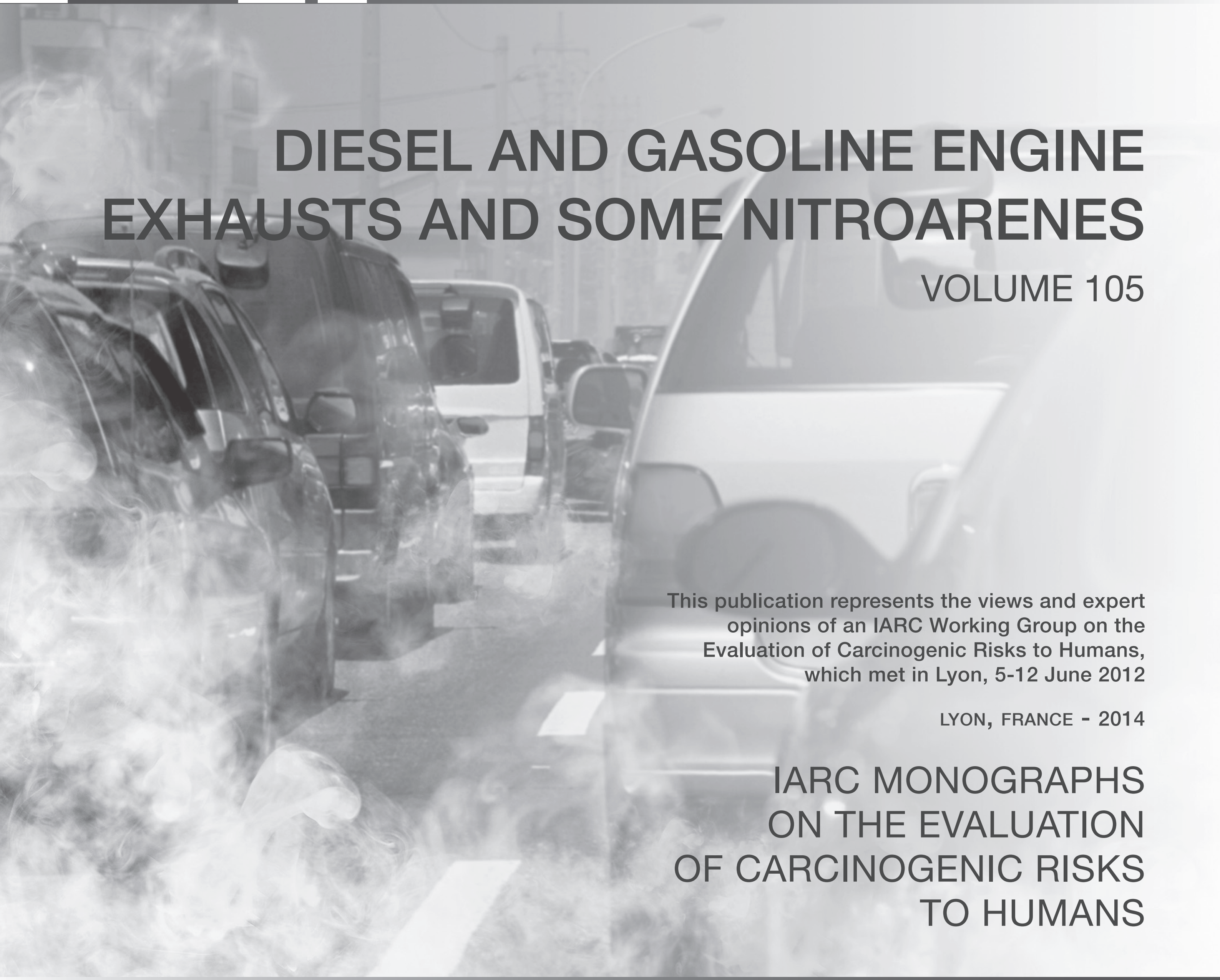
IARC MONOGRAPHS



# DIESEL AND GASOLINE ENGINE EXHAUSTS AND SOME NITROARENES

## VOLUME 105

This publication represents the views and expert opinions of an IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, which met in Lyon, 5-12 June 2012

LYON, FRANCE - 2014

## IARC MONOGRAPHS ON THE EVALUATION OF CARCINOGENIC RISKS TO HUMANS

International Agency for Research on Cancer

World Health Organization

# GENERAL REMARKS

This one-hundred-and-fifth Volume of the *IARC Monographs* contains evaluations of the carcinogenic hazard to humans of exposure to diesel and gasoline engine exhausts and 10 nitroarenes that have been identified as components of these exhausts. This Volume is the fifth in a series of *Monographs* that have evaluated exposures related to air pollution. In 2004, an *IARC Monographs* Advisory Group recommended that the IARC develop such a series, in view of the probable widespread human exposure to and potential carcinogenicity of these compounds (Straif *et al.*, 2013). The agents and related exposures evaluated to date following this recommendation include non-heterocyclic polycyclic aromatic hydrocarbons (Volume 92; IARC, 2010a), some particles and fibres (Volume 93; IARC, 2010b), indoor air pollution (Volumes 95, 100E; IARC, 2010c, 2012), and bitumens, bitumen emissions and some heterocyclic polycyclic aromatic hydrocarbons (Volume 103; IARC, 2013).

Diesel and gasoline engine exhausts were evaluated previously in Volume 46 of the *IARC Monographs* (IARC, 1989). At that time, diesel engine exhaust was classified as *probably carcinogenic to humans (Group 2A)* on the basis of *limited evidence* from epidemiological studies in humans and *sufficient evidence* for the carcinogenicity in experimental animals of whole diesel engine exhaust and of extracts of particles from diesel engine exhaust. The evaluation of gasoline engine exhaust in 1989 was based on *inadequate evidence* in humans and *sufficient evidence* in experimental animals for the carcinogenicity of condensates or extracts of gasoline engine emissions, which resulted in a classification of gasoline engine exhaust as *possibly carcinogenic to humans (Group 2B).* A series of 10 nitroarenes, all of which have been detected in diesel engine exhaust, was also reviewed. All of these nitroarenes, except for one (3-nitrobenzanthrone), were evaluated previously in Volume 46 of the *IARC Monographs* (IARC, 1989), when the Working Group classified six of them (1,3-dinitropyrene, 1,8-dinitropyrene, 6-nitrochrysene, 2-nitrofluorene, 1-nitropyrene and 4-nitropyrene) as *possibly carcinogenic to humans (Group 2B)* and three (3,7-dinitrofluoranthene, 3,9-dinitrofluoranthene and 1,3-dinitropyrene) as *not classifiable as to their carcinogenicity to humans* (Group 3).

A summary of the findings of this Volume appears in *The Lancet Oncology* (Benbrahim-Tallaa *et al.*, 2012).

## Diesel and gasoline engine exhausts

Diesel-driven engines are used for on-road traffic (e.g. passenger cars, buses and heavy goods vehicles), off-road transport (e.g. trains and ships), (heavy) equipment in various industrial sectors (e.g. mining and construction) and in electricity generators, particularly in developing countries. Gasoline-driven engines are used for cars and hand-held equipment (e.g. chainsaws). Emissions from these engines are complex and may vary widely in composition. The gas phase comprises carbon monoxide, nitrogen oxides and volatile organic compounds, such as benzene and formaldehyde. The particle fraction comprises elemental and organic carbon, ash, sulfate and metals. Polycyclic aromatic hydrocarbons and nitroarenes are distributed within the gas and the particle phases. The qualitative and quantitative composition of engine exhausts depends on the fuel, the type and age of the engine, the state of its tuning and maintenance, the use of an emission-control system and the pattern of use. The *Monograph* on diesel and gasoline engine exhausts is not a review of data on these individual compounds in engine exhausts, and covers only studies in which the whole exhaust or a major fraction of this exhausthas been investigated.

In anticipation of the availability of new epidemiological studies, an Advisory Group to the *IARC Monographs* Programme recommended in 1998 that diesel engine exhaust be treated as a high priority for re-evaluation because a large study by the US National Cancer Institute/National Institute for Occupational Safety and Health of occupational exposure to such emissions in underground miners was being performed at that time. The publication of the results of this study was delayed several times (Furlow, 2012), and the re-evaluation therefore was only undertaken after their publication in March 2012, together with updates of studies in the railroad and transport industry that included refined exposure assessments.

In evaluating the carcinogenic hazard of exposure to gasoline engine exhaust, the Working Group made attempts to disentangle their effects from those of diesel engine exhaust. Apart from those occupational environments in which diesel engine exhaust is the only or primary source of exposure (see above), many occupations involve exposures to a mixture of the two. Therefore, it is possible that a risk observed in association with exposure to gasoline engine exhaust is confounded by concomitant exposure to diesel engine emissions.

Every attempt was made to identify the exhaust tested in the cancer bioassays considered by the Working Group, taking into account the differences in the characteristics of exhausts from different types of motor (diesel/gasoline, light duty/heavy duty). When interpreting the results of studies of complex mixtures, it is important to characterize the exposures of the animals to the greatest extent possible. Therefore, with respect to experimental studies, several early bioassays in which the type of engine exhaust was not specified were not considered by the Working Group.

Diesel engine technology has changed over time in response to and in support of increasingly stringent regulations to control engine emissions. The stringency of these regulations has been increased most progressively for on-road light-duty vehicles, followed by heavy-duty on-road and off-road vehicles, and are at present largely absent for other heavy-duty engine applications, such as in trains and ships. Moreover, in many developing countries, emission standards are not enforced for either on-road or off-road use of diesel- or gasoline-driven engines. To meet the most stringent current emission-control regulations, diesel engines must be designed and constructed according to modern technology, which includes wall-flow particulate filters and diesel oxidation catalysts, in combination with the use of diesel fuel that has a very low sulfur content; the most rigorous technology measures will be required only after 2014. The new diesel engine technology has been shown to reduce particulate mass emissions by more than two orders of magnitude. Although the implications for carcinogenicity are not yet known, the 'new technology' diesel engines, due to their much lower emissions of particulate matter, will probably bring about an improvement with regard to public health. It should be noted that the human epidemiological studies reviewed in this *Monograph* were conducted before the introduction of the modern diesel engine technology.

## Nitroarenes, components of diesel engine emissions

Biomonitoring studies conducted in workers and the general population showed that both are exposed to these substances (Scheepers *et al.*, 1994; Seidel *et al.*, 2002; Zwirner-Baier & Neumann, 1999). All of the nitro- and dinitroarenes (nitroarenes that carry one or two nitro groups) evaluated in this Volume of *Monographs* were genotoxic to different extents in a series of genetic toxicology assays. In general, the dinitroarenes exhibited greater genotoxic activity than the mononitroarenes, which is consistent with their tumorigenic activities. Although only a few studies were available, the metabolites of several nitroarenes have been found in urine samples collected from populations exposed to diesel engine exhaust. Two major metabolic pathways were identified for this group of compounds. First, the reduction of the nitro group to produce the hydroxylamine, which––either by itself or after conjugation to a sulfate by sulfotransferases or conjugation to an acetate by *N*-acetyltransferases–– yields the ultimate carcinogenic aryl nitrenium ion that binds covalently to DNA to form adducts. In the case of dinitroarenes, only one nitro group is metabolically activated in this way. Second, ring oxidation to yield oxides, phenols and dihydrodiols, many of which are found as detoxification products conjugated to sulfate or glucuronic acid. Some nitroarenes formed products via both ring-oxidation and nitroreduction. Strong evidence of genotoxicity led to three nitroarenes being upgraded to *Group 2B* or *Group 2A*.

## References

Benbrahim-Tallaa L, Baan RA, Grosse Y *et al.*; International Agency for Research on Cancer Monograph Working Group (2012). Carcinogenicity of diesel-engine and gasoline-engine exhausts and some nitroarenes. *Lancet Oncol*, 13: 663–664. doi:10.1016/S1470-2045(12)70280-2 PMID:22946126

Furlow B (2012). Industry group “threatens” journals to delay publications. *Lancet Oncol*, 13: 337 doi:10.1016/S1470-2045(12)70094-3 PMID:22577661

IARC (1989). Diesel and gasoline engine exhausts. *IARC Monogr Eval Carcinog Risks Hum*, 46: 41–185. PMID:2483418

IARC (2010a). Some non-heterocyclic polycyclic aromatic hydrocarbons and some related exposures. *IARC Monogr Eval Carcinog Risks Hum*, 92: 1–853. PMID:21141735

IARC (2010b). Carbon black, titanium dioxide, and talc. *IARC Monogr Eval Carcinog Risks Hum*, 93: 1–413. PMID:21449489

IARC (2010c). Household use of solid fuels and high-temperature frying. *IARC Monogr Eval Carcinog Risks Hum*, 95: 1–430. PMID:20701241

IARC (2012). Personal habits and indoor combustions. *IARC Monogr Eval Carcinog Risks Hum*, 100E: 1–575. PMID:23193840

IARC (2013). Bitumens and bitumen emissions, and some *N*- and *S*- heterocyclic polycyclic aromatic hydrocarbons. *IARC Monogr Eval Carcinog Risks Hum*, 103: 1–342. Available at: http://monographs.iarc.fr/ENG/Monographs/vol103/index.php

Scheepers PTJ, Velders DD, Martens MHJ *et al.* (1994). Gas chromatographic-mass spectrometric determination of nitro polycyclic aromatic hydrocarbons in airborne particulate matter from workplace atmosphere. *J Chromatogr A*, 677: 107–121. doi:10.1016/0021-9673(94)80550-4

Seidel A, Dahmann D, Krekeler H, Jacob J (2002). Biomonitoring of polycyclic aromatic compounds in the urine of mining workers occupationally exposed to diesel exhaust. *Int J Hyg Environ Health*, 204: 333–338. doi:10.1078/1438-4639-00116 PMID:11885357

Straif K, Cohen A, Samet J (2013). *Air pollution and Cancer. IARC Scientific Publication No 161*, Lyon, France: International Agency for Research on Cancer.

Zwirner-Baier I & Neumann HG (1999). Polycyclic nitroarenes (nitro-PAHs) as biomarkers of exposure to diesel exhaust. *Mutat Res*, 441: 135–144. doi:10.1016/S1383-5718(99)00041-8 PMID:10224330