

CORRECTIONS TO THE CANCER INHALATION UNIT RISK FACTORS FOR COBALT SULFATE HEPTAHYDRATE AND WATER-SOLUBLE COBALT COMPOUNDS AND TO THE TECHNICAL SUPPORT DOCUMENT

Office of Environmental Health Hazard Assessment

May 5, 2023

The Office of Environmental Health Hazard Assessment (OEHHA) adopted a Cancer Inhalation Unit Risk (IUR) Factor for cobalt sulfate heptahydrate and water-soluble cobalt compounds in October 2020 (OEHHA, 2020) following public comment and review by the Scientific Review Panel on Air Toxic Contaminants. The IUR was based on research from the National Toxicology Program (NTP) that was published in NTP Technical Report Number 471 (NTP, 1998). The NTP report was summarized by NTP researchers in Bucher et al. (1999). A correction was published in 2022, stating that the exposure concentrations of cobalt sulfate in the text, tables, and figures in Bucher et al. (1999) should have been expressed as anhydrous cobalt sulfate, and not cobalt sulfate heptahydrate (Anonymous 2022). OEHHA assumes this correction also applies to the text, tables, and figures of the NTP Technical Report.

OEHHA has updated the Cobalt and Cobalt Compounds Cancer IUR Factor and supporting document adopted in October 2020 in accordance with the published correction. OEHHA also discovered an error in its calculation of the adjusted Cancer Slope Factor (CSF) in the final assessment and the update also reflects correction of this error.

Revisions to the OEHHA IUR were made to address both issues. Accordingly, for water-soluble cobalt compounds, normalized to cobalt content, the IUR was revised from 8.6×10^{-4} to $1.0 \times 10^{-2} (\mu\text{g}/\text{m}^3)^{-1}$ and the Inhalation Slope Factor was revised from 3.0 to 35 $(\text{mg}/\text{kg}\text{-day})^{-1}$ (Section II - Health Assessment Values and Section V, Calculation of inhalation unit risk). The extra cancer risk associated with continuous lifetime adult exposure to $1 \mu\text{g}/\text{m}^3$ cobalt in cobalt sulfate heptahydrate, and by extension all water-soluble cobalt compounds, was revised from 860 in 1 million to 10,000 in 1 million (Section V, Calculation of inhalation unit risk).

The IURs for cobalt metal and insoluble cobalt compounds were unaffected by the errors and are unchanged.

The following is a list of specific revisions to the OEHHA Cobalt and Cobalt Compounds Cancer Inhalation Unit Risk Factors document:

- Footnote added to Section II to explain the reasoning for the updates.

- The sentence in Section III paragraph 2, “The IUR for insoluble cobalt (i.e., cobalt metal) is ninefold greater than the IUR for soluble cobalt sulfate heptahydrate, when normalized to cobalt content”, was deleted because the apparent 9-fold difference in IURs was an artifact of the incorrect dose information reported in NTP (1998) and the calculation error by OEHHA. The following sentence was then slightly re-worded to more clearly reference the deductions of Smith et al. (2014).
- Footnote added to Section III under Cobalt sulfate heptahydrate, stating that the exposure group concentrations (0, 0.3, 1.0 or 3.0 mg/m³) in the tables and text of the NTP study were expressed as the cobalt sulfate anhydrous salt and do not represent exposure concentrations expressed as cobalt sulfate heptahydrate (Anonymous, 2022). The footnote also states that the term “cobalt sulfate heptahydrate” will be used to describe the rodent exposures, as the heptahydrate was the test compound, for consistency purposes.
- In Section III under Cobalt sulfate heptahydrate, paragraph 1, a sentence was modified noting that environmental exposure to cobalt sulfate will include both the hexahydrate and heptahydrate forms, and not just the heptahydrate as previously implied.
- In table legends and text where cobalt sulfate heptahydrate exposure concentrations are shown, it is noted that the exposure concentrations are expressed as anhydrous cobalt sulfate.
- In Section IV paragraph 3, a sentence was revised to note that the exposure concentrations were expressed as anhydrous cobalt sulfate in the tables and text of the NTP study, and that the cobalt sulfate concentrations of 0, 0.3, 1.0 and 3.0 mg/m³ CoSO₄ should be normalized to 0, 0.114, 0.38 and 1.14 mg Co/m³ [as indicated in Behl et al. (2015)]. Corrections were made in several sentences in Section IV to present the true normalized concentrations of cobalt for comparisons with the cobalt metal NTP study.
- In Section V under Cobalt Sulfate Heptahydrate - Calculation of single- and multi-site tumor cancer slope factors, a sentence stating that exposure of the animals was to cobalt sulfate hexahydrate, and not the heptahydrate, was removed because this statement is now presented earlier in the document and is not particularly relevant to the IUR Derivation Section. Additionally, the calculation of the cobalt-normalized CSF was corrected to show that the molecular weight fraction of cobalt in cobalt sulfate is divided into, rather than multiplied by, the CSF to calculate the adjusted CSF.

- Footnote added to Section V under Cobalt Sulfate Heptahydrate - Calculation of inhalation unit risk to note that the same CSF of $35 \text{ (mg Co/kg-day)}^{-1}$ was also calculated when starting with normalized cobalt concentrations of 0, 0.114, 0.38, and 1.14 mg Co/m^3 .
- Minor clarifying edits were also made to improve the understanding of the document that were not related to the Cobalt Sulfate Heptahydrate corrections. These clarifying edits are considered non-substantive.

OEHHA is accepting public comment on these changes until June 5, 2023. For information on how to comment, see the [Notice of Public Comment Period](#).

References

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Smith LJ, Holmes AL, Kandpal SK, Mason MD, Zheng T and Wise JP, Sr. (2014). The cytotoxicity and genotoxicity of soluble and particulate cobalt in human lung fibroblast cells. *Toxicol Appl Pharmacol* 278(3): 259-65.