# CHROMIUM AND CHROMIUM COMPOUNDS: CHROMIUM METAL (Group 3) TRIVALENT CHROMIUM COMPOUNDS (Group 3) HEXAVALENT CHROMIUM COMPOUNDS (Group 1*)

A. Evidence for carcinogenicity to humans (*inadequate* for chromium metal and trivalent chromium compounds; *sufficient* for hexavalent chromium compounds)

An increased incidence of lung cancer has been observed among workers in both the bichromate-producing industry and chromate-pigment manufacturing. There is evidence of

*This evaluation applies to the group of chemicals as a whole and not necessarily to all individual chemicals within the group (see also Methods, p. 38).

a similar risk among chromium platers and chromium alloy workers. The incidences of cancers at other sites may also be increased in such populations. However, a clear distinction between the relative carcinogenicity of chromium compounds of different oxidation states or solubilities has been difficult to achieve[1].

Recent studies of chromate-pigment makers and users[2-10], chrome platers[11], welders[12-16] and chrome-alloy foundry workers[17] have shed some light on this problem. For chromate-pigment makers and users, respiratory cancer excesses have usually been found. Chromium pigments are usually hexavalent and commonly include zinc, lead (see p. 230) or strontium chromate. A small Norwegian study identified 24 workers primarily exposed to zinc chromate out of a total chromium-pigment worker population of 133. All six lung cancer cases, with more than three years' exposure, occurred among the zinc chromate group (0.14 expected)[9]. One report from the UK contrasts the mortality experience of three plants, in one of which only lead chromate was used. The lung cancer excess was restricted to the plants in which there was mixed exposure to lead and zinc chromate. In the lead chromate plant, there was no lung cancer excess, whereas in the other two the observed:expected ratios for high-/medium-exposed workers ranged from 13:5.9 to 5:0.9[10].

Chrome platers have also been found to have excess lung cancer[11]. Stainless-steel welding involves the greatest exposure to hexavalent chromium, as well as to nickel[14] (see p. 264), and observed:expected ratios for lung cancer for this subgroup of welders ranged from 4.4 (based on three cases)[12] to 1.7 (based on six cases)[13]. One study of chromium-nickel alloy foundry workers showed a statistically significant excess of lung cancer in the 65-99-year age group only[17].

Excess ratios for tumours at other sites are an unusual finding, but they have been reported for chromate paint workers (gastrointestinal tract)[1,18], chromate-pigment users (stomach and pancreas)[6] and chrome platers (gastrointestinal tract)[11]. The observed numbers are, however, small, and the observed:expected ratios do not reach statistical significance. In a post-mortem investigation of lung cancer deaths, it was found that, of the cases diagnosed as small-cell carcinoma, many had been exposed mainly to hexavalent chromium compounds[19].

**B. Evidence for carcinogenicity to animals** (*inadequate* for chromium metal and trivalent chromium compounds; *sufficient* for hexavalent chromium compounds)

Chromium metal and chromium compounds have been tested for carcinogenicity by a wide variety of routes in mice, rats and rabbits. Calcium chromate produced bronchial carcinomas after implantation of an intrabronchial pellet in rats[1,20] and injection-site sarcomas after intramuscular implantation in rats and mice and after intrapleural injection in rats[1]. Bronchial carcinomas were produced in rats after intrabronchial implantation of strontium chromate and zinc chromate[20]. Injection-site sarcomas were produced in rats and mice after intramuscular, intrapleural and subcutaneous injections of chromite ore, strontium chromate, chromium trioxide, lead chromate and zinc chromate, but few or no sarcomas were induced by barium chromate, sodium chromate or dichromate, or chromic acetate. Chromium powder has been tested inadequately in mice, rats and rabbits[1].

## C. Other relevant data

The available evidence indicates that the carcinogenicity of chromium-containing materials can be related to both valency and bioavailability. Trivalent and hexavalent chromium have markedly different chemical and biological properties. Trivalent chromium is the more stable oxidation state, and under physiological conditions it may form complexes with ligands such as nucleic acids, proteins and organic acids. Biological membranes are thought to be impermeable to trivalent chromium, although phagocytosis of particulate trivalent chromium can occur. Hexavalent chromium usually forms strongly oxidizing chromate and dichromate ions, which readily cross biological membranes and are easily reduced under physiological conditions to trivalent chromium. Trivalent chromium compounds may be contaminated with hexavalent chromium compounds (and *vice versa*)[21]. Chromium compounds that are sparingly soluble in water appear to have greater carcinogenic activity than those substances that are either highly soluble or insoluble.

People occupationally exposed to hexavalent chromium compounds (in chromate production and in electroplating factories) had elevated incidences of chromosomal aberrations in their peripheral blood lymphocytes; reports on sister chromatid exchange induction were conflicting. Workers exposed to chromium compounds during stainless-steel welding did not show increased incidences of chromosomal aberrations, micronuclei or sister chromatid exchanges in peripheral blood lymphocytes[21].

No data were available on the genetic and related effects of trivalent chromium compounds in humans.

Hexavalent chromium induced dominant lethal mutations, chromosomal aberrations and micronuclei in rodents treated *in vivo*. In human cells *in vitro*, it caused chromosomal aberrations, sister chromatid exchanges and DNA damage. In cultured rodent cells, it induced transformation, chromosomal aberrations, sister chromatid exchanges, mutation and DNA damage. It induced aneuploidy in *Drosophila* and mitotic recombination in yeast. It was mutagenic and caused DNA damage in bacteria[21].

There is no consistent evidence that water-soluble trivalent chromium has genetic activity. The few positive results were obtained only with doses about 100 times higher than those of hexavalent chromium required to produce such effects[21].

Trivalent chromium did not induce micronuclei in bone-marrow cells of mice treated *in vivo*. Conflicting results were obtained for the induction of chromosomal aberrations in human lymphocytes *in vitro*, and neither sister chromatid exchange nor unscheduled DNA synthesis was induced in human cells *in vitro*. Conflicting results were obtained concerning the induction of chromosomal aberrations, mutation and sister chromatid exchanges in rodent cells in culture. Trivalent chromium did not induce mutation in bacteria, but it induced DNA damage[21].

Insoluble crystalline chromium oxide ($Cr_2O_3$) induced sister chromatid exchanges and mutation in cultured Chinese hamster cells, which were shown to contain particles of the test material[21].

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