GENERAL REMARKS ON THE AGENTS CONSIDERED

This forty-sixth volume of *IARC Monographs* covers diesel and gasoline engine exhausts and 15 nitroarenes. It is related to Volume 45 (IARC, 1989), which dealt with occupational exposures in petroleum refining and with crude oil and the major petroleum fuels, since the engine exhausts considered in the present volume originate from the use of two major petroleum fuels — gasoline and diesel fuel — primarily in vehicles. This volume also complements Volume 35 (IARC, 1985), in which the relevant data on soots formed during the domestic or institutional combustion of heating fuels are summarized and evaluated. Diesel and gasoline engine exhaust emissions all contain soot, which is defined as carbon-containing material produced as a by-product of incomplete combustion or pyrolysis. The genetic activity and tumorigenicity of soot extracts (tars) from diesel and gasoline engine exhausts have been compared with those of soot extracts from coal, wood and fuel oil (Lewtas, 1985).

Engine exhausts

The main sources of engine exhausts are vehicles: automobiles, buses, trucks, trains, ships, boats, heavy construction equipment, fork-lift trucks, tractors and jet aircraft, although diesel- and gasoline-fuelled engines are also used as stationary power sources. Jet engine exhausts were not considered in this volume, since no study relevant to an evaluation of their carcinogenicity was available. The Working Group was aware of some data on the analysis of the chemical composition of jet engine exhaust (Black *et al.*, 1977; McCammon & Crandall, 1980; McCartney *et al.*, 1986) and on pollutant concentrations in airports (Judd, 1971; Bastress, 1973). One study showed, however, that emissions from diesel- and gasoline-driven tank trucks and other vehicles at airports may cause heavier exposure than emissions from jet airplanes (McCammon *et al.*, 1981). Particle extracts from jet airplanes have been shown to be mutagenic (McCartney *et al.*, 1986). One epidemiological study addressed exposure to jet fuel exhaust (Siemiatycki *et al.*, 1988); due to the small number of exposed subjects, however, risk estimates were difficult to evaluate.

Engine exhausts are complex mixtures containing thousands of chemical compounds in the particulate and gaseous phases. Many components of engine exhausts have also been found in tobacco smoke and other combustion products. Table 1 lists agents that have been identified in engine exhausts and that have been evaluated by the IARC. The monograph on diesel and gasoline engine exhausts is not a review of data on these or other specific substances in engine exhausts but covers only experimental studies in which the whole exhaust or a major fraction of it has been tested. The few studies of exhaust irradiated with ultraviolet light are also discussed.

Table 1. Agents identified in engine exhausts that have been evaluated in *IARC Monographs* volumes

Agent	Evidence of carcinogenicity[a]		
	Humans	Animals	Group
Acetaldehyde	I	S	2B
Acridines			
Benz[*c*]acridine	ND	L	3
Dibenz[*a*,*h*]acridine	ND	S	2B
Dibenz[*a*,*j*]acridine	ND	S	2B
Acrolein	I	I	3
Benzene	S	S	1
1,3-Butadiene	I	S	2B
1,2-Dibromoethane (ethylene dibromide)	I	S	2A
1,2-Dichloroethane	ND	S	2B
Ethylene	ND	ND	3
Formaldehyde	L	S	2A
Lead and lead compounds			
Inorganic	I	S	2B
Organolead	I	I	3
Methylbromide	I	L	3
Nitroarenes			
3,7-Dinitrofluoranthene[b]	ND	L	3
3,9-Dinitrofluoranthene[b]	ND	L	3
1,3-Dinitropyrene[b]	ND	L	3
1,6-Dinitropyrene[b]	ND	S	2B
1,8-Dinitropyrene[b]	ND	S	2B
9-Nitroanthracene	ND	ND	3
6-Nitrobenzo[*a*]pyrene[b]	ND	L	3
3-Nitrofluoranthene	ND	I	3
2-Nitrofluorene[b]	ND	S	2B
1-Nitronaphthalene[b]	ND	I	3
2-Nitronaphthalene[b]	ND	I	3
1-Nitropyrene[b]	ND	S	2B
Polycyclic aromatic compounds			
Anthanthrene	ND	L	3
Anthracene	ND	I	3
Benz[*a*]anthracene	ND	S	2A
Benzo[*b*fluoranthene	ND	S	2B
Benzo[*j*]fluoranthene	ND	S	2B
Benzo[*k*]fluoranthene	ND	S	2B
Benzo[*ghi*]fluoranthene	ND	I	3
Benzo[*a*]fluorene	ND	I	3
Benzo[*b*]fluorene	ND	I	3
Benzo[*ghi*]perylene	ND	I	3
Benzo[*c*]phenanthrene	ND	I	3
Benzo[*a*]pyrene	ND	S	2A
Benzo[*e*]pyrene	ND	I	3
Chrysene	ND	L	3

Table 1 (contd)

Agent	Evidence of carcinogenicity[a]		
	Humans	Animals	Group
Coronene	ND	I	3
Cyclopenta[*cd*]pyrene	ND	L	3
Dibenz[*a*,*h*]anthracene	ND	S	2A
Dibenzo[*a*,*e*]pyrene	ND	S	2B
Dibenzo[*a*,*h*]pyrene	ND	S	2B
1,4-Dimethylphenanthrene	ND	I	3
Fluoranthene	ND	I	3
Fluorene	ND	I	3
Indeno[1,2,3-*cd*]pyrene	ND	S	2B
2-Methylchrysene	ND	L	3
3-Methylchrysene	ND	L	3
4-methylchrysene	ND	L	3
5-Methylchrysene	ND	S	2B
6-Methylchrysene	ND	L	3
1-Methylphenanthrene	ND	I	3
Perylene	ND	I	3
Phenanthrene	ND	I	3
Pyrene	ND	I	3
Triphenylene	ND	I	3
Propylene	ND	ND	3

[a]From Supplement 7 (IARC, 1987), unless otherwise indicated; I, inadequate evidence; L, limited evidence; ND, no adequate data; S, sufficient evidence; 1, Group 1 — the agent is carcinogenic to humans; 2A, Group 2A — the agent is probably carcinogenic to humans; 2B, Group 2B — the agent is possibly carcinogenic to humans; 3, Group 3 — the agent is not classifiable as to its carcinogenicity to humans

[b]In this volume

In 1980, there were approximately 320 million passenger cars in the world, and approximately 75 million trucks and 20 million buses. The major increase in the world vehicle fleet occurred during 1950–70, with a substantial tapering off of this increase in subsequent years (Swedish Ministry of Agriculture, 1983). Diesel cars have virtually disappeared from the US market but currently account for 18% of new registrations in the countries of the European Community (Henssler & Gospage, 1987).

Intensive research was begun in the 1970s to develop internal combustion engines capable of meeting the emission control standards adopted in various parts of the world. This has resulted in the development of control techniques common to gasoline and diesel engines, including improved engine design and the use of exhaust gas recirculation and oxidation catalysts. Gasoline engines have been adapted for use of double and three-way catalysts, primarily intended to reduce emission of nitrogen oxides (Swedish Ministry of Agriculture, 1983). Air pollution standards which became effective in 1975 in the USA (US Environmental Protection Agency, 1972, 1974) necessitated the use of catalytic converters

on passenger cars sold in that country, which entailed the simultaneous introduction of unleaded gasoline to avoid poisoning the active catalyst within the converter. Unleaded gasoline was introduced in Japan in 1972 (Swedish Ministry of Agriculture, 1979). The introduction of unleaded gasoline in the European Community was proposed in 1984 (Commission of the European Communities, 1984; Henssler & Gospage, 1987); with effect from 1 October 1989, new vehicles with engine capacities greater than 2 l must have a catalytic converter (Commission of the European Communities, 1985). Leaded regular gasoline has been banned in the Federal Republic of Germany since 1 February 1988 (Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit, 1987; CONCAWE, 1988). The sale of leaded regular gasoline was prohibited in Switzerland from 1 July 1986 (Conseil Fédéral Suisse, 1985), and, since 1 October 1987, all cars have had to be equipped with a catalytic converter; the same regulation has applied to light motorcycles since 1 October 1988 (Département Fédéral de l'Intérieur de Suisse, 1986).

Diesel engines have become the predominant source of industrial power, due in part to their ruggedness and power efficiency. Diesel locomotives were introduced on railroads in Canada and the USA in 1928 and in Germany in 1932. The 'dieselization' of railroads occurred rapidly in the USA: 5% of the locomotives used in 1943 had diesel engines (Anon., 1966), but 95% conversion had taken place by 1959 (Garshick *et al.*, 1987). The introduction of diesel engines into underground coal mines began in Germany in 1927, in Belgium and France soon after, and in the UK in 1939 (Harrington & East, 1947). In the USA, diesel engines were first used in a Pennsylvania limestone mine in 1939 and in underground coal mines in 1946; their use in coal mines in the USA was not common as recently as 1977, but since that time there has been a five-fold increase. The worldwide use of diesel engines in mining applications has advanced steadily since their introduction (Daniel, 1984).

A substantial effort throughout the world during the late 1970s and 1980s resulted in improved characterization of emissions from light-duty diesel engines. Unfortunately, much less information is available with regard to heavy-duty diesel engines. It would be particularly important to characterize exhaust emissions from diesel railroad locomotives, which might be of value in interpreting the results of epidemiological studies of railroad workers.

Because of the differences in the characteristics of exhausts from different types of motors — diesel/gasoline, light duty/heavy duty, catalytic/noncatalytic — every attempt was made to identify the exhaust tested in the studies considered. With respect to experimental studies, therefore, a number of early studies in which the type of engine exhaust was not specified were not considered by the Working Group, except in the absence of comparable data on specific exhaust types.

In interpreting the results of studies of complex mixtures, such as those in which animals are exposed to vehicle exhausts, it is important that the atmospheres to which the animals were exposed be characterized in as much detail as possible. The relevance of characterizing the various components, such as specific gases (e.g., nitrogen dioxide) and particulate material (e.g., diesel soot and associated organic compounds), is apparent when it is recognized that each may play a role in producing disease. For example, nitrogen dioxide

and carbonaceous particles may irritate respiratory tract epithelium, and organic compounds may interact with DNA.

In rats exposed to high levels of whole diesel exhaust, long-term clearance of soot particles from the lungs is impaired and there is a build-up of the lung burden of soot that is in excess of the levels predicted from observations at low levels of exposure. At high levels of exposure, chronic active inflammation accompanies the focal accumulation of 'sequestered' soot in alveolar macrophages. In these areas, epithelial cell hyperplasia, progressive fibrosis and squamous metaplasia have been observed. Similar changes have been noted in studies with other materials in which increased incidences of lung tumours have been observed. The potential role of the lung 'overload' phenomenon and the associated pathology in the pathogenesis of lung tumours due to inhaled particles is not yet clear, and further research is needed in view of the prominent role of lung carcinogenicity in rats exposed to diesel engine exhaust.

The relevance to the human situation of impaired clearance in animals also awaits clarification. There is a severe lack of information on the effects on humans of engine exhausts. In particular, there are no data on the deposition and clearance of inhaled diesel exhaust particles. However, it should be noted that impairment of the pulmonary clearance of insoluble particles has been observed in cigarette smokers (Bohning *et al.*, 1982; Freedman *et al.*, 1984), who deposit gram quantities of tar per week (Pritchard, 1987). On the basis of a 320-day half-time for the pulmonary clearance of insoluble particles (Bailey *et al.*, 1982), life-time occupational exposure to, for example, 0.3 mg/ m^3 (Gamble *et al.*, 1987) would result in a lung burden of approximately 50 mg. Scaling down to rats on the basis of relative lung weights by a factor of 250 (human:rat; Xu & Yu, 1987) would bring this burden to within an order of magnitude of that which impairs pulmonary clearance in rats.

Although it is clear that exposure of animals to engine exhausts results in the induction of lung tumours, it should be noted that complete necropsies were performed in only a few studies (e.g., Heinrich *et al.*, 1986; Mauderly *et al.*, 1987), and the presence or absence of tumours at sites other than the lung was not reported. Such data would be of interest in view of the epidemiological evidence of bladder cancer. It is to be hoped that site-specific tumour incidences will be reported in future studies. In considering data on bladder tumours, it should be noted that there are species differences in their induction by certain classes of chemicals.

Nitroarenes

Nitroarenes are found mainly in engine exhausts, and diesel engines, especially, produce considerable amounts. Monographs on some nitroarenes are included in this volume on the basis of the availability of data on carcinogenic activity in experimental animals; no epidemiological data were available on individual nitroarenes. It should be noted that 6-nitrochrysene, 7-nitrobenz[*a*]anthracene, 3-nitroperylene, 2-nitropyrene and 4-nitropyrene have not been found in engine exhausts, although three of these (6-nitrochrysene, 2-nitropyrene and 4-nitropyrene) have been found in extracts of environmental airborne particles.

The nitroarenes found in engine exhausts are listed in Table 1. Some were evaluated previously (IARC, 1984), and only those for which additional data on carcinogenicity have become available since the earlier evaluation have been re-evaluated in this volume. It was originally planned to include 3,4-dinitrofluoranthene in this volume, but no data on its carcinogenicity were available. It induced DNA damage (Nakagawa *et al.*, 1987) and mutation in bacteria (Tokiwa *et al.*, 1986; Nakagawa *et al.*, 1987).

It should be noted that most of the biological data on the nitroarenes considered in this volume relate to the compounds alone; however, in the environment, nitroarenes occur predominantly in association with carbonaceous particles. As demonstrated in the monograph on 1-nitropyrene, association with particles substantially prolongs residence time. In the evaluation and testing of polycyclic aromatic compounds for carcinogenicity, detailed knowledge of impurities is important, and identification of possibly carcinogenic impurities is essential if lack of carcinogenicity is to be established and if a compound is carcinogenic only when administered at high doses. Thus, the levels of impurities present in a substance and the limit of detection of the analytical method used are stated as precisely as possible.

Genetic activity profiles were prepared for the individual nitroarenes but not for diesel or gasoline engine exhaust materials, since it would not be appropriate to plot data on complex mixtures on the basis of dissimilar samples. The most extensive data base exists for particle extracts of engine exhausts, for which the units (e.g., μg/ml for *in-vitro* tests and mg/kg for *in-vivo* tests) would be suitable for use in profiles.

Mindful of the procedures adopted in the preparation of earlier volumes in this series of *Monographs* (see Preamble, p. 15, section 4), the Working Group reviewed and referred to reports other than those published as part of the general scientific literature only when this was considered to be pertinent to making a final evaluation of carcinogenicity and provided that the reports were readily available. The Working Group wishes to draw attention to a series of peer-reviewed reports available from the Health Effects Institute (Cambridge, MA, USA) that include information on the health effects of automobile emissions and of some of the nitroarenes described in this volume.

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