Cancérogénicité des effluents des moteurs diesel et essence et de certains hydrocarbures aromatiques polycycliques nitrés (nitro-HAP ou nitroarènes).

Carcinogenicity of diesel-engine and gasoline-engine Exhausts and some Nitroarenes

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In June 2012, an IARC *Monographs* Working Group reevaluated the carcinogenic hazards to humans of diesel and gasoline engine exhausts, and of some nitroarenes that are found in these emissions. Diesel engine exhaust was classified as "carcinogenic to humans" (Group 1) and gasoline engine exhaust as "possibly carcinogenic to humans" (Group 2B). The most influential epidemiological studies on cancer associated with diesel-engine exhausts were conducted among non-metal miners, railroad workers, and workers in the trucking industry in the USA. The miners study included a cohort analysis [Attfield *et al.*, 2012] and a nested case-control analysis that was adjusted for tobacco smoking [Silverman *et al.*, 2012]. Both showed positive trends in lung cancer risk with increasing exposure, with a 2-3-fold increased risk in the highest categories of cumulative or average exposure. There were few potential confounding exposures in these underground mines, and high exposures were well documented in current surveys. A 40% increased risk for lung cancer was observed in railroad workers exposed to diesel exhaust [Garshick *et al.*, 2004]. Indirect adjustment for smoking suggested that differences in smoking could not have influenced this excess risk substantially. When extended with more accurate exposure assessment, the study showed a 70-80% increase in risk for exposed workers positive trends were observed with duration of exposure, but not with cumulative exposure [Laden *et al.*, 2006]. A large cohort study in the US trucking industry [Garshick *et al.*, 2008] reported a 15-40% increased lung cancer risk in truck drivers and dockworkers with regular exposure to diesel exhaust. There was a significant trend of increasing risks with longer duration of employment, with 20 years of employment roughly doubling the risk after adjusting for tobacco smoking. These trends were more pronounced when adjustment for duration of work was included [Garshick *et al.*, 2008]. These findings were supported by those in other occupational groups and by case-control studies including various occupations involving similar exposures. An increased risk for bladder cancer was also noted in many case-control studies, but not in cohort studies. The Working Group concluded that there was *"sufficient evidence"* in humans for the carcinogenicity of diesel-engine exhaust. In experimental animals, whole diesel-engine exhaust caused an increased incidence of lung tumours in rats [Heinrich *et al.*, 1995], diesel-engine exhaust particles instilled intratracheally caused benign and malignant lung tumours in rats [Pott and Roller, 1995], and extracts of the particles also caused lung carcinomas in rats and sarcomas at the injection site in mice [Kunitake *et al.*, 1986 ; Grimmer *et al.*, 1987]. The Working Group concluded that there was *"sufficient evidence"* in experimental animals for the carcinogenicity of these three agents, which also induced, *in vitro* and *in vivo*, various forms of DNA damage. Gas-phase diesel-engine exhaust – without particles – did not increase the incidence of respiratory tumours in any species tested. Positive genotoxicity biomarkers of exposure and effect were also observed in humans exposed to diesel engine exhaust. The Working Group concluded that there is "strong evidence" for the ability of whole diesel-engine exhaust to induce cancer in humans through genotoxicity.

Gasoline exhaust and cancer risk was investigated in only a few epidemiological studies and, because of the difficulty to separate the effect of diesel and gasoline exhaust, evidence for carcinogenicity was evaluated as "inadequate". Organic extracts of gasoline engine-exhaust condensate induced a significant increase in lung carcinomas and papillomas of the skin in mice [Brune *et al.*, 1978]. In rats, the gasoline exhaust condensate induced a significant increase in lung carcinomas [Grimmer *et al.*, 1984]. The Working Group concluded that there was "sufficient evidence" in experimental animals for the carcinogenicity of condensates of gasoline-engine exhaust.

Evaluation for the nitroarenes, all of which have been detected in diesel engine exhaust, each of them carrying one or two nitro groups, are shown in Table 1. No epidemiological studies of these nitroarenes have been reported but studies have shown that workers and also the general population are exposed to these

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substances [Scheepers *et al.*, 1994 ; Seidel and Dahmann, 2002 ; Zwirner-Baier and Neumann, 1999]. All the nitroarenes studies were genotoxic to different extents in a series of assays. The Working Group reaffirmed the Group 2B classification of seven of theses nitroarenes. Studies in experimental systems provided strong evidence for genotoxicity, which led to an upgrade for 1-nitropyrene, 6-nitrochrysene (to Group 2A), and 3-Nitrobenzanthrone (to Group 2B) (see table for details).

Tableau I.
Evaluation of the nitroarenes.

Agent	Evidence of carcinogenicity in experimental animals	Mechanistic evidence	Overall evaluation
3,7-Dinitrofluoranthene	Sufficient	Weak	2B
3,9-Dinitrofluoranthene	Sufficient	Weak	2B
1,3-Dinitropyrene	Sufficient	Weak	2B
1,6-Dinitropyrene	Sufficient	Moderate	2B
1,8-Dinitropyrene	Sufficient	Moderate	2B
3-Nitrobenzanthrone	Limited	Strong	2B*
6-Nitrochrysene	Sufficient	Strong	2A*
2-Nitrofluorene	Sufficient	Weak	2B
1-Nitropyrene	Sufficient	Strong	2A*
4-Nitropyrene	Sufficient	Moderate	2B

*Strong mechanistic evidence contributed to the overall evaluation (see text).

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