

Cyanogen bromide; CASRN 506-68-3

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 Cyanogen bromide

File First On-Line 09/26/1988

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	09/26/1988*
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	not evaluated	

*A comprehensive review of toxicological studies was completed (2004) - 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 — Cyanogen bromide

CASRN — 506-68-3

Last Revised — 09/26/1988

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

Critical Effect	Experimental Doses*	UF	MF	RfD
Rat Chronic Oral Study Howard and Hanzal, 1955	NOAEL: 10.8 mg/kg/day cyanide converted to 44 mg/kg/day of cyanogen	100	5	9E-2 mg/kg/day

Weight loss, thyroid effects and myelin degeneration

LOAEL: 30 mg/kg/day cyanide (122 mg/kg/day cyanogen)

Rat Subchronic to Chronic Oral Bioassay

Philbrick et al., 1979

*Conversion Factors: Based on food consumption and body weight data, the 100 ppm level (NOAEL) was equal to CN-doses of 7.5 mg/kg/day for males and 10.8 mg/kg/day for females. Multiplying 10.8 mg CN-/kg/day by the ratio of the molecular weights of cyanogen bromide to CN- (105.93/26.02) yields a dose of 44 mg/kg/day for cyanogen bromide.

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

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

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. Health.* 5: 579-592.

Groups of 10 male and 10 female rats were exposed to dietary hydrogen cyanide levels reported to be 0, 100 and 300 ppm for 2 years (Howard and Hanzal, 1955). There were no treatment-related effects on growth rate or hematological parameters, no gross signs of toxicity and no histopathological lesions of major organs, including the brain, detected after examination with routine light microscopy.

In the Philbrick et al. (1979) study, groups of 10 male weanling rats were treated with diets containing potassium cyanide at a concentration that provided 0 or 30 mg/kg/day of cyanide for 11.5 months. Decreased thyroxine levels in the serum and decreased body weight gain were reported in rats consuming 30 mg/kg/day of cyanide. Vacuolization and membrane degeneration were observed in the ventral white matter of the spinal cord after examination of thick and thin sections with the electron microscope but not after routine light microscopic evaluation. In addition, Philbrick et al. (1979) reported that the effect of CN⁻ on nerve tissue was exacerbated by a diet deficient in DL-methionine, potassium iodide and vitamin B12.

Thus, 30 mg/kg/day is the LOAEL and the 300 ppm dietary level, converted to 10.8 mg/kg/day, is the NOAEL for cyanide. Correcting for the molecular weight difference yields a dose of 44 mg/kg/day for cyanogen bromide.

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

UF — The uncertainty factor of 100 includes 10 to account for interspecies extrapolation and 10 for the range of sensitivity within the human population to xenobiotics.

MF — A modifying factor of 5 was used to account for "possible problems associated with the use of a dietary study to estimate a drinking water criterion" (U.S. EPA, 1985a,b).

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

No teratogenicity, reproductive, subchronic or chronic toxicity studies on cyanogen bromide were available. 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. Decreased protein efficiency ratio was produced by dietary cyanide treatment of rats during gestation, lactation and postweaning growth phase in the Tewe and Maner (1981) 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. Although the toxicity of cyanogen bromide appears to be related to the release of cyanide in

chronic exposure to low levels of cyanogen bromide (Hartung, 1982), the toxicity of undissociated cyanogen bromide has not been evaluated. Data from acute exposure indicate that cyanogen is less potent, albeit more irritating, than other cyanides (Hartung, 1982). For example, cyanogen chloride is one order of magnitude less toxic (lethal dose, 20 mg/kg) than sodium cyanide (lethal dose, 2.2 mg/kg) when administered to rabbits subcutaneously (ACGIH, 1986). This difference in toxicity cannot be accounted for only by the differences in molecular weight and may be related to the covalent nature of the chemical bonds. Despite the lack of studies that evaluate the toxicity of chronic oral exposure to cyanogen bromide specifically, the available data indicate that cyanogen bromide is soluble in water and dilute acid, that full dissociation would result in a maximum of one mole equivalent of cyanide and that of the three possible breakdown products of cyanogen bromide (cyanide, bromide and cyanogen bromide), cyanide is probably the most toxic to mammals. Therefore, until specific data on cyanogen bromide become available, the RfD for cyanogen bromide is derived by analogy to cyanide.

I.A.5. Confidence in the Oral RfD

Study — Medium

Database — Medium

RfD — Low

The level of confidence in the Howard and Hanzal (1955) study is rated medium because, despite both sexes being tested by an appropriate route for 2 years with no overt toxicity, no hematological effects or histopathological lesions (including brain lesions), only 10 rats/sex/group were evaluated and myelin degeneration could not be properly evaluated by the techniques used by Howard and Hanzal (1955). Confidence in the database is low because, although there are several studies (including human studies) on the effects of cyanide that provide substantial information on the toxicity of cyanide, data specifically on the toxicity of cyanogen bromide are not available. The low confidence in the RfD for cyanogen bromide follows.

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

Source Document — U.S. EPA, 1985a,b

Extensive peer review and Agency-wide review, 1985.

Other EPA Documentation — None

Agency Work Group Review — 12/15/1987

Verification Date — 12/15/1987

A comprehensive review of toxicological studies published prior to 2004 was conducted. No new health effects data were identified that would be directly useful in the revision of the existing RfD for Cyanogen bromide and a change in the RfD is not warranted at this time.

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 — Cyanogen bromide
CASRN — 506-68-3

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Cyanogen bromide
CASRN — 506-68-3

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 — Cyanogen bromide
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VI.A. Oral RfD References

ACGIH (American Conference of Government Industrial Hygienists). 1986. TLVs - Threshold Limit Values for chemical substances and physical agents in the workroom environment with intended changes for 1984-1985. ACGIH, Cincinnati, OH. p. 10, 14-15.

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

Hartung, R. 1982. Cyanides and nitriles. In: Patty's Industrial Hygiene and Toxicology, Vol. IIC, G.D. Clayton and F.E. Clayton, Ed. John Wiley and Sons, NY. p. 4845-4900.

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

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

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

U.S. EPA. 1985a. Consensus Regarding Quantification of Noncarcinogenic Effects of Cyanide. From Cynthia Sonich-Mullin, ECAO-Cin to Edward Ohanian, Office of Drinking Water (WH550).

U.S. EPA. 1985b. 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. (Final Draft)

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Cyanogen bromide

CASRN — 506-68-3

Date	Section	Description
09/26/1988	I.A.	Oral RfD summary on-line
10/28/2003	I.A.6.	Screening-Level Literature Review Findings message has been added.
09/29/2004	I.A.6.	Screening-Level Literature Review Findings message has been removed and replaced by comprehensive literature review conclusions.

VIII. Synonyms

Substance Name — Cyanogen bromide

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Last Revised — 09/26/1988

- 506-68-3
- bromine cyanide
- Cyanogen bromide