

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 Evaluation¹

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)*.

¹For definitions of the italicized terms, see Preamble, pp. 25–28.

