Cyclohexylamine; CASRN 108-91-8

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 Cyclohexylamine

File First On-Line 09/07/1988

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	09/07/1988
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 — Cyclohexylamine
CASRN — 108-91-8
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

Critical Effect	Experimental Doses*	UF	MF	RfD
Testicular damage **Rat Chronic Oral Study** **Gaunt et al., 1976** **Testicular damage** **Rat Chronic Reproductive Study** **Oser et al., 1976**	NOAEL: 600 ppm cyclohexylamine-HCl in diet (18 mg/kg/day) LOAEL: 2000 ppm cyclohexylamine-HCl in diet (60 mg/kg/day)	100	1	2E-1 mg/kg/day

*Conversion Factors: Investigators estimated intake of cyclohexylamine-HCl in male rats at 600 ppm at 24 mg/kg/day; thus, 24 mg/kg/day x 99.17/135.63 (ratio of mol. wt. of cyclohexylamine to cyclohexylamine-HCl) results in a dosage of cyclohexylamine of 18 mg/kg/day.

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

Gaunt, I.F., J. Hardy, P. Grasso, S.D. Gangolli and K.R. Butterworth. 1976. Long-term toxicity of cyclohexylamine hydrochloride in the rat. Food Cosmet. Toxicol. 14(4): 255-268.

Oser, B.L., S. Carson, G.E. Cox, E.E. Vogin and S.S. Steinberg. 1976. Long- term and multigeneration toxicity studies with cyclohexylamin hydrochloride. Toxicologist. 6(1): 47-65.

Groups of 48 male and 48 female Wistar rats were fed diets containing 0, 600, 2000 or 6000 ppm cyclohexylamine hydrochloride for 104 weeks (Gaunt et al., 1976). The investigators estimated ingested dosages of cyclohexylamine hydrochloride at 24, 82 and 300 mg/kg/day for males and 35, 120 and 440 mg/kg/day for females. Parameters of toxicity investigated included behavior

and appearance, body weight gain and body weights, food and water consumption, limited hematology, urinalysis and tests of kidney function, necropsy examination and histopathologic examination of a large number of tissues. Effects attributed to treatment included a dose-related decrease in mortality, decreased body weight gain and decreased terminal body weights. Food consumption was decreased at greater than or equal to 2000 ppm. Females at greater than or equal to 2000 ppm had elevated relative thyroid weights; males at greater than or equal to 2000 ppm had testicular degeneration, which was severe at 6000 ppm; minor hematologic effects occurred in both sexes at greater than or equal to 2000 ppm; and an increased frequency of pulmonary alveoli with foamy macrophages was observed in rats at 6000 ppm. The effects on body weight gain and body weights were observed in both sexes in all treated groups throughout the experiment.

In a six-generation dietary study (Oser et al., 1976), FDRL strain rats (30/sex/group) were fed diets of 0, 15, 50, 100 or 150 mg/kg/day of cyclohexylamine-HCl in the parental (F0) generation. During the course of a 24-month chronic toxicity study, all F0 rats were bred six times. Parameters of toxicity investigated included behavior, appearance and survival, recorded body weights, food consumption, histopathology and hematology, blood chemistry and urinalysis. There was a statistically significant decrease in the rate of body weight gain in treated males (100 and 150 mg/kg/day groups) and treated females (greater than or equal to 50 mg/kg/day groups). This effect was attributed to decreased food intake. The incidence of testicular atrophy was statistically significant at both 50 and 150 mg/kg/day cyclohexylamine; however, the incidence was not elevated at 100 mg/kg/day relative to controls. There was reduced fertility in the 150 mg/kg/day group after the 4th and 5th mating, and at 100 and 150 mg/kg/day groups, there was a reduced number of live young/litter and the growth rate of the pups was reduced.

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

UF — The UF of 100 allows for uncertainty in the extrapolation from experimental animals to humans (10A) and to protect unusually sensitive individuals (10H).

MF — None

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

A subchronic rat study performed by the same group of investigators found adverse effects on body weight gain at 2000 but not at 600 ppm cyclohexylamine hydrochloride (Gaunt et al., 1974). Long-term (Hardy et al., 1976) and multigeneration studies (Kroes et al., 1977) in mice indicate that mice are less sensitive than rats to the adverse effects of cyclohexylamine. The chemical has not been associated with teratogenicity in rats or rabbits (Oser et al., 1976; Lorke and Machemer, 1983; Kennedy et al., 1969).

I.A.5. Confidence in the Oral RfD

Study — High
Database — High
RfD — High

Confidence in the study is rated high because it was well-planned and conducted with adequate numbers of animals and evaluated the appropriate parameters of toxicity. Confidence in the database is high because the developmental and reproductive toxicity of cyclohexylamine has been adequately investigated. High confidence in the RfD follows.

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

Source Document — U.S. EPA, 1987

Limited peer review and extensive Agency-wide review, 1987.

Other EPA Documentation — None

Agency Work Group Review — 09/17/1987

Verification Date — 09/17/1987

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 Cyclohexylamine conducted in September 2002 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to 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 — Cyclohexylamine
CASRN — 108-91-8

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Cyclohexylamine
CASRN — 108-91-8

Not available at this time.

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

VI. Bibliography

Substance Name — Cyclohexylamine
CASRN — 108-91-8

VI.A. Oral RfD References

Gaunt, I.F., M. Sharratt, P. Grasso, A.B.G. Lansdown and S.D. Gangolli. 1974. Short-term toxicity of cyclohexylamine hydrochloride in the rat. Food Cosmet. Toxicol. 12(5-6): 609-624.

Gaunt, I.F., J. Hardy, P. Grasso, S.D. Gangolli and K.R. Butterworth. 1976. Long-term toxicity of cyclohexylamine hydrochloride in the rat. Food Cosmet. Toxicol. 14(4): 255-268.

Oser, B.L., S. Carson, G.E. Cox, E.E. Vogin and S.S. Steinberg. 1976. Long- term and multigeneration toxicity studies with cyclohexylamin hydrochloride. Toxicologist. 6(1): 47-65.

Hardy, J., I.F. Gaunt, J. Hooson, R.J. Hendy and K.R. Butterworth. 1976. Long-term toxicity of cyclohexylamine hydrochloride in mice. Food Cosmet. Toxicol. 14(4): 269-276.

Kennedy, G.L., P.G. Sanders, M.S. Weinberg, D.W. Arnold and M.L. Keplinger. 1969. Reproduction studies in rats and rabbits with cyclohexylamine sulfate. Toxicol. Appl. Pharmacol. 14: 656.

Kroes, R., P.W.J. Peters, J.M. Berkvens, H.G. Verschuuren, T. DeVries and G.J. Van Esch. 1977. Long-term toxicity and reproduction study (including a teratogenicity study) with cyclamate, saccharin, and cyclohexylamine. Toxicology. 8(3): 285-300.

Lorke, D. and L. Machemer. 1983. The effect of cyclohexylamine on the embryo following oral administration to mice and rats. Toxicol. Lett. 17: 137-143.

U.S. EPA. 1987. Health and Environmental Effects Document on Cyclohexylamine. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Cyclohexylamine
CASRN — 108-91-8

Date	Section	Description
09/07/1988	I.A.	Oral RfD summary on-line
12/03/2002	I.A.6.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Cyclohexylamine
CASRN — 108-91-8
Last Revised — 09/07/1988

- 108-91-8
- aminocyclohexane
- Cyclohexylamine
- hexahydroaniline