# Copper; CASRN 7440-50-8

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the IRIS assessment development process. Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the guidance documents located on the IRIS website.

STATUS OF DATA FOR Copper

**File First On-Line 09/07/1988**

| Category (section) | Assessment Available? | Last Revised |
|---|---|---|
| **Oral RfD (I.A.)** | not evaluated | |
| **Inhalation RfC (I.B.)** | not evaluated | |
| **Carcinogenicity Assessment (II.)** | yes | 09/07/1988 |

## I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

### I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name — Copper
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Not available at this time.

### I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name — Copper
CASRN — 7440-50-8

Not available at this time.

## II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Copper
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Last Revised — 09/07/1988

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

### II.A. Evidence for Human Carcinogenicity

#### II.A.1. Weight-of-Evidence Characterization

Classification — D; not classified

Basis — There are no human data, inadequate animal data from assays of copper compounds, and equivocal mutagenicity data.

#### II.A.2. Human Carcinogenicity Data

None.

## II.A.3. Animal Carcinogenicity Data

Inadequate. Bionetics Research Labs (1968) studied the carcinogenicity of a copper-containing compound, copper hydroxyquinoline, in two strains of mice (B6C3F1 and B6AKF1). Groups of 18 male and 18 female 7-day-old mice were administered 1000 mg copper hydroxyquinoline/kg bw (180.6 mg Cu/kg) suspended in 0.5% gelatin daily until they were 28 days old, after which they were administered 2800 ppm (505.6 ppm Cu) in the feed for 50 additional weeks. No statistically significant increases in tumor incidence were observed in the treated 78-week-old animals.

In the same study, Bionetics Research Labs (1968) administered a single subcutaneous injection of gelatin (control) or 1000 mg of copper hydroxyquinoline/kg bw (180.6 mg Cu/kg) suspended in 0.5% gelatin to groups of 28-day-old mice of both strains. After 50 days of observation, the male B6C3F1 had an increased incidence of reticulum cell sarcomas compared with controls. No tumors were observed in the treated male B6AKF1 mice, and a low incidence of reticulum cell sarcomas was observed in the treated female mice of both strains.

Gilman (1962) administered intramuscular injections containing 20 mg of cupric oxide (16 mg Cu), cupric sulfide (13.3 mg Cu), and cuprous sulfide (16 mg Cu) into the left and right thighs of 2- to 3-month-old Wistar rats. After 20 months of observations, no injection-site tumors were observed in any animals, but other tumors were observed at very low incidence in the animals receiving cupric sulfide (2/30) and cuprous sulfide (1/30). As the relevance of the organic copper compound to the observation of sarcoma induction is uncertain and the incidence of tumors in rats treated i.m. with inorganic copper was very low, data are considered inadequate for classification.

## II.A.4. Supporting Data for Carcinogenicity

Moriya et al. (1983) reported no increase in mutations in E. coli and S. typhimurium strains TA98, TA1535, TA1537 and TA1538 incubated with up to 5 mg copper quinolinolate/plate and in S. typhimurium TA98 and TA100 incubated with up to 5 mg copper sulfate/plate. Demerec et al. (1951) reported dose-related mutagenic effects in E. coli with 2 to 10 ppm copper sulfate in a reverse mutation assay. Negative results were obtained with copper sulfate or copper chloride in assays using S. cerevisiae (Singh, 1983) and Bacillus subtilis (Nishioka, 1975, Matsui, 1980, Kanematsu et al., 1980). Errors in DNA synthesis from poly(c)templates have been induced in viruses incubated with copper chloride or copper acetate (Sirover and Loeb, 1976). Chromosomal aberrations were induced in isolated rat hepatocytes when incubated with copper sulfate (Sina et al., 1983). Casto et al. (1979) showed enhanced cell transformation in Syrian hamster embryo cells infected with simian adenovirus with the addition of cuprous sulfide and copper sulfate. High concentrations of copper compounds have been reported to induce mitosis

in rat ascites cells and recessive lethals in Drosophila melanogaster. Law (1938) reported increases in the percent lethals observed in Drosophila larvae and eggs when exposed to copper by microinjection (0.1% copper sulfate) or immersion (concentrated aqueous copper sulfate), respectively.

## II.B. Quantitative Estimate of Carcinogenic Risk from Oral Exposure

Not available.

## II.C. Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure

Not available.

## II.D. EPA Documentation, Review, and Contacts (Carcinogenicity Assessment)

### II.D.1. EPA Documentation

Source Document — U.S. EPA, 1987

The values in the 1987 Drinking Water Criteria Document for Copper have received peer and administrative review.

### II.D.2. EPA Review (Carcinogenicity Assessment)

Agency Work Group Review — 09/15/1987

Verification Date — 09/15/1987

### II.D.3. EPA Contacts (Carcinogenicity Assessment)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or hotline.iris@epa.gov (internet address).

## III. [reserved]
## IV. [reserved]
## V. [reserved]

## VI. Bibliography

Substance Name — Copper
CASRN — 7440-50-8

### VI.A. Oral RfD References

None

### VI.B. Inhalation RfC References

None

### VI.C. Carcinogenicity Assessment References

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Demerec, M., G. Bertani and J. Flint. 1951. A survey of chemicals for mutagenic action on E. coli. Am. Natur. 85(821): 119-136.

Gilman, J.P.W. 1962. Metal carcinogenesis. II. A study on the carcinogenic activity of cobalt, copper, iron and nickel compounds. Cancer Res. 22: 158-166.

Kanematsu, N., M. Hara and T. Kada. 1980. Rec assay and mutagenicity studies on metal compounds. Mutat. Res. 77: 109-116.

Law, L.W. 1938. The effects of chemicals on the lethal mutation rate in drosophilia melanogaster. Proc. Natl. Acad. Sci., USA. 24: 546-550.

Matsui, S. 1980. Evaluation of a Bacillus subtilis rec-assay for the detection of mutagens which may occur in water environments. Water Res. 14(11): 1613-1619.

Moriya, M., T. Ohta, K. Watanabe, T. Miyazawa, K. Kato and Y. Shirasu. 1983. Further mutagenicity studies on pesticides in bacterial reversion assay systems. Mutat. Res. 116(3-4): 185-216.

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Singh, I. 1983. Induction of reverse mutation and mitotic gene conversion by some metal compounds in Saccharomyces cerevisiae. Mutat. Res. 117(1-2): 149-152.

Sirover, M.A. and L.A. Loeb. 1976. Infidelity of DNA synthesis in vitro: Screening for potential metal mutagens or carcinogens. Science. 194: 1434-1436.

U.S. EPA. 1987. Drinking Water Criteria Document for Copper. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Drinking Water, Washington, DC.

## VII. Revision History

Substance Name — Copper
CASRN — 7440-50-8

| Date | Section | Description |
|---|---|---|
| **09/07/1988** | II. | Carcinogen summary on-line |

## VIII. Synonyms

Substance Name — Copper
CASRN — 7440-50-8
Last Revised — 09/07/1988

- 7440-50-8
- Copper