

Review Summary of the NTP Executive Committee Working Group for the Report on Carcinogens (RG2)

Nomination: Cobalt sulfate

Review Committee: NTP Executive Committee Working Group for the Report on Carcinogens - RG2

Meeting Date: 05/01/2002

Application of Criteria:

◆ Exposure

The RG2 members felt that there was adequate evidence for exposure to cobalt sulfate based on information on importation, consumption, and potential exposure from the many different uses of cobalt sulfate. Cobalt sulfate is mainly used in the occupational setting; it is used in electroplating and electrochemical industries, as a coloring agent in ceramics, enamels and glazes, as a drier for lithographic inks, varnishes, paints and linoleum and in storage batteries. Past uses include mineral supplement in animal feed, veterinary medicine, food additive, fertilizer supplement that was used on cobalt-deficient pastures, and to treat some hematological abnormalities in humans. Some of the RG2 members were concerned that specific information (such as number of workers) on occupational and environmental exposure (including environmental fate) was only available for cobalt compounds as a class and was not available for cobalt sulfate. The RG2 felt that the exposure information on cobalt presented in Section 2 (Human Exposure) of the background document should have been subdivided into information specific for exposure to cobalt sulfate and general exposure information on cobalt compounds as a class. Moreover, the exposure information needs to be updated based on the recently published (September 2001) ATSDR toxicological profile on cobalt. In response to these concerns, RG2 proposed that an addendum should be added to the cobalt sulfate background document that would update and reorganize the information on human exposure.

◆ Carcinogenicity

The RG2 felt that the NTP two-year inhalation bioassay in rats and mice provided sufficient evidence of carcinogenicity for cobalt sulfate in experimental animals as evident by a significant increased incidence of malignant and/or a combination of malignant and benign tumors at multiple tissue sites (lung and adrenal pheochromocytomas) in multiple species of experimental animals (mice and rats). There was clear evidence of carcinogenicity in male and female B6C3F₁ mice and female F344/N rats based on significant increases in alveolar/bronchiolar lung tumors. In addition, female rats had an increased incidence of pheochromocytoma of the adrenal medulla. Some evidence of carcinogenicity was observed in male F344/N rats based on significant increased incidence of alveolar/bronchiolar lung tumors at the highest exposure level studied.

Other Scientific Concerns:

◆ Human Studies

There are no human studies reported in which exposure to cobalt sulfate is specifically mentioned. Studies on cobalt as a class are inadequate for the specific evaluation of cobalt sulfate.

◆ Genotoxicity and Mechanistic Concerns

In general cobalt sulfate was not mutagenic in most bacteria systems but was genotoxic in many mammalian systems. The mechanism of carcinogenicity of cobalt sulfate has not yet been elucidated.

Recommendation:

Motion

Recommend Cobalt Sulfate to be listed as *reasonably anticipated to be a human carcinogen* based on sufficient evidence in animals which indicates there is an increased incidence of malignant and/or a combination of malignant and benign tumors at multiple tissue sites in multiple species of experimental animals. The motion also included the recommendation that a commentary to the background document be included with the RG2 cobalt sulfate review summary, which updates and reorganizes the human exposure information according to specific information on exposure to cobalt sulfate and general information on exposure to cobalt as a class. This commentary should be written using the 2001 ATSDR Toxicological Profile for cobalt.

◆ Vote

8 yes votes to 1 no vote

Reason for dissenting vote: Revision of exposure information for cobalt sulfate should be included in Section 2 of the actual background document rather than as an addendum.