

CARBON BLACK

(Group 2B)

[The text of these Summaries and Evaluations may be edited for language and clarity during the checking of the main text of the Monographs.]

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5. Summary of Data Reported

5.1 Exposure data

Carbon black is a generic term for a particulate form of elemental carbon manufactured by the vapour-phase pyrolysis and partial combustion of hydrocarbons. Carbon blacks are categorized, on the basis of different production processes by which they are made, as acetylene black, channel black, furnace black, lampblack or thermal black. Acetylene, furnace and thermal blacks have been produced since the early twentieth century. Over 95% of all carbon black produced today is furnace black. Worldwide production capacity of carbon black in 2005 was approximately 10 million tonnes.

Carbon blacks are characterized by the size distribution of the primary particles and the degree of their aggregation and agglomeration. Human exposure is primarily to carbon black particles in aggregate and agglomerate forms. Average aggregate particle diameters in several commercially produced carbon blacks range from 50 to 600 nm and the more loosely associated agglomerates can reach up to many micrometers in diameter. The majority of carbon blacks currently manufactured have small quantities (< 1%) of organic compounds, including polycyclic aromatic hydrocarbons, adsorbed onto their surface.

About 90% of carbon black is used in rubber products, predominantly in tyres. Carbon black is also used as a pigment in inks, paints and coatings and in plastics.

Exposures to carbon black vary markedly between and within production facilities and over time. The highest levels of exposure are experienced by packers and site cleaners. Some studies prior to 1970 found that extremely high levels of carbon black exposure could have occurred in the carbon black manufacturing industry. Exposure studies in this industry in the USA and western Europe after the late 1970s found personal inhalable dust exposures to be less than 5 mg/m³ (geometric mean). By the mid to late 1990s the inhalable dust levels were below 2 mg/m³ (geometric mean); the respirable dust levels were below 0.5 mg/m³. No data were available that would allow the characterization or quantification of exposure to ultrafine primary particles. Exposure in the user industries is difficult to assess because of the lack of data from such industries and concomitant exposure to many other particles. However, exposure levels are assumed to be lower in the user industries, with the possible exception of workers who handle large quantities of carbon black. No significant exposure to carbon black is thought to occur during the use of products in which carbon black is bound to other materials, such as rubber, printing ink or paint.

5.2 Human carcinogenicity data

The greatest potential for elucidating the carcinogenicity of carbon black is in the carbon black production industry where it has been the prime industrial exposure. Cohort studies of carbon black production workers have been conducted in the United Kingdom, Germany and the USA.

The study of workers in five carbon black production facilities in the United Kingdom involved a large group with a long follow-up. When compared with national mortality rates, there was a clear excess of mortality from lung cancer. Although smoking histories were not known, there was no corresponding excess of other diseases known to be associated with smoking. The excess risk was manifest in two of the five factories. Exposure was assessed using last job from worker records and a job–exposure matrix based on expert judgement and measurements from two of the five plants. When adjusted for age and divided into four subgroups based on cumulative exposure levels, relative risk for lung cancer did not increase monotonically with increasing exposure, although the two highest exposure categories showed higher relative risks than the two lowest categories. There was no excess risk for cancer at any other site.

A cohort study was conducted among blue-collar workers in a long-standing, large German carbon black production plant. When mortality was compared with regional rates, there was an approximate doubling of risk for lung cancer. Exposure was assessed using full work history records from the plant and expert judgements. Further, company medical records provided some information on tobacco smoking for most of the workers. Compared with the lowest exposure group, after adjusting for smoking, and using several indices of exposure, there was no indication that workers with higher exposure to carbon black had higher risks. However, the precision of these subgroup risk estimates was low. There were no excess risks for most other cancer sites, including oesophagus, stomach and urinary bladder, although the numbers were small.

Another group of investigators analysed the same German cohort of carbon black workers, but used rather different methods. They confirmed that there was no exposure–response relationship within the cohort between estimated exposure to carbon black and lung cancer. After accounting for regional variations in cancer and different methods of adjustment for tobacco smoking and other exposures, the overall risk for lung cancer was slightly elevated, although the Working Group was not persuaded that all the adjustments were warranted.

The US study included a large cohort of workers from 18 plants with good ascertainment of cohort members and effective mortality follow-up over a long period of time. There was no indication of excess risk for cancer at any of the reported cancer sites. There was no indication that long-service workers had higher risks than short-service workers. For most types of cancer, including lung cancer, the numbers of deaths observed did not exceed the numbers expected on the basis of national rates. No results were provided according to levels of exposure to carbon black, and the analyses did not take into account tobacco smoking habits.

Additional evidence is provided by studies of workers who were exposed to carbon black in some other industries.

Within a study of a large cohort of German rubber industry workers, an attempt was made to assess exposure to carbon black. The exposure assessment was rather crude. In statistical analyses of carbon black without other exposure variables as potential confounders, there were significant excess risks for lung cancer and for stomach cancer. When exposure to nitrosamines, asbestos and talc were considered, the excess risks were no longer statistically significant.

A cohort study was carried out among workers in the USA to assess cancer risks due to exposure to formaldehyde in 10 participating plants that were spread across several industries. To control for confounding and modification of effect by other exposures, workers' exposures to various other chemicals, including carbon black, were assessed by industrial hygienists. Overall, among carbon black-exposed workers, there was a slight non-significant excess of lung cancer. There was no clear trend by duration of exposure.

A study of Italian dockyard workers was based on the undocumented but reasonable premise that those who unloaded and carried bags of carbon black experienced exposures. Apart from mesothelioma and malignant melanoma, neither of which was probably attributable to exposure to carbon black, only one cancer site – urinary bladder – showed some evidence of a statistically significant excess. For lung cancer, stomach cancer and cancer at several other sites, there was no indication of excess risk.

In a community-based case–control study in Montreal, Canada, interviews were designed to obtain detailed lifetime job histories and information on potential confounders. Potential occupational exposures were identified for each job description; carbon black was among the exposures assessed. Few if any of the exposed subjects had worked in the manufacture of carbon black. Many workers were exposed to carbon black in bound matrices such as paint or rubber. It is probable that workers exposed to carbon black in this study were exposed to lower levels than those in other studies. There was indication of excess risk in relation to relatively high exposure to carbon black and cancer of the lung, oesophagus and kidney, but not for cancer of the stomach, urinary bladder or at other sites.

A Swedish community-based case–control study reported a non-statistically significantly increased risk for urothelial cancer for men exposed to carbon black.

Overall, seven studies were considered to be informative for lung cancer, of which three were among carbon black production workers. The Working Group considered the studies of carbon black production workers in the United Kingdom, Germany and the USA to be the most informative for assessing cancer risk. The two studies from the United Kingdom and Germany indicated excess risk compared with external references. Confounding by smoking could not be excluded, although it was unlikely to have explained the entire excess risk. However, in both cohorts, internal analyses by level of exposure to carbon black gave equivocal but mainly null results. The study of carbon black workers in the USA suggested no excess mortality, but did not assess risk by level of exposure. In studies that assessed risks for lung cancer among user industries, the most informative study of German rubber workers showed some indication of excess risk that disappeared when asbestos and talc were adjusted for in the analysis. Of the remaining studies, two others showed non-significant excesses (US formaldehyde cohort and the Canadian community-based case–control study) and one showed no excess risk for lung cancer linked to the handling of carbon black (Italian dockworkers).

For cancers of the urinary bladder, kidney, stomach and oesophagus, isolated results indicate excess risks, but these are not sufficient to support an evaluation of human carcinogenicity. There is no evidence of an effect of carbon black for other cancer sites.

5.3 Animal carcinogenicity data

Two different carbon black products were tested by inhalation exposure in two studies in female rats and in one study in rats of both sexes. Significant increases in the incidence of malignant lung tumours and the incidence of benign and malignant lung tumours combined were observed in female rats in all three studies. In addition, increased incidences of lesions described as benign cystic keratinizing squamous-cell tumours or squamous-cell cysts were observed. In one study in female mice exposed by inhalation, carbon black did not increase the incidence of respiratory tract tumours.

There were three studies of intratracheal administration to female rats: one study used two types of carbon black, another study used toluene extracts of two types of carbon black, and the third used a single type of carbon black. All three studies showed an increased incidence of benign and malignant lung tumours. In several studies of dermal application in mice that used various carbon blacks (some of which are no longer commercially available), no carcinogenic effect on the skin was observed; the dermal application of benzene extracts of several carbon blacks resulted in skin tumours. In a series of studies in male and female mice using the same types of carbon black by subcutaneous injection, a carbon black that contained demonstrable quantities of carcinogenic polycyclic aromatic hydrocarbons produced local sarcomas, whereas a carbon black in which no polycyclic aromatic hydrocarbon was detected did not produce such sarcomas. In several studies in mice, solvent extracts of carbon black produced sarcomas following subcutaneous injection.

No adequate study of the carcinogenicity of carbon black administered by the oral route was available.

5.4 Mechanistic considerations and other relevant data

The deposition pattern of carbon black particles depends on the particle size (aerodynamic or thermodynamic) and on the anatomical and physiological characteristics of the host. The deposition fraction of carbon black influences the dose to a given region of the respiratory tract. Several studies describe the retention of carbon black in the respiratory tract of exposed workers, as well as the health effects of these exposures. For example, lung tissues from workers in carbon black factories contain deposits of carbon black. Lung diseases or conditions may influence the deposition and retention of particles such as carbon black. For instance, asthmatics had a higher total deposition of ultrafine carbon particles in the respiratory tract compared with healthy individuals. The amount of carbon particles deposited can also increase with increasing minute ventilation, for instance in individuals taking exercise or during heavy physical labour. High retained mass lung burdens and decreased lung clearance have been observed in coal miners.

Non-cancer respiratory effects in carbon black workers that have been reported include cough, sputum production, bronchitis, chest radiographic opacities (e.g. pneumoconiosis) and decrements in lung function.

There are many studies on the deposition and retention kinetics of inhaled carbon particles following intratracheal instillation or inhalation in rodents. In general, all rodent species investigated show evidence of rapid clearance of inhaled carbon particles when exposure concentrations did not result in impaired clearance resulting in accumulation of particles in the lung (i.e. lung overload). The experimental studies of ultrafine particles of carbon black have shown that rodents experience dose-dependent impairment of alveolar macrophage-mediated clearance, which occurs at lower mass doses of ultrafine particles than with larger particles. Overloading has been observed in rats, mice and hamsters exposed to carbon black. Hamsters appear to exhibit the most efficient clearance of carbon black particles compared with rats and mice. Adverse lung responses to inhaled carbon black (pulmonary inflammation and epithelial injury) increase significantly with increasing retained lung dose of carbon black particles. Fine and ultrafine carbon black particles can translocate beyond the lungs to other organs.

A number of toxic effects of carbon black have been reported in various rodent species. The toxic effects reported are dose-dependent and include inflammation, lung epithelial cell injury and lung lesions that are more severe and prolonged in rats than in mice and hamsters. Exposure to carbon black particles modulates the immune system. In-vitro studies show evidence that carbon black particles can generate reactive oxygen species in cell-free systems, increase the production of tumour necrosis factor- α and activate serum factors such as complement.

The genotoxicity of carbon black has been evaluated in various in-vivo and in-vitro systems. In rats exposed to carbon black by inhalation for 13 weeks, the *Hprt* mutant frequency and the level of pro-mutagenic 8-oxo-deoxyguanosine adducts were elevated in lung epithelial cells. *In vitro*, catalase inhibited the increase in *Hprt* mutation frequency in lung epithelial cells induced by lavage fluid from carbon black-instilled rats, which implies a role for cell-derived oxidants in this response. In two of five studies, carbon black induced an increase in DNA adducts in the peripheral lung tissue of rats after inhalation exposure. Mutations in *K-Ras* and *p53* do not seem to be induced by exposure to carbon black. In separate in-vitro studies with hamster cells, carbon black caused micronucleus induction and cell transformation, but no sister chromatid exchange. The results of most bacterial mutagenicity studies of carbon black were negative.

6. Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of carbon black.

There is *sufficient evidence* in experimental animals for the carcinogenicity of carbon black.

There is *sufficient evidence* in experimental animals for the carcinogenicity of carbon black extracts.

Overall evaluation

Carbon black is *possibly carcinogenic to humans (Group 2B)*.

Rationale

To follow

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