Copper cyanide; CASRN 544-92-3

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 cyanide

File First On-Line 01/31/1987

<table>
<thead>
<tr>
<th>Category (section)</th>
<th>Assessment Available?</th>
<th>Last Revised</th>
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<tr>
<td>Oral RfD (I.A.)</td>
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<td>09/07/1988*</td>
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<tr>
<td>Inhalation RfC (I.B.)</td>
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<td></td>
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<tr>
<td>Carcinogenicity Assessment (II.)</td>
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*A comprehensive review of toxicological studies was completed 01/10/05 - please see section I.A.6 for more information.

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Copper cyanide
CASRN — 544-92-3
Last Revised — 09/07/1988

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the
human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

I.A.1. Oral RfD Summary

<table>
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<tr>
<th>Critical Effect</th>
<th>Experimental Doses*</th>
<th>UF</th>
<th>MF</th>
<th>RfD</th>
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<tr>
<td>Decreased body and organ weights, histopathologic alterations in liver and kidney</td>
<td>NOAEL: 5 mg/kg/day</td>
<td>1000</td>
<td>1</td>
<td>5E-3 mg/kg/day</td>
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<tr>
<td></td>
<td>LOAEL: 15 mg/kg/day</td>
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Rat Oral Subchronic Study

U.S. EPA, 1986

*Conversion Factors -- None

I.A.2. Principal and Supporting Studies (Oral RfD)


In a 90-day subchronic study, Sprague-Dawley rats (20/sex/group) were administered by gavage at 0, 0.5, 5, 15 and 50 mg/kg/day copper cyanide in a 1.5% carboxymethylcellulose vehicle. Data generated from this study included body weight changes, food consumption, ophthalmological examinations, clinical, biochemical and gross morphological changes, and histopathology of the target organs. CuCn treatment-related deaths were observed in the 0.5, 5, 15 and 50 mg/kg/day dose groups with a total of 3, 1, 2 and 23 deaths, respectively. No rats died in control groups. Detailed examination of histopathologic data, however, indicated that eight male and four female vehicle control rats had hemorrhage in the lungs; and three males and two females from the low-
dose group had hemorrhage in the lungs. Lung congestion was also reported in both male and female rats treated with different levels of CuCn thus suggesting possible dosing error-related mortality in the 0.5, 5 and 15 mg/kg dose groups. Mean body weights, body weight gains and weekly food consumption values for CuCn-treated rats were significantly decreased when compared with control groups, with male rats being more sensitive than female rats. Rats primarily in the 15 and 50 mg/kg/day dose groups were observed as having labored respiration, fixed and prolonged posture, and thin appearance. Lethargy, red urine, discolored inguinal fur and diarrhea were observed primarily in the 50 mg/kg/day dose group. There was a significant decrease in globulin and an increase in SGOT and SGPT levels in the 50 mg/kg/day group; male rats were more sensitive than females. There was also a significant increase in total and direct bilirubin in male rats, but not female rats, and an overall increase in alkaline phosphatase. Male rats displayed decreased Hb, Hct, and MCH values, while females displayed slightly decreased Hg and MCH values only. Generally the 50 mg/kg/day group showed decreased RBC values and increased MCV and platelet values. Increased MCV also occurred in the 15 mg/kg/day group. CuCn affected both absolute organ weights and relative organ weight ratios of the kidney, spleen and brain in the 50 mg/kg/day group. Again, males appeared more sensitive than females when evaluating absolute organ weights only. The histopathology suggested that both male and female rats treated with 50 mg/kg/day CuCn died of hemolytic anemia. These rats also displayed a paroxysmal hemolytic disorder of either chronic or episodic hemolysis with hematopoietic hyperplasia. Relative and pertinent microscopic findings include the presence of hemoglobin in the cytoplasm of the renal convoluted tubule epithelium, pigmentation in the spleen and liver and hyperplasia of hematopoietic tissue. Based on data available from this study, 5 mg/kg/day could be considered as a NOAEL and 15 mg/kg/day as a LOAEL (decreased body and organ weights and morphological alterations of female liver and kidney tissues).

I.A.3. Uncertainty and Modifying Factors (Oral RfD)

UF — 1000 is applied; 10 to extrapolate from subchronic to chronic data, 10 for species extrapolation and 10 to account for interspecies variability.

MF — None

I.A.4. Additional Studies/Comments (Oral RfD)

In a 2-year chronic study, rats (10/sex/group) were administered food fumigated with HCN (Howard and Hanzal, 1955). The average daily concentrations were 73 and 183 mg CN/kg diet from the data reported on food consumption and body weight, daily estimated doses were 4.3 and 10.8 mg Cn/kg bw. The average food CN concentrations were estimated based on the authors' data for concentration at the beginning and end of each food preparation period and by
assuming a first-order rate of loss for the intervening period. There was no treatment-related effects on growth rate, no gross signs of toxicity and no histopathological lesions.

Studies by Philbrick et al. (1979) showed decreased weight gain and thyroxin levels, and myelin degeneration in rats at 30 mg/kg/day CN. Other chronic studies either gave higher effect levels or used subcutaneous routes (Crampton et al., 1979; Lessell, 1971; Hertting et al., 1960).

Decreased protein efficiency ratio was produced by dietary cyanide (10.6 mg/kg/day) in rats during gestation, lactation and postweaning growth phase (Tewe and Maner, 1981a). A further study by Tewe and Maner (1981b) in which sows were fed approximately 9.45 mg/kg/day CN, there was proliferation of the glomerular cells of the kidneys and reduced activity of the thyroid glands. The number of animals in this study, however, was very small. A Japanese study (Amo, 1973) indicated that 0.05 mg/kg/day of cyanide obtained from drinking water decreased the fertility rate and survival rate in the F1 generation and produced 100% mortality in the F2 generation. However, these data are not consistent with the body of available literature.

**I.A.5. Confidence in the Oral RfD**

Study — Medium  
Database — Medium  
RfD — Medium

The critical study is given a medium confidence because it is a well-designed 90-day oral study with adequate toxicologic endpoints. Confidence in the data base is rated medium because the database contains both a chronic toxicity study and reproductive studies. Medium confidence in the RfD follows.

**I.A.6. EPA Documentation and Review of the Oral RfD**


Other EPA Documentation — None

Agency Work Group Review — 08/05/1985, 07/16/1987

Verification Date — 07/16/1987

A comprehensive review of toxicological studies published through 2004 was conducted. No new health effects data were identified that would be directly useful in the revision of the
existing RfD for Copper cyanide and a change in the RfD is not warranted at this time. For more information, IRIS users may contact the IRIS Hotline at hotline.iris@epa.gov or (202)566-1676.

I.A.7. EPA Contacts (Oral RfD)

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).

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

Substance Name — Copper cyanide
CASRN — 544-92-3

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Copper cyanide
CASRN — 544-92-3

This substance/agent has not undergone a complete evaluation and determination under US EPA's IRIS program for evidence of human carcinogenic potential.

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

VI. Bibliography

Substance Name — Copper cyanide
CASRN — 544-92-3
VI.A. Oral RfD References


Crampton, R.F., I.F. Gaunt, R. Harris et al. 1979. Effects of low cobalamin diet and chronic cyanide toxicity in baboons. Toxicology. 12: 221-234.


VI.B. Inhalation RfC References

None
VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Copper cyanide
CASRN — 544-92-3

<table>
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<th>Description</th>
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<td>03/03/2005</td>
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VIII. Synonyms

Substance Name — Copper cyanide
CASRN — 544-92-3
Last Revised — 01/31/1987

- 544-92-3
- Copper cyanide
- Cupricin
- Cuprous cyanide
- RCRA waste number P029