Ethylene diamine; CASRN 107-15-3

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 Ethylene diamine

File First On-Line 05/01/1991

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	message	05/01/1991
Carcinogenicity Assessment (II.)	yes	11/01/1992

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Ethylene diamine
CASRN — 107-15-3

Not available at this time.

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

Substance Name — Ethylene diamine
CASRN — 107-15-3

The health effects data for ethylene diamine were reviewed by the U.S. EPA RfD/RfC Work Group and determined to be inadequate for the derivation of an inhalation RfC. For additional information on the health effects of this chemical, interested parties are referred to the EPA documentation listed below.

U.S. EPA. 1988. Health and Environmental Effects Document for Ethylene diamine. 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. EPA/600/8-89/004.

Agency Work Group Review — 12/18/1990

EPA Contacts:

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).

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfC for Ethylene diamine 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.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Ethylene diamine
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Last Revised — 11/01/1992

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 classifiable as to human carcinogenicity

Basis — Based on no human data and inadequate animal data.

II.A.2. Human Carcinogenicity Data

None.

II.A.3. Animal Carcinogenicity Data

Inadequate. As discussed in Yang et al. (1984a,b), Union Carbide researchers conducted a 2-year carcinogenicity study of oral ethylene diamine dihydrochloride in F344 rats in which 25 male and 26 female rats (FO) were fed a diet containing either 0.05, 0.15 or 0.5 g/kg/day (50, 150 or 500 mg/kg/day, respectively). These doses were determined from a previous study (Yang and Tallant, 1982). A control group of 50 males and 52 females was fed a basal diet. The FO parents were treated for 100 days then mated. After mating, the males were used in another assay. The offspring of the treated animals, 15 males and 26 females (F1), were fed the same three doses in the diet. Necropsies were performed on F1 weanlings (5 rats/sex/dose and 10 control rats/sex) and F1 adults (10 rats/sex/dose and 20 control rats/sex). Yang et al. (1984b) indicated that the most significant microscopic lesion observed was hepatocellular pleomorphism, which is characterized by enlarged hepatocytes and hepatocyte nuclei, variations in nuclear shape, and increased numbers of multinucleate hepatocytes.

DePass et al. (1984) conducted a lifetime dermal bioassay of 99.1% pure ethylene diamine in male C3H/HeJ mice. Twenty-five uL of a 1% ethylene diamine solution in deionized water was applied to the skin of two groups of 50 mice 3 times/week until death. (The mean survival time for the three groups was at least 598 days.) (Two different chemical manufacturers supplied ethylene diamine for the groups.) A control group of 50 mice received similar applications of the vehicle and a positive control group of 40 mice received repeated applications of 0.1% 3-methylcholanthrene in acetone. The mean survival times of the two treated groups, the vehicle control group, and the positive control group were 639, 598, 626 and 204 days, respectively.

Animals in all groups were individually housed, except for the positive control group, which was housed 5/cage. Another group of 40 mice housed 5/cage was used as a housing control for the positive control group. The mean survival time of the housing controls was 488 days. The investigators conducted complete gross necropsies on all the mice, and subjected the dorsal skin and all gross lesions to histologic examination. No evidence of epidermal tumors was found in either group of treated mice, the individually-housed vehicle controls, or the group-housed vehicle controls. In contrast, 98% of positive control mice had skin tumors, including 92% with squamous cell carcinomas.

II.A.4. Supporting Data for Carcinogenicity

Ethylene diamine produced a weakly mutagenic response in four Salmonella typhimurium strains, both in the presence and the absence of an S9 homogenate fraction (Haworth et al., 1983; Hedenstedt, 1978; Hulla et al., 1981). Ethylene diamine was negative in a sister chromatid exchange assay and HGPRT gene mutation assay in Chinese hamster ovary cells, both in the presence and the absence of metabolic activation. It was also negative in an unscheduled DNA synthesis assay in Sprague-Dawley rat hepatocytes (Slesinski et al., 1983). Zimmering et al. (1985) found that both dietary and injected ethylene diamine was negative in sex-linked recessive lethal assays in Drosophila.

Ethylene diamine is a water-soluble molecule with little affinity for body fat (Yang et al., 1984a). This study is unusual in that it was designed to provide both cancer and pharmacokinetic data. The major urinary and fecal metabolite after oral administration in rats is N-acetylethylenediamine, which may subsequently undergo further metabolism to ethylene diamine, aminoacetaldehyde, ethanolamine, and, eventually, carbon dioxide (Yang and Tallant, 1982).

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

None.

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

None.

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

II.D.1. EPA Documentation

Source Document — U.S. EPA, 1988

The 1988 Health and Environmental Effects Document for Ethylene diamine has received full review from the Office of Health and Environmental Assessment and from the Office of Pesticides and Toxic Substances.

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

Agency Work Group Review — 07/25/1991

Verification Date — 07/25/1991

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the cancer assessment for Ethylene diamine 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.

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 — Ethylene diamine
CASRN — 107-15-3

VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

U.S. EPA. 1988. Health and Environmental Effects Document for Ethylene diamine. 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. EPA/600/8-89/004.

VI.C. Carcinogenicity Assessment References

DePass, L.R., E.H. Fowler and R.S.H. Yang. 1984. Dermal oncogenicity studies on ethylenediamine in male C3H mice. Fund. Appl. Toxicol. 4(4): 641-645.

Haworth, S., T. Lawlor, M. Mortelmans, W. Speck and E. Zeiger. 1983. Salmonella mutagenicity test results for 250 chemicals. Environ. Mutagen. Suppl. 5(Suppl. 1): 10-11, 94-95.

Hedenstedt, A. 1978. Mutagenicity screening of industrial chemicals: Seven aliphatic amines and one amide tested in the Salmonella/microsomal assay. Mutat. Res. 53: 198-199.

Hulla, J.E., S.J. Rogers and G.R. Warren. 1981. Mutagenicity of a series of polyamines. Environ. Mutagen. 3: 332-333.

Slesinski, R.S., P.J. Guzzie, W.G. Hengler, P.G. Watanabe, M.D. Woodside and R.S.H. Yang. 1983. Assessment of genotoxic potential of ethylenediamine: In vitro and in vivo studies. Mutat. Res. 124(3-4): 299-314.

U.S. EPA. 1988. Health and Environmental Effects Document for Ethylene diamine. 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.

Yang, R.S.H. and M.J. Tallant. 1982. Metabolism and pharmacokinetics of ethylenediamine in the rat following oral, endotracheal or intravenous administration. Fund. Appl. Toxicol. 2(5): 252-260.

Yang, R.S.H., M.J. Tallant and J.A. McKelvey. 1984a. Age-dependent pharmacokinetic changes of ethylenediamine in Fischer 344 rats parallel to a 2-year chronic toxicity study. Fund. Appl. Toxicol. 4(4): 663-670.

Yang, R.S.H., R.H. Garman, E.V. Weaver and M.D. Woodside. 1984b. Two- generation reproduction study of ethylenediamine in Fischer 344 rats. Fund. Appl. Toxicol. 4(4): 539-546.

Zimmering, S., J.M. Mason, R. Valencia and R.C. Woodruff. 1985. Chemical mutagenesis testing in Drosophila. 2. Results of 20 coded compounds tested for the National Toxicology Program. Environ. Mutagen. 7: 87-100.

VII. Revision History

Substance Name — Ethylene diamine
CASRN — 107-15-3

Date	Section	Description
05/01/1991	I.B.	Inhalation RfC message on-line
11/01/1992	II.	Carcinogenicity assessment on-line
10/28/2003	I.B., II.D.2.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Ethylene diamine
CASRN — 107-15-3
Last Revised — 05/01/1991

- 107-15-3
- 1,2-Ethanediamine
- Aethaldiamin [German]
- Aethylenediamin [German]
- Algicode 106L
- Amerstat 274
- BETA-AMINOETHYLAMINE
- Caswell No. 437
- Dimethylenediamine
- EPA Pesticide Chemical Code 004205
- Ethyleendiamine [Dutch]
- Ethylendiamine
- ETHYLENE-DIAMINE [French]
- Ethylenediamine
- Etilendiamina [Spanish]
- HSDB 535
- NCI-C60402
- UN 1604
- 1,2-DIAMINO-ETHAAN [Dutch]
- 1,2-DIAMINO-ETHANO [Italian]
- 1,2-DIAMINOAETHAN [German]
- 1,2-diaminoethane
- 1,2-ETHANEDIAMINE
- 1,2-ETHYLENEDIAMINE