mutagenic and carcinogenic activity. In: Stich, H.F., ed., *Carcinogens and Mutagens in the Environment*, Vol. V, *The Workplace: Sources of Carcinogens*, Boca Raton, FL, CRC Press, pp. 59–74.

Lewtas, J. & Williams, K. (1986) A retrospective view of the value of short-term genetic bioassays in predicting the chronic effects of diesel soot. In: Ishinishi, N., Koizumi, A., McClellan, R.O. & Stöber, W., eds, *Carcinogenicity and Mutagenic Effects of Diesel Engine Exhaust*, Amsterdam, Elsevier, pp. 119–140. [PubMed: 2435484]

Li A. P., Royer R.E. Diesel-exhaust-particle extract enhancement of chemical-induced mutagenesis in cultured Chinese hamster ovary cells: possible interaction of diesel exhaust with environmental carcinogens. Mutat. Res. 1982;103:349–355. [PubMed: 6178024]

Liber, H.L., Andon, B.M., Hites, R.A. & Thilly, W.G. (1980) Diesel soot: mutation measurements in bacterial and human cells. In: Pepelko, W.E., Danner, R.M. & Clarke, N.A., eds, *Health Effects of Diesel Engine Emissions* (*EPA-600/9-80-05 7a*), Cincinnati, OH, US Environmental Protection Agency, pp. 404–412.

Liber H.I., Andon B.M., Hites R.A., Thilly W.G. Diesel soot: mutation measurements in bacterial and human cells. Environ. int. 1981;5:281–284.

Liberti A., Ciccioli P., Cecinato A., Brancaleoni E., Di Palo C. Determination of nitrated-polyaromatic hydrocarbons (nitro-PAHs) in environmental samples by high resolution chromatographic techniques. J. high Resolut. Chromatogr. Chromatogr. Commun. 1984;7:389–397.

Lies, K.-H., Härtung, A., Postulka, A., Gring, H. & Schuetzle, J. (1986) Composition of diesel exhaust with particular reference to particle bound organics including formation of artifacts. In: Ishinishi, N., Koizumi, A., McClellan, R.O. & Stöber, W., eds, *Carcinogenic and Mutagenic Effects of Diesel Engine Exhaust*, Amsterdam, Elsevier, pp. 65–82.

Lindner W., Posch W., Wolfbeis O.S., Tritthart P. Analysis of nitro-PAHs in diesel exhaust particulate extracts with multicolumn HPLC. Chromatographia. 1985;20:213–218.

Lioy P.J., Daisey J.M. Airborne toxic elements and organic substances. Environ. Sci. Technol. 1986;20:8–14. [PubMed: 22300144]

Lockard J.M., Kaur P., Lee-Stephens C., Sabharwal P.S., Pereira M. A., McMillan L., Mattox J. Induction of sister-chromatid exchanges in human lymphocytes by extracts of particulate emissions from a diesel engine. Mutat. Res. 1982;104:355–359. [PubMed: 6287249]

Löfroth, G. (1981a) Comparison of the mutagenic activity in carbon particulate matter and in diesel and gasoline engine exhaust. In: Waters, M.D., Sandhu, S.S., Lewtas Huisingh, J., Claxton, L. & Nesnow, S., eds, *Short-term Bioassays in the Analysis of Complex Environmental Mixtures, II*, New York, Plenum, pp. 319–336.

Löfroth G. *Salmonella/*microsome mutagenicity assays of exhaust from diesel and gasoline powered motor vehicles. Environ. int. 1981b;5:255–261.

Malanchuk, M. (1980) Exposure chamber atmospheres. Sampling and analysis. In: Stara, J.F., Dungworth, D.L., Orthoefer, J.G. & Tyler, W.S., eds, *Long-term Effects of Air Pollutants: in Canine Species* (*EPA-6008-80-014*), Washington DC, US Environmental Protection Agency, pp. 41–54.

Malker, H. & Weiner, J. (1984) *Cancer-miljöregistret. Exempelpå Utnyuttjande av Registerepidemiologi inom Arbetsmiljöområdet* [The Cancer-Environment Registry 1961–1973. Examples of the Use of Register Epidemiology in Studies in the Work Environment] (*Arbete och Hälsa 1984:9*), Solna, Arbetarskyddsstyrelsen.

Manabe Y., Kinouchi T., Ohnishi Y. Identification and quantification of highly mutagenic nitroacetoxypyrenes and nitrohydroxypyrenes in diesel-exhaust particles. Mutat. Res. 1985;158:3–18. [PubMed: 2413353]

Maruna R.F.L., Maruna H. Lead load in taxi drivers characterized by delta aminolaevulinic acid in the urine (Ger.). Wien. med. Wochenschr. 1975;125:615–620. [PubMed: 58483]

Massad E., Saldiva P.H.N., Saldiva C.D., Pires do Rio Caldeira M., Cardoso L.M.N., Méri Steves de Morais A., Calheiros D.F., da Silva R., Böhm G.M. Toxicity of prolonged exposure to ethanol and gasoline autoengine exhaust gases. Environ. Res. 1986;40:479–486. [PubMed: 2426102]

Matsushita, H., Goto, S., Endo, O., Lee, J.-H. & Kawai, A. (1986) Mutagenicity of diesel exhaust and related chemicals. In: Ishinishi, N., Koizumi, A., McClellan, R.O. & Stöber, W., eds, *Carcinogenic and Mutagenic Effects of Diesel Engine Exhaust*, Amsterdam, Elsevier, pp. 103–118.

Mauderly, J.L., Jones, R.K., McClellan, R.O., Henderson, R.F. & Griffith, W.C. (1986) Carcinogenicity of diesel exhaust inhaled chronically by rats. In: Ishinishi, N., Koizumi, A., McClellan, R.O. & Stöber, W., eds, *Carcinogenic and Mutagenic Effects of Diesel Engine Exhaust*, Amsterdam, Elsevier, pp. 397–409.

Mauderly J.L., Jones R.K., Griffith W.C., Henderson R.F., McClellan R.O. Diesel exhaust is a pulmonary carcinogen in rats exposed chronically by inhalation. Fundam. appl. Toxicol. 1987;9:208–221. [PubMed: 2443412]

Maziarka S., Strusiński A., Wyszyńska H. Lead compounds in the atmosphere of Polish towns (Pol.). Roczn. Panstw. Zakl. Hig. 1971;22:399–406. [PubMed: 5139098]

McClellan R.O. Health effects of diesel exhaust: a case study in risk assessment. Am. ind. Hyg. Assoc. J. 1986;47:1–13. [PubMed: 2418672]

McClellan, R.O., Brooks, A.L., Cuddihy, R.G., Jones, R.K., Mauderly, J.L. & Wolff, R.K. (1982) Inhalation toxicology of diesel exhaust particles. In: Lewtas, J., ed., *Toxicological Effects of Emissions from Diesel Engines*, Amsterdam, Elsevier, pp. 99–120.

McCormick, J.J., Zator, R.M., DaGue, B.B. & Maher, V.M. (1980) Studies on the effects of diesel particulate on normal and xeroderma pigmentosum cells. In: Pepelko, W.E., Danner, R.M. & Clarke, N.A., eds, *Health Effects of Diesel Engine Emissions* (*EPA-60019-80-057a*), Cincinnati, OH, US Environmental Protection Agency, pp. 413–415.

Meiss R., Robenek H., Schubert M., Themann H., Heinrich U. Ultrastructural alterations in the livers of golden hamsters following experimental chronic inhalation of diluted diesel exhaust emission. Int. Arch. occup. environ. Health. 1981;48:147–157. [PubMed: 6167522]

Menck H.R., Henderson B.E. Occupational differences in rates of lung cancer. J. occup. Med. 1976;18:797–801. [PubMed: 993873]

Mentnech M.S., Lewis D.M., Olenchock S.A., Mull J.C., Koller W. A. Effects of coal dust and diesel on immune competence in rats. J. Toxicol environ. Health. 1984;13:31–41. [PubMed: 6201622]

Metz, N., Lies, K.-H. & Hartung, A. (1984) Polynuclear aromatic hydrocarbons in diesel soot: round robin test results from eight European laboratories of the Committee of Common Market Automobile Constructors (CCMC). In: Cooke, M. & Dennis, A. J., eds, *Polynuclear Aromatic Hydrocarbons, 8th International Symposium: Mechanisms, Methods and Metabolism*, Columbus, OH, Battelle, pp. 899–912.

Milham, S., Jr, (1983) *Occupational Mortality in Washington State 1950–1979* (*DHHS (NIOSH*) *Publ. No. 83–116*), Cincinnati, OH, US Department of Health and Human

Services.

Mitchell A.D., Evans E.L., Jotz M.M., Riccio E.S., Mortelmans K.E., Simmon V.F. Mutagenic and carcinogenic potency of extracts of diesel and related environmental emissions: in vitro mutagenesis and DNA damage. Environ. int. 1981;5:393–401.

Mohr U., Reznik-Schüller H., Reznik G., Grimmer G., Misfeld J. Investigations on the carcinogenic burden by air pollution in man. XIV. Effects of automobile exhaust condensate on the Syrian golden hamster lung. Zbl. Bakt. Hyg., I. Abt. Orig. B. 1976;163:425–432. [PubMed: 65878]

Moore, W., Orthoefer, J., Burkart, J. & Malanchuk, M. (1978) Preliminary findings of the deposition and retention of automotive diesel particulate in rat lungs. In: *Proceedings of the 71st Annual Meeting of the Air Pollution Control Association*, Vol. 3, Pittsburg, PA, Air Pollution Control Association, pp. 3–15.

Moorman W.J., Clark J.C., Pepelko W.E., Mattox J. Pulmonary function responses in cats following long-term exposure to diesel exhaust. J. appl. Toxicol. 1985;5:301–305. [PubMed: 2414357]

Morandi M., Eisenbud M. Carbon monoxide exposure in New York City: a historical overview. Bull. N.Y. Acad. Med. 1980;56:817–828. [PMC free article: PMC1808364] [PubMed: 6936059]

Morgan A., Holmes A. The fate of lead in petrol-engine exhaust particulates inhaled by the rat. Environ. Res. 1978;15:44–56. [PubMed: 74332]

Morimoto, K., Kitamura, M., Kondo, H. & Koizumi, A. (1986) Genotoxicity of diesel exhaust emissions in a battery of in-vitro short-term and in-vivo bioassays. In: Ishinishi, N., Koizumi, A., McClellan, R.O. & Stöber, W., eds, *Carcinogenic and Mutagenic Effects of Diesel Engine Exhaust*, Amsterdam, Elsevier, pp. 85–101.

The Motor Vehicle Manufacturers Association of the United States and The Engine Manufacturers Association (1986) *Analysis of the Environmental Protection Agency's 'Diesel Particulate Study' and a Diesel Particulate Emission Projection*, Detroit, MI.

Nakagawa R., Kitamori S., Horikawa K., Nakashima K., Tokiwa H. Identification of dinitropyrenes in diesel-exhaust particles: their probable presence as the major mutagens. Mutat. Res. 1983;124:201–211. [PubMed: 6197647]

Nathanson B., Nudelman H. Ambient lead concentrations in New York City and their health implications. Bull. N. Y. Acad. Med. 1980;56:866–875. [PMC free article: PMC1808369] [PubMed: 6161662]

National Air Pollution Control Administration (1970) *Air Quality Criteria for Hydrocarbons* (*AP-64; US NTIS PB190-489*), Washington DC, US Department of Health, Education, and Welfare.

National Research Council (1972a) *Biological Effects of Atmospheric Pollutants: Particulate Polycyclic Organic Matter*, Washington DC, National Academy of Sciences.

National Research Council (1972b) *Biological Effects of Atmospheric Pollutants: Lead*, Washington DC, National Academy of Sciences.

National Research Council (1977a) *Medical and Biological Effects of Environmental Pollutants: Carbon Monoxide*, Washington DC, National Academy of Sciences.

National Research Council (1977b) *Medical and Biological Effects of Environmental Pollutants: Nitrogen Oxides*, Washington DC, National Academy of Sciences.

National Research Council (1981) *Formaldehyde and Other Aldehydes*, Washington DC, National Academy of Sciences.

National Research Council (1982) *Diesel Technology — Impacts of Diesel-powered Light-duty Vehicles*, Washington DC, National Academy of Sciences.

National Research Council (1983) *Feasibility of Assessment of Health Risks from Vapor-phase Organic Chemicals in Gasoline and Diesel Exhaust*, Washington DC, National Academy of Sciences.

Nesnow S., Triplett L.L., Slaga T.J. Comparative tumor-initiating activity of complex mixtures from environmental particulate emissions on SENCAR mouse skin. J. natl Cancer Inst. 1982a;68:829–834. [PubMed: 6951092]

Nesnow, S., Evans, C., Stead, A., Creason, J., Slaga, T.J. & Triplett, L.L. (1982b) Skin carcinogenesis studies of emission extracts. In: Lewtas, J., ed., *Toxicological Effects of Emissions from Diesel Engines*, Amsterdam, Elsevier, pp. 295–320.

Nesnow S., Triplett L.L., Slaga T.J. Mouse skin tumor initiation-promotion and complete carcinogenesis bioassays: mechanisms and biological activities of emission samples. Environ. Health Perspect. 1983;47:255–268. [PMC free article: PMC1569412] [PubMed: 6825618]

Nielsen T. Isolation of polycyclic aromatic hydrocarbons and nitro derivatives in complex mixtures by liquid chromatography. Anal Chem. 1983;55:286–290.

Nilsson C.-A., Lindahl R., Norström Å. Occupational exposure to chain saw exhausts in logging operations. Am. ind. Hyg. Assoc. J. 1987;48:99–105. [PubMed: 3565274]

Nishioka, M.G., Petersen, B.A. & Lewtas, J. (1982) Comparison of nitro-aromatic content and direct-acting mutagenicity of diesel emissions. In: Cooke, M., Dennis, A.J. & Fisher, G.L., eds, *Polynuclear Aromatic Hydrocarbons, 6th International Symposium: Physical and Biological Chemistry*, Columbus, OH, Battelle, pp. 603–613.

Nishioka, M.G., Petersen, B.A. & Lewtas, J. (1983) Comparison of nitro-aromatic content and direct-acting mutagenicity of passenger car engine emissions. In: Rondia, D., Cooke, M. & Haroz, R.K., eds, *Mobile Source Emissions Including Polycyclic Organic Species*, Dordrecht, D. Reidel, pp. 197–210.

Nordenson I., Sweins A., Dahlgren E., Beckman L. A study of chromosomal aberrations in miners exposed to diesel exhausts. Scand. J. Work Environ. Health. 1981;7:14–17. [PubMed: 6171879]

Norpoth K., Jacob J., Grimmer G., Mohtashamipur E. Determination of mutagenic activities in different fractions of automobile exhaust condensate by the *Salmonella/*oxygenase mutagenicity test system. Zbl. Bakt. Hyg., I. Abt. Orig B. 1985;180:540–547. [PubMed: 2411064]

Oberdoerster G., Green F.H.Y., Freedman A.P. Clearance of $^{59}Fe_3O_4$ particles from the lungs of rats during exposure to coal mine dust and diesel exhaust. J. Aerosol Sci. 1984;15:235–237.

Office of Population Censuses and Surveys (1978) *Occupational Mortality. The Registrar General's Decennial Supplement for England and Wales 1970–1912* (*Series DS No. 1*), London, Her Majesty's Stationery Office.

Ohnishi Y., Kachi K., Sato K., Tahara I., Takeyoshi H., Tokiwa H. Detection of mutagenic activity in automobile exhaust. Mutat. Res. 1980;77:229–240. [PubMed: 6155611]

Ohnishi Y., Okazaki H., Wakisaka K., Kinouchi T., Kikuchi T., Furuya K. Mutagenicity of particulates in small engine exhaust. Mutat. Res. 1982;103:251–256. [PubMed: 6178022]

Olsen, J.H. & Jensen, O.M. (1987) Occupation and risk of cancer in Denmark. An analysis of 93 810 cancer cases, 1970–1979. *Scand. J. Work Environ. Health, 13* (*Suppl. 1*) [PubMed: 3659854]

Olufsen, B.S. & Bjørseth, A. (1983) Analysis of polycyclic aromatic hydrocarbons by gas chromatography. In: Bjørseth, A., ed., *Handbook of Aromatic Hydrocarbons*, New York, Marcel Dekker, pp. 257–300.

Ong T., Whong W.-Z., Xu J., Burchell B., Green F.H.Y., Lewis T. Genotoxicity studies of rodents exposed to coal dust and diesel emission particulates. Environ. Res. 1985;37:399–409. [PubMed: 2410249]

Orthoefer J.G., Bhatnagar R.S., Rahman A., Yang Y.Y., Lee S.D., Stara J.F. Collagen and prolyl hydroxylase levels in lungs of beagles exposed to air pollutants. Environ. Res. 1976;12:299–305. [PubMed: 63369]

Paputa-Peck M.C., Marano R.S., Schuetzle D., Riley T.L., Hampton C.V., Prater T.J., Skewes L.M., Jensen T.E., Ruehle P.H., Bosch L.C., Duncan W.P. Determination of nitrated polynuclear aromatic hydrocarbons in particulate extracts by capillary column gas chromatography with nitrogen selective detection. Anal. Chem. 1983;55:1946–1954.

Pederson T.C., Siak J.-S. The role of nitroaromatic compounds in the direct-acting mutagenicity of diesel particle extracts. J. appl. Toxicol. 1981;1:54–60. [PubMed: 6206114]

Pepelko W.E. Effects of 28 days exposure to diesel engine emissions in rats. Environ. Res. 1982a;27:16–23. [PubMed: 6175514]

Pepelko, W.E. (1982b) EPA studies on the toxicological effects of inhaled diesel engine emissions. In: Lewtas, J., ed., *Toxicological Effects of Emissions from Diesel Engines*, Amsterdam, Elsevier, pp. 121–142. [PubMed: 6176418]

Pepelko W.E., Peirano W.B. Health effects of exposure to diesel engine emissions. A summary of animal studies conducted by the US Environmental Protection Agency's Health Effects Research Laboratory at Cincinnati, OH. J. Am. Coll. Toxicol. 1983;2:253–306.

Pepelko W.E., Orthoefer J.G., Yang Y.-Y. Effects of 90 days exposure to catalytically treated automobile exhaust in rats. Environ. Res. 1979;19:91–101. [PubMed: 92404]

Pepelko W.E., Mattox J.K., Yang Y.-Y., Moore W. Jr. Pulmonary function and pathology in cats exposed 28 days to diesel exhaust. J. environ. Pathol Toxicol. 1980;4:449–458. [PubMed: 6161980]

Pepelko W.E., Mattox J., Moorman W.J., Clark J.C. Pulmonary function evaluation of cats after one year of exposure to diesel exhaust. Environ. int. 1981;5:373–376.

Pereira, M.A. (1982) Genotoxicity of diesel exhaust emissions in laboratory animals. In: Lewtas, J., ed., *Toxicological Effects of Emissions from Diesel Engines*, Amsterdam, Elsevier, pp. 265–276.

Pereira M.A., Shinozuka H., Lombardi B. Test of diesel exhaust emissions in the rat liver foci assay. Environ. int. 1981a;5:455–458.

Pereira M. A., Sabharwal P.S., Kaur P., Ross C.B., Choi A., Dixon T. In vivo detection of mutagenic effects of diesel exhaust by short-term mammalian bioassays. Environ. int. 1981b;5:439–443.

Pereira M.A., Connor T.H., Meyne J., Legator M.S. Metaphase analysis, micronuclei assay, and urinary mutagenicity assay of mice exposed to diesel emissions. Environ. int. 1981c;5:435–438.

Pereira M. A., McMillan L., Kaur P., Gulati D.K., Sabharwal P.S. Effect of diesel exhaust emissions, particulates, and extract on sister chromatid exchange in transplacentall exposed fetal hamster liver. Environ. Mutagenesis. 1982;4:215–220. [PubMed: 6178584]

Petersen, B.A. & Chuang, C.C. (1982) Methodology of fractionation and partition of diesel exhaust particulate samples. In: Lewtas, J., ed., *Toxicological Effects of Emissions from Diesel Engines*, Amsterdam, Elsevier, pp. 51–67. [PubMed: 6176435]

Petersen, G.R. & Milham, S., Jr (1980) *Occupational Mortality in the State of California 1959–61* (*DHEW (NIOSH) Publ. No. 80–104*), Cincinnati, OH, US Department of Health, Education, and Welfare.

del Piano, M., Gaudiuso, M., Rimatori, V., Sessa, R. & Bellanti, M. (1986) Exposure of workers to chemical pollutants in a public transport company (Abstract). In: *Proceedings of the International Congress on Industrial Hygiene, Rome, October* 5–9 1986, Rome, Pontificia Università Urbaniana, pp. 125–127.

Pierce R.C., Katz M. Dependency of polynuclear aromatic hydrocarbon content on size distribution of atmospheric aerosols. Environ. Sci. Technol. 1975;9:347–353.

Pierson W.R., Brachaczek W. W. Particulate matter associated with vehicles on the road. II. Aerosol Sci. Technol. 1983;2:1–40.

Pierson W.R., Gorse R.A. Jr, Szkarlat A.C., Brachaczek W.W., Japar S.M., Lee F.S.-C., Zweidinger R.B., Claxton L.D. Mutagenicity and chemical characteristics of carbonaceous particulate matter from vehicles on the road. Environ. Sci. Technol. 1983;17:31–44. [PubMed: 22304549]

Pitts J.N. Jr. Formation and fate of gaseous and particulate mutagens and carcinogens in real and simulated atmospheres. Environ. Health Perspect. 1983;47:115–140. [PMC free article: PMC1569386] [PubMed: 6337822]

Pitts J.N. Jr, Van Cauwenberghe K.A., Grosjean D., Schmid J.P., Fitz D.R., Belser W.L. Jr, Knudson G.B., Hynds P.M. Atmospheric reactions of polycyclic aromatic hydrocarbons: facile formation of mutagenic nitro derivatives. Science. 1978;202:515–519. [PubMed: 705341]

Pitts J.N. Jr, Lokensgard D.M., Harger W., Fisher T.S., Mejia V., Schuler J.J., Scorziell G.M., Katzenstein Y.A. Mutagens in diesel exhaust particulate: identification and direct activities of 6-nitrobenzo[*a*]pyrene, 9-nitroanthracene, 1-nitropyrene and 5*H*-phenanthro[4,5-*bcd*]pyran-5-one. Mutat. Res. 1982;103:241–249. [PubMed: 6178021]

Pott, F., Tomingas, R. & Misfeld, J. (1977) Tumours in mice after subcutaneous injection of automobile exhaust condensates. In: Mohr, U., Schmähl, D. & Tomatis, L., eds, *Air Pollution and Cancer in Man* (*IARC Scientific Publications No. 16*), Lyon, International

Agency for Research on Cancer, pp. 79–87.

Pritchard, J.N. (1987) *Particle growth in the airways and the influence of airflow*. In: Newman, S.P., Morén, F. & Crompton, G.K., eds, *A New Concept in Inhalation Therapy*, Bussum, Medicom, pp. 3–24.

Pryor, P. (1983) *Trailways Bus System, Denver, CO* (*Health Hazard Evaluation Report No. HETA 81-416-1334*), Cincinnati, OH, National Institute for Occupational Safety and Health.

Purdham J.T., Holness D.L., Pilger C.W. Environmental and medical assessment of stevedores employed in ferry operations. Appl. ind. Hyg. 1987;2:133–139.

Quinto J., De Marinis E. Sperm abnormalities in mice exposed to diesel particulate. Mutat. Res. 1984;130:242.

Raab, O.G., Yeh, H.-C., Newton, G.J., Phalen, R.F. & Velasquez, D.J. (1977) Deposition of inhaled monodisperse aerosols in small rodents. In: Walton, W.H., ed., *Inhaled Particles*, IV, Part 1, Oxford, Pergamon, pp. 3–21. [PubMed: 1236165]

Rabovsky J., Petersen M.R., Lewis T.R., Marion K.J., Groseclose R.D. Chronic inhalation of diesel exhaust and coal dust: effect of age and exposure on selected enzyme activities associated with microsomal cytochrome P-450 in rat lung and liver. J. Toxicol environ. Health. 1984;14:655–666. [PubMed: 6084065]

Raffle P.A.B. The health of the worker. Br. J. ind. Med. 1957;14:73–80. [PMC free article: PMC1037773] [PubMed: 13426428]

Ramdahl, T. (1984) Polycyclic aromatic ketones in source emissions and ambient air. In: Cooke, M. & Dennis, A.J., eds, *Polynuclear Aromatic Hydrocarbons, 8th International Symposium: Mechanisms, Methods and Metabolism*, Columbus, OH, Battelle, pp. 1075–1087.

Ramdahl T., Urdal K. Determination of nitrated polycyclic aromatic hydrocarbons by fused silica capillary gas chromatography/negative ion chemical ionization mass spectrometry. Anal. Chem. 1982;54:2256–2260.

Ramsey J.M. Carboxyhemoglobinemia in parking garage employees. Arch. environ. Health. 1967;15:580–583. [PubMed: 4169238]

Randerath E., Reddy M.V., Avitts T.A., Randerath K. ^{32}P-Postlabeling test for genotoxicity of environmental carcinogens/mutagens in condensates of cigarette smoke, gasoline exhaust and diesel exhaust (Abstract No. 332). Proc. Am. Assoc. Cancer Res. 1985;26:84.

Rannug U. Data from short-term tests on motor vehicle exhausts. Environ. Health Perspect. 1983;47:161–169. [PMC free article: PMC1569413] [PubMed: 6186476]

Rannug U., Sundvall A., Westerholm R., Alsberg T., Stenberg U. Some aspects of mutagenicity testing of the particulate phase and the gas phase of diluted and undiluted automobile exhaust. Environ. Sci. Res. 1983;27:3–16.

Rappaport S.M., Wang Y.Y., Wei E.T., Sawyer R., Watkins B.E., Rapoport H. Isolation and identification of a direct-acting mutagen in diesel-exhaust particulates. Environ. Sci. Technol. 1980;14:1505–1509. [PubMed: 22279997]

Reger R., Hancock J., Hankinson J., Hearl F., Merchant J. Coal miners exposed to diesel exhaust emissions. Ann. occup. Hyg. 1982;26:799–815. [PubMed: 7181308]

Reznik-Schüller H., Mohr U. Pulmonary tumorigenesis in Syrian golden hamsters after intratracheal instillations with automobile exhaust condensate. Cancer. 1977;40:203–210. [PubMed: 69482]

Risch H.A., Burch J.D., Miller A.B., Hill G.B., Steele R., Howe G.R. Occupational factors and the incidence of cancer of the bladder in Canada. Br. J. ind. Med. 1988;45:361–367. [PMC free article: PMC1009613] [PubMed: 3395572]

Ritter, J. A., Stedman, D.H, & Kelly, T.J. (1979) Ground level measurements of nitric oxide, nitrogen dioxide and ozone in rural air. In: Grosjean, D., ed., *Nitrogenous Air Pollutants, Proceedings of a Symposium, 175th National Meeting, American Chemical Society, Anaheim, California, March 12–17, 1978*, Ann Arbor, MI, Ann Arbor Science, pp. 325–343.

Robertson A., Dodgson J., Collings P., Seaton A. Exposure to oxides of nitrogen: respiratory symptoms and lung function in British coalminers. Br. J. ind. Med. 1984;41:214–219. [PMC free article: PMC1009286] [PubMed: 6722049]

Rosenkranz H.S., McCoy E.C., Mermelstein R., Speck W.T. A cautionary note on the use of nitroreductase-deficient strains of *Salmonella typhimurium* for the detection of nitroarenes as mutagens in complex mixtures including diesel exhausts. Mutat. Res. 1981;91:103–105. [PubMed: 7019692]

Rouser, G. & Aloia, R. (1980) The effects of air pollutants on membrane lipids. In: Stara, J.F., Dungworth, D.L., Orthoefer, J.G. & Tyler, W.S., eds, *Long-term Effects of Air Pollutants: in Canine Species* (*EPA-600/8-80-014*), Washington DC, US Environmental Protection Agency, pp. 87–91.

Rudd, C.J. (1980) Diesel particulate extract in cultured mammalian cells. In: Pepelko, W.E., Danner, R.M. & Clarke, N.A., eds, *Health Effects of Diesel Engine Emissions* (*EPA-60019-80-057a*), Cincinnati, OH, US Environmental Protection Agency, pp. 385–403.

Rushton L., Alderson M.R., Nagarajah C.R. Epidemiological survey of maintenance workers in London Transport executive bus garages and Chiswick works. Br. J. ind. Med. 1983;40:340–345. [PMC free article: PMC1069332] [PubMed: 6871124]

Sakuma, T., Davidson, W.R., Lane, D.A., Thomson, B.A., Fulford, J.E. & Quan, E.S.K. (1981) The rapid analysis of gaseous PAH and other combustion related compounds in hot gas streams by APCI/MS and APCI/MS/MS. In: Cooke, M. & Dennis, A.J., eds, *Polynuclear Aromatic Hydrocarbons, 5th International Symposium: Chemical Analysis and Biological Fate*, Columbus, OH, Battelle, pp. 179–188.

Salmeen I., Durisin A.M., Prater T.J., Riley T., Schuetzle D. Contribution of 1-nitropyrene to direct-acting Ames assay mutagenicities of diesel particulate extracts. Mutat. Res. 1982;104:17–23. [PubMed: 6176864]

Sanders B.M., White G.C., Draper G.J. Occupations of fathers of children dying from neoplasms. J. Epidemiol. Commun. Health. 1981;35:245–250. [PMC free article: PMC1052171] [PubMed: 7338698]

Sawicki, E. (1976) Analysis of atmospheric carcinogens and their cofactors. In: Rosenfeld, C. & Davis, W., eds, *Environmental Pollution and Carcinogenic Risks* (*IARC Scientific Publications No. 13*), Lyon, International Agency for Research on Cancer, pp. 297–354.

Sawicki E., Elbert W.C., Hauser T.R., Fox F.T., Stanley T.W. Benzo(a)pyrene content of the air of American communities. Am. ind. Hyg. Assoc. J. 1960;21:443–451. [PubMed: 13746945]

Sawicki E., Meeker J.E., Morgan M.J. Polynuclear aza compounds in automotive exhaust. Arch. environ. Health. 1965;11:773–775. [PubMed: 4158652]

Sayers, R.R., Yant, W.P., Levy, E. & Fulton, W.B. (1929) *Effect of Repeated Daily Exposure of Several Hours to Small Amounts of Automobile Exhaust Gas* (*Public Health Bulletin No. 186*), Washington DC, US Government Printing Office.

Schiller C.F., Gebhart J., Heyder J., Rudolf G., Stahlhofen W. Factors influencing total deposition of ultrafine aerosol particles in the human respiratory tract. J. Aerosol Sci. 1986;17:328–332.

Schoenberg J.B., Stemhagen A., Mogielnicki A.P., Altman R., Abe T., Mason T.J. Case-control study of bladder cancer in New Jersey. I. Occupational exposures in white males. J. natl Cancer Inst. 1984;72:973–981. [PubMed: 6585596]

Schuetzle D. Sampling of vehicle emissions for chemical analysis and biological testing. Environ. Health Perspect. 1983;47:65–80. [PMC free article: PMC1569398] [PubMed: 6186484]

Schuetzle, D. & Frazier, J. A. (1986) Factors influencing the emission of vapor and particulate phase components from diesel engines. In: Ishinishi, N., Koizumi, A., McClellan, R.O. & Stöber, W., eds, *Carcinogenic and Mutagenic Effects of Diesel Engine Exhaust*, Amsterdam, Elsevier, pp. 41–63.

Schuetzle, D. & Jensen, T.E. (1985) Analysis of nitrated polycyclic aromatic hydrocarbons (nitro-PAH) by mass spectrometry. In: White, C., ed., *Nitrated Polycyclic Aromatic Hydrocarbons*, Heidelberg, A. Hüthig Verlag, pp. 121–167.

Schuetzle D., Lewtas J. Bioassay-directed chemical analysis in environmental research. Anal. Chem. 1986;58:1060A–1075A. [PubMed: 3532864]

Schuetzle, D. & Perez, J.M. (1981) A CRC cooperative comparison of extraction and HPLC techniques for diesel particulate emissions (Paper 81–56.4). In: *Proceedings of the 74th Annual Meeting of the Air Pollution Control Association, Philadelphia, PA, June 16–21 1981*, Pittsburg, PA, Air Pollution Control Association.

Schuetzle D., Perez J.M. Factors influencing the emissions of nitrated-polynuclear aromatic hydrocarbons (nitro-PAH) from diesel engines. J. Air Pollut. Control Assoc. 1983;33:751–755.

Schuetzle D., Lee F.S.-C., Prater T.J., Tejada S.B. The identification of polynuclear aromatic hydrocarbon (PAH) derivatives in mutagenic fractions of diesel particulate extracts. Int. J. environ. anal. Chem. 1981;9:93–144. [PubMed: 7012053]

Schuetzle, D., Riley, T.L., Prater, T.J., Salmeen, I. & Harvey, T.M. (1982) The identification of mutagenic chemical species in air particulate samples. In: Albaiges, J., ed., *Analytical Techniques in Environmental Chemistry*, Vol. 2, Oxford, Pergamon, pp. 259–280.

Schuetzle D., Jensen T.E., Ball J.C. Polar polynuclear aromatic hydrocarbon derivatives in extracts of particulates: biological characterization and techniques for chemical analysis. Environ. int. 1985;11:169.

Schuler R.L., Niemeier R.W. A study of diesel emissions on *Drosophila*. Environ. int.

1981;5:431–434.

Seemayer N.H., Hadnagy W., Tomingas R. The effect of automobile exhaust particulates on cell viability, plating efficiency and cell division of mammalian tissue culture cells. Sci. total Environ. 1987;61:107–115. [PubMed: 2437649]

Seifert B., Ullrich D. Concentration of inorganic and organic air pollutants at a traffic intersection in Berlin (Ger.). Staub-Reinhalt. Luft. 1978;38:359–363.

Shefner, A.M., Collins, B.R., Dooley, L., Fiks, A., Graf, J.L. & Preache, M.M. (1982) Respiratory carcinogenicity of diesel fuel emissions. Interim results. In: Lewtas, J., ed., *Toxicological Effects of Emissions from Diesel Engines*, Amsterdam, Elsevier, pp. 329–350. [PubMed: 6176431]

Siak J.S., Chan J.L., Lee P.S. Diesel particulate extracts in bacterial test systems. Environ. int. 1981;5:243–248.

Siemiatycki J., Gérin M., Stewart P., Nadon L., Dewar R., Richardson L. Associations between several sites of cancer and ten types of exhaust and combustion products: results from a case-referent study in Montreal. Scand. J. Work Environ. Health. 1988;14:79–90. [PubMed: 2455336]

Silverman D.T., Hoover R.N., Albert S., Graff K.M. Occupation and cancer of the lower urinary tract in Detroit. J. natl Cancer Inst. 1983;70:237–245. [PubMed: 6571931]

Silverman D.T., Hoover R.N., Mason T.J., Swanson G.M. Motor exhaust-related occupations and bladder cancer. Cancer Res. 1986;46:2113–2116. [PubMed: 2418962]

Smith E.M., Miller E.R., Woolson R.F., Brown C.K. Bladder cancer risk among auto and truck mechanics and chemically related occupations. Am. J. publ. Health. 1985;75:881–883. [PMC free article: PMC1646348] [PubMed: 2411155]

Speizer F.E., Ferris B.G. Jr. The prevalence of chronic nonspecific respiratory disease in road tunnel employees. Am. Rev. respir. Dis. 1963;88:205–212. [PubMed: 14045225]

Stanley T.W., Meeker J.E., Morgan M.J. Extraction of organics from airborne particulates. Effects of various solvents and conditions on the recovery of benzo(*a*)pyrene, benz(*c*)acridine, and 7*H*-benz(*de*)anthracen-7-one. Environ. Sci. Technol. 1967;1:927–931. [PubMed: 22148409]

Stara, J.F., Dungworth, D.L., Orthoefer, J.G. & Tyler, W.S., eds (1980) *Long-term Effects of Air Pollutants: in Canine Species* (*EPA-600/8-80-014*), Cincinnati, OH, US Environmental Protection Agency.

Stauff J., Tsai W.-L., Stärk G., Miltenburger H. Chemiluminescence and mutagenic activity of exhaust gas after combustion (Ger.). Staub-Reinhalt. Luft. 1980;40:284–289.

Steenland K. Lung cancer and diesel exhaust: a review. Am. J. ind. Med. 1986;10:177–189. [PubMed: 2428240]

Steenland K., Burnett C., Osorio A.M. A case-control study of bladder cancer using city directories as a source of occupational data. Am. J. Epidemiol. 1987;126:247–257. [PubMed: 3605053]

Stenberg, U., Alsberg, T. & Bertilsson, B.M. (1981) *A Comparison of the Emission of Polynuclear Aromatic Hydrocarbons from Automobiles Using Gasoline or a Methanol/Gasoline Blend (SAE Technical Paper No. 810441)*, Warrendale, PA, Society of

Automotive Engineers.

Stenberg U., Alsberg T., Westerholm R. Applicability of a cryogradient technique for the enrichment of PAH from automobile exhausts: demonstration of methodology and evaluation experiments. Environ. Health Perspect. 1983;47:43–51. [PMC free article: PMC1569390] [PubMed: 6186482]

Stenburg R.L., von Lehmden D.J., Hangebrauck R.P. Sample collection techniques for combustion sources — benzopyrene determination. Am. ind. Hyg. Assoc. J. 1961;22:271–275.

Stern F.B., Curtis R.A., Lemen R.A. Exposure of motor vehicle examiners to carbon monoxide: a historical prospective mortality study. Arch. environ. Health. 1981;36:59–66. [PubMed: 6163400]

Strom K. A. Response of pulmonary cellular defenses to the inhalation of high concentrations of diesel exhaust. J. Toxicol. environ. Health. 1984;13:919–944. [PubMed: 6208373]

Stupfel M., Magnier M., Romary F., Tran M.-H., Moutet J.-P. Lifelong exposure of SPF rats to automotive exhaust gas. Dilution containing 20 ppm of nitrogen oxides. Arch. environ. Health. 1973;26:264–269. [PubMed: 4121280]

Sun J.D., McClellan R.O. Respiratory tract clearance of ^{14}C-labelled diesel exhaust compounds associated with diesel particles or as a particle-free extract. Fundam. appl. Toxicol. 1984;4:388–393. [PubMed: 6204900]

Sun J.D., Wolff R.K., Kanapilly G.M., McClellan R.O. Lung retention and metabolic fate of inhaled benzo(*a*)pyrene associated with diesel exhaust particles. Toxicol. appl. Pharmacol. 1984;73:48–59. [PubMed: 6200954]

Swarin, S.J. & Williams, R.L. (1980) Liquid chromatographic determination of benzo[*a*]pyrene in diesel exhaust particulate: verification of the collection and analytical methods. In: Bjørseth, A. & Dennis, A.J., eds, *Polynuclear Aromatic Hydrocarbons, 4th International Symposium: Chemistry and Biological Effects*, Columbus, OH, Battelle, pp. 771–806.

Takafuji S., Suzuki S., Koizumi K., Tadokoro K., Miyamoto T., Ikemori R., Muranaka M. Diesel-exhaust particulates inoculated by the intranasal route have an adjuvant activity for IgE production in mice. J. Allerg. clin. Immunol. 1987;79:639–645. [PubMed: 2435776]

Takemoto, K., Yoshimura, H. & Katayama, H. (1986) Effects of chronic inhalation exposure to diesel exhaust on the development of lung tumors in di-isopropanol-nitrosamine-treated F344 rats and newborn C57BL and ICR mice. In: Ishinishi, N., Koizumi, A., McClellan, R.O. & Stöber, W., eds, *Carcinogenic and Mutagenic Effects of Diesel Engine Exhaust*, Amsterdam, Elsevier, pp. 311–327. [PubMed: 2435493]

Tejada, S.B., Zweidinger, R.B. & Sigsby, J.E., Jr (1983) *Analysis of Nitroaromatics in Diesel and Gasoline Car Emissions* (*SAE Technical Paper No. 820775*), Warrendale, PA, Society of Automotive Engineers.

Thurston G.D., Spengler J.D. A quantitative assessment of source contributions to inhalable particulate matter pollution in metropolitan Boston. Atmos. Environ. 1985;19:9–25.

Tokiwa, H., Otofuji, T., Nakagawa, R., Horikawa, K., Maeda, T., Sano, N., Izumi, K. &

Otsuka, H. (1986) Dinitro derivatives of pyrene and fluoranthene in diesel emission particulates and their tumorigenicity in mice and rats. In: Ishinishi, N., Koizumi, A., McClellan, R.O. & Stöber, W., eds, *Carcinogenic and Mutagenic Effects of Diesel Engine Exhaust*, Amsterdam, Elsevier, pp. 253–270.

Tong H.Y., Karasek F.W. Quantitation of polycyclic aromatic hydrocarbons in diesel exhaust particulate matter by high-performance liquid chromatography fractionation and high-resolution gas chromatography. Anal Chem. 1984;56:2129–2134. [PubMed: 6209996]

Törnqvist M., Kautiainen A., Gatz R.N., Ehrenberg L. Hemoglobin adducts in animals exposed to gasoline and diesel exhausts. 1. Alkenes. J. appl. Toxicol. 1988;8:159–170. [PubMed: 2459181]

Tsani-Bazaca E., McIntyre A.E., Lester J.N., Perry R. Concentrations and correlations of 1,2-dibromoethane, 1,2-dichloroethane, benzene and toluene in vehicle exhaust and ambient air. Environ. Technol Lett. 1981;2:303–316.

Tucker J.D., Xu J., Stewart J., Baciu P.C., Ong T.-M. Detection of sister chromatid exchanges induced by volatile genotoxicants. Teratog. Carcinog. Mutagenesis. 1986;6:15–21. [PubMed: 2426822]

Tyrer H.W., Cantrell E.T., Horres R., Lee I.P., Peirano W.B., Danner R.M. Benzo(*a*)pyrene metabolism in mice exposed to diesel exhaust: I. Uptake and distribution. Environ. int. 1981;5:307–311.

Ulfvarson, U., Alexandersson, R., Aringer, L., Anshelm-Olson, B., Ekholm, U., Hedenstierna, G., Hogstedt, C., Holmberg, B., Lindstedt, G., Randma, E., Rosen, G., Sorsa, M. &Svensson, E. (1985) *Hälsoeffekter vid Exponering för Motoravgaser* [Health Effects of Exposure to Motor Exhaust Gases] (*Arbete och Hälsa 1985:5*), Solna, Arbetarskyddsstyrelsen.

Ulfvarson U., Alexandersson R., Aringer L., Svensson E., Hedenstierna G., Hogstedt C., Holmberg B., Rosén G., Sorsa M. Effects of exposure to vehicle exhaust on health. Scand. J. Work Environ. Health. 1987;13:505–512. [PubMed: 2448871]

Ungers, L.J. (1984) *Measurement of Exhaust Emissions from Diesel-powered Forklifts during Operations in Ammunition Storage Magazines (Phase I* (*AD-A141-792*), Cincinnati, OH, PEDCo Environmental.

Ungers, L.J. (1985) *Measurement of Exhaust Emissions from Diesel-powered Forklifts during Operations in Ammunition Storage Magazines (Phase II*(*AD-A153-092*), Cincinnati, OH, PEI Associates.

US Environmental Protection Agency (1977) Protection of the environment, Chapter 1, Part 8B, Subpart B, section 86. *US Code fed Regul., Title 40*, 113–178.

US Environmental Protection Agency (1979) *Air Quality Criteria for Carbon Monoxide* (*Report No. EPA 60018-79-022; US NTIS PB81-244840*), Research Triangle Park, NC, Environmental Criteria and Assessment Office.

US Environmental Protection Agency (1982) *Air Quality Criteria for Oxides of Nitrogen. Final Report* (*Report No. EPA 600/8-82-026F; US NTIS Pb83-163337*), Research Triangle Park, NC, Environmental Criteria and Assessment Office.

US Environmental Protection Agency (1986) *Air Quality for Lead, Volume 4* (*EPA-600/8-83-028dF; US NTIS PB87-142378*), Research Triangle Park, NC, Environmental Criteria and Assessment Office.

US Environmental Protection Agency (1987) *USEPA Mobile Source Emission Standards Summary*, Bethesda, MD, Office of Air and Radiation.

Vallyathan V., Virmani R., Rochlani S., Green F.H.Y., Lewis T. Effect of diesel emissions and coal dust inhalation on heart and pulmonary arteries of rats. J. Toxicol., environ. Health. 1986;19:33–41. [PubMed: 2427732]

VDI-Kommision (1987) *Emission Measurement. Measurement of Polycyclic Aromatic Hydrocarbons (PAH). Measurement of PAH in the Exhaust Gas from Gasoline and Diesel Engines of Passenger Cars — Gas Chromatographic Determination* (Ger.) (*VDI-Handbuch Reinhaltung der Luft Vol 5*), Düsseldorf, VDI (Verein Deutscher Ingenieure)-Verlag GmbH.

Vianna N.J., Kovasznay B., Polan A., Ju C. Infant leukemia and paternal exposure to motor vehicle exhaust fumes. J. occup. Med. 1984;26:679–682. [PubMed: 6207280]

Vineis P., Magnani C. Occupation and bladder cancer in males: a case-control study. Int. J. Cancer. 1985;35:599–606. [PubMed: 3997281]

Vostal J.J. Bioavailability and biotransformation of the mutagenic component of particulate emissions present in motor exhaust samples. Environ. Health Perspect. 1983;47:269–281. [PMC free article: PMC1569410] [PubMed: 6186478]

Vostal J. J., Chan T.L., Garg B.D., Lee P.S., Strom K.A. Lymphatic transport of inhaled diesel particles in the lungs of rats and guinea pigs exposed to diluted diesel exhaust. Environ. int. 1981;5:339–347.

Vostal, J.J., White, H.J., Strom, K. A., Siak, J.-S., Chen, K.-C. & Dziedzic, D. (1982) Response of the pulmonary defense system to diesel particulate exposure. In: Lewtas, J., ed., *Toxicological Effects of Emissions from Diesel Engines*, Amsterdam, Elsevier, pp. 201–221.

Wadden R.A., Uno I., Wakamatsu S. Source discrimination of short-term hydrocarbon samples measured aloft. Environ. Sci. Technol. 1986;20:473–483. [PubMed: 19994931]

Wallace W.E., Keane M.J., Hill C.A., Xu J., Ong T.-M. Mutagenicity of diesel exhaust particles and oil shale particles dispersed in lecithin surfactant. J. Toxicol environ. Health. 1987;21:163–171. [PubMed: 2437315]

Waller R. E. Trends in lung cancer in London in relation to exposure to diesel fumes. Environ. int. 1981;5:479–483.

Waller R.E., Commins B.T., Lawther P.J. Air pollution in road tunnels. Br. J. ind. Med. 1961;18:250–259. [PMC free article: PMC1038239] [PubMed: 14004693]

Waller R.E., Hampton L., Lawther P.J. A further study of air pollution in diesel bus garages. Br. J. ind. Med. 1985;42:824–830. [PMC free article: PMC1007586] [PubMed: 4074654]

Wang Y.Y., Rappaport S.M., Sawyer R.F., Talcott R.E., Wei E.T. Direct-acting mutagens in automobile exhaust. Cancer Lett. 1978;5:39–47. [PubMed: 80258]

Waxweiler R.J., Wagoner J.K., Archer V.E. Mortality of potash workers. J. occup. Med. 1973;15:486–489. [PubMed: 4704225]

Weller M.A., Chen S.-T., Barnhart M.I. Acid phosphatase in alveolar macrophages exposed *in vivo* to diesel engine exhaust. Micron. 1981;12:89–90.

Wells, A.C., Venn, J.B. & Heard, M.J. (1977) Deposition in the lung and uptake to blood of motor exhaust labelled with ^{203}Pb. In: Walton, W.H., ed., *Inhaled Particles*, IV, Part 1, Oxford, Pergamon, pp. 175–189. [PubMed: 70403]

Westerholm R.N., Alsberg T.E., Frommelin A.B., Strandell M.E., Rannug U., Winquist L., Grigoriadis V., Egebäck K.E. Effect of fuel polycyclic aromatic hydrocarbons content on the emissions of polycyclic aromatic hydrocarbons and other mutagenic substances from a gasoline-fueled automobile. Environ. Sci. Technol. 1988;22:925–930. [PubMed: 22195714]

Wheeler R.W., Hearl F.J., McCawley M. An industrial hygiene characterization of exposure to diesel emissions in an underground coal mine. Environ. int. 1981;5:485–488.

Whitby R.A., Altwicker E.R. Acetylene in the atmosphere: sources, representative ambient concentrations and ratios to other hydrocarbons. Atmos. Environ. 1978;12:1289–1296.

White, C.M. (1985) Analysis of nitrated polycyclic aromatic hydrocarbons by gas chromatography. In: White, C.M., ed., *Nitrated Polycyclic Aromatic Hydrocarbons*, Heidelberg, A. Hüthig Verlag, pp. 1–86.

White H.J., Garg B.D. Early pulmonary response of the rat lung to inhalation of high concentration of diesel particles. J. appl. Toxicol. 1981;1:104–110. [PubMed: 6206108]

Wiester M.J., Iitis R., Moore W. Altered function and histology in guinea pigs after inhalation of diesel exhaust. Environ. Res. 1980;22:285–297. [PubMed: 6157525]

Wilkins J.R. III, Sinks T.H. Jr. Paternal occupation and Wilms' tumour in offspring. J. Epidemiol. Commun. Health. 1984;38:7–11. [PMC free article: PMC1052307] [PubMed: 6323612]

Williams M.L. The impact of motor vehicles on air pollutant emissions and air quality in the UK — an overview. Sci. total Environ. 1987;59:47–61.

Williams, R.L. & Swarin, S.J. (1979) *Benzo[a]pyrene Emissions from Gasoline and Diesel Automobiles* (*Technical Paper Series No. 790419*), Warrendale, PA, Society of Automotive Engineers.

Williams R.R., Stegens N.L., Goldsmith J.R. Associations of cancer site and type with occupation and industry from the Third National Cancer Survey interview. J. natl Cancer Inst. 1977;59:1147–1185. [PubMed: 903993]

Wise, S.A. (1983) High-performance liquid chromatography for the determination of polycyclic aromatic hydrocarbons. In: Bjørseth, A., ed., *Handbook of Polycyclic Aromatic Hydrocarbons*, New York, Marcel Dekker, pp. 183–256.

Wise, S.A., Bonnett, W.J. & May, W.E. (1980) Normal- and reverse-phase liquid chromatographic separations of polycyclic aromatic hydrocarbons. In: Bjørseth, A. & Dennis, A.J., eds, *Polynuclear Aromatic Hydrocarbons, 4th International Symposium: Chemistry and Biological Effects*, Columbus, OH, Battelle, pp. 791–806.

Wolff R.K., Kanapilly G.M., DeNee P.B., McClellan R.O. Deposition of 0.1 μm chain aggregate aerosols in beagle dogs. J. Aerosol Sci. 1981;12:119–129.

Wolff R.K., Kanapilly G.M., Gray R.H., McClellan R.O. Deposition and retention of inhaled aggregate $^{67}Ga_2O_3$ particles in beagle dogs, Fischer-344 rats, and CD-1 mice. Am. ind. Hyg. Assoc. J. 1984;45:377–381. [PubMed: 6741792]

Wolff, R.K., Henderson, R.F., Snipes, M.B., Sun, J.D., Bond, J.A., Mitchell, C.E., Mauderly, J.L. & McClellan, R.O. (1986) Lung retention of diesel soot and associated organic compounds. In: Ishinishi, N., Koizumi, A., McClellan, R.O. & Stöber, W., eds, *Carcinogenic and Mutagenic Effects of Diesel Engine Exhaust*, Amsterdam, Elsevier, pp. 199–211.

Wolff R.K., Henderson R.F., Snipes M.B., Griffith W.C., Mauderly J.L., Cuddihy R.G., McClellan R.O. Alterations in particle accumulation and clearance in lungs of rats chronically exposed to diesel exhaust. Fundam. appl. Toxicol. 1987;9:154–166. [PubMed: 2442056]

Wong O., Morgan R.W., Kheifets L., Larson S.R., Whorton M.D. Mortality among members of a heavy construction equipment operators union with potential exposure to diesel exhaust emissions. Br. J. ind. Med. 1985;42:435–448. [PMC free article: PMC1007508] [PubMed: 2410010]

Wong D., Mitchell C.E., Wolff R.K., Mauderly J.L., Jeffrey A.M. Identification of DNA damage as a result of exposure of rats to diesel engine exhaust. Carcinogenesis. 1986;7:1595–1597. [PubMed: 2427242]

Woskie S.R., Smith T.J., Hammond S.K., Schenker M.B., Garshick E., Speizer F.E. Estimation of the diesel exhaust exposures of railroad workers: I. Current exposures. Am. J. ind. Med. 1988a;13:381–394. [PubMed: 3354586]

Woskie S.R., Smith T.J., Hammond S.K., Schenker M.B., Garshick E., Speizer F.E. Estimation of the diesel exhaust exposures of railroad workers: II. National and historical exposures. Am. J. ind. Med. 1988b;13:395–404. [PubMed: 3281456]

Wright E.S. Effects of short-term exposure to diesel exhaust on lung cell proliferation and phospholipid metabolism. Exp. Lung Res. 1986;10:39–55. [PubMed: 2419123]

Wynder E.L., Hoffmann D. A study of air pollution carcinogenesis. III. Carcinogenic activity of gasoline engine exhaust condensate. Cancer. 1962;15:103–108. [PubMed: 14008627]

Wynder E.L., Dieck G.S., Hall N.E.L., Lahti H. A case-control study of diesel exhaust exposure and bladder cancer. Environ. Res. 1985;37:475–489. [PubMed: 2410250]

Xu G.B., Yu C.P. Deposition of diesel exhaust particles in mammalian lungs. A comparison between rodents and man. Aerosol Sci. Technol. 1987;7:117–123.

Yamaki, N., Kohno, T., Ishiwata, S., Matsushita, H., Yoshihara, K., Iida, Y., Mizoguchi, T., Okuzawa, S., Sakamoto, K., Kachi, H., Goto, S., Sakamoto, T. & Daishima, S. (1986) The state of the art on the chemical characterization of diesel particulates in Japan. In: Ishinishi, N., Koizumi, A., McClellan, R.O. & Stöber, W., eds, *Carcinogenic and Mutagenic Effects of Diesel Engine Exhaust*, Amsterdam, Elsevier, pp. 17–40.

Yoshimura H. The influence of air pollution in the development of pulmonary cancer, with special reference to gasoline engines (Jpn.). Nippon Eiseigaku Zasshi (Jpn. J. Hyg.). 1983;37:848–865. [PubMed: 6191062]

Yu C.P., Xu G.B. Predictive models for deposition of diesel exhaust particulates in human and rat lungs. Aerosol Sci. Technol. 1986;5:337–347.

Yu C.P., Xu G.B. Predicted disposition of diesel particles in young humans. J. Aerosol Sci. 1987;18:419–423.

Zack M., Cannon S., Loyd D., Heath C.W. Jr, Falletta J.M., Jones B., Housworth J., Crowley S. Cancer in children of parents exposed to hydrocarbon-related industries and occupations. Am. J. Epidemiol. 1980;111:329–336. [PubMed: 7361757]

Zaebst, D.D., Blade, L.M., Morris, J.A., Schuetzle, D. & Butler, J. (1988) Elemental carbon as a surrogate index of diesel exhaust exposure. In: *Proceedings of the American Industrial Hygiene Conference, 15–20 May 1988, San Francisco, CA*, Cincinnati, OH, National Institute for Occupational Safety and Health, Division of Surveillance, Hazard Evaluation and Field Studies.

Zamora P.O., Gregory R.E., Brooks A.L. In vitro evaluation of the tumor-promoting potential of diesel-exhaust-particle extracts. J. Toxicol., environ. Health. 1983;11:187–197.

Ziskind, R.A., Carlin, T.J. & Ballas, J. (1978) Evaluating toxic gas hazards inside heavy duty diesel truck cabs. In: *Proceedings of the 4th Joint Conference on Sensing Environmental Pollutants, New Orleans, 1977*, Washingon DC, American Chemical Society, pp. 377–383.

Zweidinger, R.B. (1982) Emission factors from diesel and gasoline powered vehicles: correlation with the Ames test. In: Lewtas, J., ed., *Toxicological Effects of Emissions from Diesel Engines*, Amsterdam, Elsevier, pp. 83–96. [PubMed: 6176437]

Footnotes

1 Subsequent to the meeting, a more detailed report of the study was published (Lewis *et al.*, 1989).

1 Subsequent to the meeting, a more detailed report of the study was published (Brightwell *et al.*, 1989; see also pp. 93,98,99, 104).

1 For definitions of the italicized terms, see Preamble, pp. 25–28.

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