

## Cobalt Sulfate

### CAS No. 10124-43-3

Reasonably anticipated to be a human carcinogen  
First Listed in the *Eleventh Report on Carcinogens* (2004)



### Carcinogenicity

Cobalt sulfate is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals. When administered by inhalation, cobalt sulfate heptahydrate (cobalt sulfate in a form associated with water molecules) significantly increased the incidences of combined malignant and benign tumors at multiple tissue sites in two species of experimental animals. It caused lung tumors in male and female mice and in female rats and adrenal-gland tumors in female rats. Evidence of carcinogenicity in male rats was limited to significant increases in the incidence of lung tumors at the highest exposure level (NTP 1998).

No studies in humans were found that evaluated the carcinogenicity of exposure specifically to cobalt sulfate. However, several studies evaluated the carcinogenicity of cobalt compounds as a class. Most of these studies investigated the effects of occupational exposure to hard metals (cobalt and tungsten carbide) or metallic cobalt (Lasfargues *et al.* 1994, Moulin *et al.* 1998, Wild *et al.* 2000). Although these studies consistently reported an increased risk of lung cancer among workers exposed to cobalt, the workers were also exposed to other agents (e.g., tungsten carbide) and probably were not exposed to soluble cobalt. Thus, these studies are of uncertain relevance for evaluating whether exposure specifically to cobalt sulfate causes cancer. Only one study investigated the effects of exposure to cobalt salts. The initial study reported an increased risk of lung cancer among cobalt production workers, but a follow-up study of the same workers found no increased risk of cancer (Mur *et al.* 1987, Moulin *et al.* 1993). Interpretation of this finding is limited by the small number of exposed workers who developed cancer.

### Additional Information Relevant to Carcinogenicity

The hydrated and non-hydrated forms of a solute will behave similarly when dissolved in water, both forming a solution of hydrated ions and water. For inhalation exposure studies with animals, the exposure atmospheres were generated as aerosols of cobalt sulfate heptahydrate, containing cobalt ions, sulfate ions, and water, which were partially dried before they entered the exposure chambers (NTP 1998).

Cobalt sulfate did not cause mutations in most bacterial test systems studied, but it did cause genetic damage in many test systems using mammalian cells (NTP 1998). In Syrian hamster embryo cells, cobalt sulfate caused cell transformation (Kerckaert *et al.* 1996) and micronucleus formation (Gibson *et al.* 1997). In mouse fibroblasts, it caused expression of the *p53* tumor-suppressor gene (Duerksen-Hughes *et al.* 1999). In the presence of hydrogen peroxide, cobalt sulfate induced single-strand breaks and apparent intrastrand cross-links in DNA, but not the formation of 8-hydroxy-2'-deoxyguanosine adducts (Lloyd *et al.* 1997, Lloyd *et al.* 1998). In human lymphocytes (white blood cells), cobalt sulfate heptahydrate decreased the mitotic index (the proportion of cells undergoing division) but did not cause micronucleus formation or chromosomal aberrations (changes in chromosome structure or number) (Olivero *et al.* 1995).

As a constituent of vitamin B<sub>12</sub> (cobalamin), cobalt is absorbed from the gastrointestinal tract, lungs, and skin and distributed throughout the body. The highest concentrations are found in the liver, kidney, and heart. Cobalt is eliminated primarily in the urine, in two phases; the first phase is rapid and occurs within days, and the second may take several years (Léonard and Lauwerys 1990).

The mechanism by which cobalt ions cause cancer has not been determined. It has been suggested that cobalt may replace other essential divalent metal ions (e.g., magnesium, calcium, iron, copper, or zinc), thus altering important cellular functions. Other potential mechanisms include inhibition of DNA repair and interaction with hydrogen peroxide to form reactive oxygen species that can damage DNA (Beyersmann and Hartwig 1992, Lison *et al.* 2001).

### Properties

Cobalt sulfate is a metallic salt occurring as red to lavender crystals or powder. It has a molecular weight of 155, a melting point of 73°C, and a specific gravity of 3.71 (25°C/4°C). It is soluble in water (36.2 g/100 mL at 20°C), slightly soluble in methanol, and insoluble in ammonia (HSDB 2003).

Cobalt sulfate heptahydrate occurs as red to pink crystals. It has a molecular weight of 281.1, a melting point of 96.8°C, and a specific gravity of 1.948 (25°C/25°C). The heptahydrate form is soluble in water (60.4 g/100 mL at 3°C) (HSDB 2003).

### Use

Cobalt sulfate is used in the electroplating and electrochemical industries; as a drier for lithographic inks, varnishes, paints, and linoleum; in storage batteries; and as a coloring agent in ceramics, enamels, glazes, and porcelain. In addition, cobalt sulfate has been used in animal feeds as a mineral supplement (Budavari *et al.* 1996, Herman *et al.* 1999) and has been used on pastures where the forage is cobalt deficient to provide enough cobalt for ruminants (e.g., cattle, sheep, or goats) to produce vitamin B<sub>12</sub> (EPA 1999, Washington State 1999). Past uses include addition to beers to improve the stability of the foam (NTP 1998), to prevent and treat cobalt deficiency in ruminants, and to improve blood values (hematocrit, hemoglobin, and erythrocyte levels) in people with forms of anemia not responsive to other treatments (Hillman and Finch 1985, HSDB 2003).

### Production

Cobalt sulfate is formed by the interaction of cobalt oxide, hydroxide, or carbonate with sulfuric acid. Production of cobalt sulfate in the United States in 1983 was estimated at 450,000 lb (204,500 kg) (NTP 1998). No other, more recent production data were available. Cobalt is no longer mined or refined in the United States, but negligible amounts are produced as byproducts of other mining operations (USGS 2003). There were 17 U.S. suppliers of cobalt sulfate in 2003 (ChemSources 2003). Imports of cobalt sulfate in 1986 were 79,700 lb (36 metric tons) (HSDB 2003). Between 1995 and 2001, U.S. imports of cobalt sulfate ranged from about 900 to over 1,600 metric tons per year (2 to 3.5 million pounds) (USGS 2003). No information on cobalt sulfate exports was found.

### Exposure

No information was found on environmental exposure specifically to cobalt sulfate. The general population may be exposed to cobalt through inhalation of ambient air or ingestion of food or drinking water (ATSDR 2004). Cobalt is an essential trace element in humans, because a cobalt atom is present in each molecule of vitamin B<sub>12</sub> (Anderson 2000). The 1999 National Health and Nutrition Examination Survey reported the geometric mean cobalt level in the urine of humans to be 0.36 µg/L of urine (95% confidence interval = 0.32 to 0.40) (CDC 2001).

No information was found on occupational exposure specifically to cobalt sulfate. However, more than a million U.S. workers potentially are exposed to cobalt or cobalt compounds (Jensen and Tüchsen 1990). Workers in the hard-metal, coal and metal mining, smelting and refining, cobalt dye painting and cobalt chemical production industries are potentially exposed to high levels of cobalt (ATSDR 2004). In

addition, many workers receive limited exposure when using cobalt-containing paint driers. Occupational exposure is primarily dermal or through inhalation of cobalt metal dusts or fumes (NTP 1998, HSDB 2003). Among workers exposed to cobalt, the concentrations of cobalt in blood and urine are closely related to the average levels of cobalt in the air during a workweek (Alexandersson 1988).

## Regulations

### EPA

#### Clean Air Act

NESHAP: Cobalt Compounds listed as a Hazardous Air Pollutant (HAP)

#### Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Cobalt Compounds are listed and subject to reporting requirements

### FDA

Cobaltous salts may not be used as foam stabilizers in beverages or in foods  
All drug products containing cobalt salts have been withdrawn from the market because they were found to be unsafe or not effective and they may not be compounded

## Guidelines

### ACGIH

Threshold Limit Value - Time-Weighted Average Limit (TLV-TWA) = 0.02 mg/m<sup>3</sup> (cobalt & inorganic cobalt compounds)

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