Carcinogenicity of carbon black, titanium dioxide, and talc

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In February, 2006, 19 scientists from eight countries met at the International Agency for Research on Cancer (IARC), Lyon, France, to reassess the carcinogenicity of carbon black, titanium dioxide, and non-asbestiform talc. These assessments will be published as volume 93 of the IARC Monographs,[1] and are the first assessments since the IARC Monograph preamble was amended.[2]

All three of the above agents are poorly soluble particles that are weakly toxic, and were chosen for assessment because evidence suggests that they cause cancer in the respiratory tract of rats through similar mechanisms: after exposure to high concentrations of these agents, deposition of particles onto the respiratory epithelium can lead to enhanced particle retention, impaired lung clearance, inflammatory response, production of reactive oxygen species, cell injury, cell proliferation, fibrosis, induction of mutations, and, ultimately, cancer. Because many of these steps arise in people who work in dusty environments (eg, coal miners),[3,4] data on cancer in animals obtained in conditions of impaired lung clearance could be relevant to human beings. Furthermore, impaired lung clearance and adverse effects in the lungs of rats that have been exposed to ultrafine particles (<100 nm) occur at much lower mass concentrations than in rats exposed to fine particles (<10 µm), increasing the potential relevance to human beings.

Carbon black is a particulate form of elemental carbon. About 90% of carbon black is used in rubber products, mainly tyres. Carbon black is also used as a pigment in inks, paints and coatings, and in plastics. Exposure to carbon-black particles occurs mainly in the form of aggregates (ie, particle size, 50–600 nm) and agglomerates (227 µm). Most types of carbon black have small quantities (ie, <1%) of organic compounds, including polycyclic aromatic hydrocarbons, adsorbed onto their surface. The highest exposures to carbon black arise during its manufacturing. Exposure in industries that use carbon black is difficult to assess because data are scarce. No substantial exposure to carbon black is thought to occur when it is bound to other materials such as rubber, printing ink, or paint.

Workers who produced carbon black in Germany[5] and the UK[6] had an excess risk of lung cancer. Confounding by smoking was unlikely to explain the entire excess risk, but no clear dose-response relation between exposure to carbon black and lung cancer was noted. A US study[7] of workers in carbon black production found no excess risk of lung cancer, but no data according to level of exposure were reported. A study[8] of workers in the rubber industry in Germany who were exposed to carbon black showed no significant excess risk of lung cancer after adjustment for potential confounding by asbestos and talc. The working group concluded that the epidemiological studies of carbon black provided inadequate evidence of carcinogenicity.

Carbon black and its extracts have been tested in rats and mice by inhalation, intratracheal instillation, dermal application, and subcutaneous injection. The overall results provided sufficient evidence in laboratory animals for the carcinogenicity of carbon black and carbon-black extracts. The working group classified carbon black as possibly carcinogenic to human beings (ie, group 2B).

Titanium dioxide accounts for 70% of the total production volume of pigments worldwide. The primary particles are typically 200–300 nm in diameter, but larger aggregates and agglomerates are formed readily. Ultrafine grades of titanium dioxide (ie, 10–50 nm) are used in sunscreens and plastics to block ultraviolet light, and in catalysts. Highest exposures occur in titanium-dioxide production during packing, milling, site cleaning, and maintenance. Exposure data for industries that use titanium dioxide are scarce.

The largest epidemiological cohort study[9] considered included workers in the titanium dioxide production industry in six European countries, and showed a small but significant increase in risk of lung cancer compared with that for the general population; however, the data did not suggest an exposure-response relation. Two cohort studies undertaken in the USA did not report excess risks of lung cancer, neither did a Canadian population-based case-control study. Overall, the working group concluded that the epidemiological studies on titanium dioxide provide inadequate evidence of carcinogenicity.

Pigment-grade titanium dioxide and ultrafine titanium dioxide have been tested in rats, mice, and hamsters by various routes of administration. Overall, results from studies of inhalation and intratracheal instillation provided sufficient evidence in animals for the carcinogenicity of titanium dioxide. The working group classified titanium dioxide as possibly carcinogenic to human beings (ie, group 2B).

Talc refers to both mineral talc and industrial products that contain 35% to >95% mineral talc. Mineral talc

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occurs naturally in a platy (flat) form, but also as asbestiform fibres; it is generally associated with other minerals, for instance, quartz and occasionally asbestos. Asbestiform talc should not be confused with talc that contains asbestos. Talc is used in agricultural products, ceramics, cosmetics, paint and other coatings, paper, pharmaceuticals, plastics, roofing materials, rubber, and for waste treatment. Occupational exposure to talc arises during mining, milling, and industrial use. Consumers are exposed during the use of loose talc-based powders—eg, baby powders and body powders used by women on the perineum or genital area.

Cohort studies from various countries of talc miners and millers were available for assessment. In US miners,[10] an excess risk of lung cancer was noted, but this risk could have been due to exposure to radon and quartz. The other cohort studies did not report an increased cancer risk. A nested case-control study of cohorts in France and Austria[11] found no higher risk of lung cancer with increasing cumulative exposure to talc dust. A study[12] of women working in the Norwegian pulp and paper industry noted an increased risk of ovarian cancer, but this risk was attributed to asbestos exposure. The working group concluded that the epidemiological studies provided inadequate evidence for the carcinogenicity of inhaled talc that does not contain asbestos or asbestiform fibres.

Talc has been tested in rats, mice, and hamsters by various routes of administration. A long-term inhalation study[13] showed increased incidences of alveolar or bronchiolar carcinoma in female rats and adrenal pheochromocytoma in rats of both sexes. This increase in incidence provided limited evidence for carcinogenicity in animals. Overall, the working group concluded that inhaled talc that does not contain asbestos or asbestiform fibres is not classifiable as to its carcinogenicity (ie, group 3).

Particular attention was paid to epidemiological data from a prospective cohort study[14] and from 19 case-control studies on the association between use of talc-based body powder and risk of ovarian cancer. Although the cohort study[14] did not lend support to an association, the case-control studies showed a high degree of consistency: the eight more-informative studies[15–22] reported a 30–60% increase in risk, and most of the other studies noted similar relative risks. Only two studies[18,20] suggested that women with the highest exposure had the highest risk. The case-control studies could have been affected by recall bias, if women with ovarian cancer were more likely to over-report body-powder use. These powders generally contain quartz. Furthermore, low concentrations of asbestos were occasionally present in these powders before the mid-1970s, but the available information is sparse and poorly reported, and analyses were often inadequate to identify the fibres detected. After careful assessment of the biases and possible confounding factors, the working group concluded that the epidemiological studies provided limited evidence for the carcinogenicity of perineal use of talc-based body powder, and classified this use as possibly carcinogenic to human beings (ie, group 2B).

The authors declare no conflicts of interest.

1 IARC. IARC monographs on the evaluation of carcinogenic risks to humans. Volume 93. Carbon black, titanium dioxide, talc. Lyon: International Agency for Research on Cancer (in press).

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