Zinc cyanide; CASRN 557-21-1

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 Zinc cyanide

File First On-Line 01/31/1987

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	01/31/1987
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	not evaluated	

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Zinc cyanide
CASRN — 557-21-1
Last Revised — 01/31/1987

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

Critical Effect	Experimental Doses*	UF	MF	RfD
Rat Chronic Oral Study **Howard and Hanzal, 1955**	NOAEL: 10.8 mg/kg/day cyanide converted to 24.3 mg/kg/day of zinc cyanide	100	5	5E-2 mg/kg/day
Weight loss, thyroid effects and myelin degeneration **Rat Subchronic to Chronic Oral Bioassay** **Philbrick et al., 1979**	LOAEL: 30 mg/kg/day cyanide (67.5 mg/kg/day zinc cyanide)			

*Conversion Factor: molecular weight conversion factor = 117/(2 x 26) [MW Zn(CN)2 = 117; MW CN = 26]; two molar equivalents of free CN released in water.

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

Howard, J.W. and R.F. Hanzal. 1955. Chronic toxicity for rats by food treated with hydrogen cyanide. Agric. Food Chem. 3: 325-329.

Since zinc is present at high levels in foods and is considerably less toxic than cyanide (CN), an RfD for zinc cyanide of 0.05 mg/kg/day or 3.4 mg/day can be calculated based on the maximum molar equivalents (2) of cyanide generated in aqueous solution or dilute acids.

In this 2-year dietary study, rats (10/sex/group) were administered food fumigated with hydrogen cyanide. 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 mg 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 were no treatment related effects on growth rate, no gross signs of toxicity, and no histopathologic 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 the subcutaneous route (Crampton et al., 1979; Lessell, 1971; Hertting et al., 1960). Human data do not provide adequate information from which to derive an RfD because effective dose levels of chronically ingested CN are not documented. Therefore, the study of Howard and Hanzel (1955) provides the highest NOAEL, 10.8 mg/kg/day for CN, and is chosen for the derivation of an RfD for CN of 1.5 mg/day or 0.02 mg/kg/day.

Cyanide is metabolized extensively in the liver, indicating that the only relevant route of administration for quantitative risk assessment in the derivation of an oral RfD is the oral route of administration.

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

UF — According to the U.S. EPA (1985), an uncertainty factor of 100 is used to derive the RfD (10 for species extrapolation, 10 for sensitive population).

MF — A modifying factor of 5 is used to account for the apparent tolerance to cyanide when it is ingested with food rather than when it is administered by gavage or by drinking water.

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

Decreased protein efficiency ratio was produced by dietary cyanide treatment of rats during gestation, lactation, and postweaning growth phase in the Tewe and Maner (1981a) experiment: the dose level of cyanide (10.6 mg/kg/ day) producing that effect is slightly lower than the currently accepted NOAEL of 10.8 mg/kg/day (U.S. EPA, 1985). Furthermore, Tewe and Maner (1981b) tested sows. Possible effects observed at about 9.45 mg/kg/day were proliferation of glomerular cells of the kidneys and reduced activity of the thyroid glands in the young sows. However, the number of animals in this experiment 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 in mice. 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 confidence in the study is medium because adequate records of food consumption and body weight were maintained and animals of both sexes were tested at two doses for 2 years. The database is rated medium because a small but sufficient number of studies support the chosen study. Medium confidence in the RfD follows. Additional chronic/reproductive studies are needed to support a higher level of confidence in the RfD.

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

Source Document — This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation — U.S. EPA, 1985

Agency Work Group Review — 08/05/1985

Verification Date — 08/05/1985

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfD for zinc cyanide conducted in August 2003 identified one or more significant new studies. IRIS users may request the references for those studies from 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 — Zinc cyanide
CASRN — 557-21-1

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Zinc cyanide
CASRN — 557-21-1

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 — Zinc cyanide
CASRN — 557-21-1

VI.A. Oral RfD References

Amo, H. 1973. Effects of oral administration of cyanide and heavy metals in long term on breeding and chromosomes analyses of mice. Nagoya shiritsu Diagaku Igakkai Zasshi. 24(1): 48-66.

Crampton, R.F., I.F. Gaunt, R. Harris, et al. 1979. Effects of low cobalamin diet and chronic

cyanide toxicity in baboons. Toxicology. 12(3): 221-234.

Hertting, G., O. Kraupp, E. Schnetz and S. Wuketich. 1960. Untersuchungen uber die Folgen einer chronischen Verabreichung akut toxischer Dosen von Naturimcyanid an Hunden. Octa Pharmacol. Toxicol. 17: 27-43. Investigations about the consequences of a chronic administration of acutely toxic doses of sodium cyanide to dogs. (Eng. trans.)

Howard, J.W. and R.F. Hanzal. 1955. Chronic toxicity for rats of food treated with hydrogen cyanide. Agric. Food Chem. 3(4): 325-329.

Lessell, S. 1971. Experimental cyanide optic neuropathy. Arch. Opthalmol. 86(2): 194-204.

Philbrick, D.J., J.B. Hopkins, D.C. Hill, J.C. Alexander and R.G. Thomson. 1979. Effects of prolonged cyanide and thiocyanate feeding in rats. J. Toxicol. Environ. Health. 5: 579-592.

Tewe, O.O. and J.H. Maner. 1981a. Long-term and carry-over effect of dietary inorganic cyanide (KNC) in the life cycle performance and metabolism of rats. Toxicol. Appl. Pharmacol. 58(1): 1-7.

Tewe, O.O. and J.H. Maner. 1981b. Performance and pathophysiological changes in pregnant pigs fed cassava diets containing different levels of cyanide. Res. Veter. Sci. 30(2): 147-151.

U.S. EPA. 1985. Drinking Water Criteria Document for Cyanide. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Drinking Water, Washington, DC.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Zinc cyanide
CASRN — 557-21-1

Date	Section	Description
10/28/2003	I.A.6	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Zinc cyanide
CASRN — 557-21-1
Last Revised — 01/31/1987

- 557-21-1
- Cyanure de zinc
- RCRA waste number P121
- UN 1713
- Zinc Cyanide
- Zinc dicyanide