Ethylene glycol; CASRN 107-21-1

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 Ethylene glycol

File First On-Line 09/30/1987

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	09/30/1987
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 — Ethylene glycol
CASRN — 107-21-1
Last Revised — 09/30/1987

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
Kidney Toxicity **Chronic Rat Oral Feeding Study** **DePass et al., 1986a**	NOEL: 200 mg/kg/day LOAEL: 1000 mg/kg/day	100	1	2E+0 mg/kg/day

*Conversion Factors -- none

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

DePass, L.R., R.H. Garman, M.D. Woodside, et al. 1986a. Chronic toxicity and oncogenicity studies of ethylene glycol in rats and mice. Fund. Appl. Toxicol. 7: 547-565.

DePass et al. (1986a) conducted 2-year studies using groups of approximately 30 rats/sex and 20 mice/sex fed diets providing ethylene glycol dosages of 0, 40, 200, or 1000 mg/kg/day. High-dose rats had increased mortality, neutrophil count, water intake, kidney hemoglobin and hematocrit, and chronic nephritis. Female rats exposed to 1000 mg/kg/day had mild fatty changes in the liver. No adverse effects occurred at other doses in rats or at any dose in mice.

Groups of Sprague-Dawley rats (16/sex/group) were fed diets containing 0, 0.1, 0.2, 0.5, 1.0, or 4.0% ethylene glycol for 2 years (Blood, 1965). Male rats at 1.0 and 4.0% and females at 4.0% had increased mortality, decreased growth, increased water consumption, proteinurea, and renal calculi. There was an increased incidence of cytoplasmic crystal deposition in renal tubular epithelium at 0.5 and 1.0%. There were no effects on organ weights or hematologic parameters. The authors concluded that 0.2% (2000 ppm) was a NOEL for rats; the LOAEL was 0.5% (5000 ppm). Assuming that a rat consumes food equivalent to 5% of its body weight/day, the NOEL and the LOAEL are equivalent to 100 mg/kg/day and 250 mg/kg/day, respectively.

The choice of the DePass et al. (1986a) study over the Blood (1965) study as the basis of the RfD reflects the greater confidence in the former study because of a greater number of animals tested and effects considered. The magnitude of the RfD in either case is similar.

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

UF — The UF of 100 included 10 for interspecies extrapolation and 10 for differences in individual human sensitivity.

MF — None

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

Blood et al. (1962) fed a diet containing 0.2 or 0.5% ethylene glycol to rhesus monkeys for 3 years. No treatment-related toxic effects on histologic appearance of kidneys or other major organs were found.

In a teratogenicity study, Maronpot et al. (1983) found increased preimplantation loss and increased incidence of poorly ossified vertebral centra in offspring of rats treated at 1000 mg/kg in the diet on days 6-15 of gestation. No effects occurred at 40 or 200 mg/kg. Lamb et al. (1985) reported that exposure of male and female mice to 1.0% ethylene glycol in drinking water for 14 weeks resulted in significantly fewer litters, decreased mean live pup weight, and decreased number of live pups/litter. DePass et al. (1986b) conducted a 3-generation study in which rats were treated with 0, 40, 200, or 1000 mg/kg/day in the diet. No treatment-related effects were observed. Price et al. (1985) treated rats with gavage doses of 0, 1250, 2500, or 5000 mg/kg/day and mice with 0, 750, 1500, or 3000 mg/kg/day on days 6-15 of gestation. The percentage of litters with malformed fetuses increased in a dose-related manner in both species at all doses. There was a dose- related increase in postimplantation losses/litter in both species, but it was significant only in high-dose rats. Maternal body weight gain was decreased at all doses in rats and at the two higher doses in mice.

I.A.5. Confidence in the Oral RfD

Study — High
Database — High
RfD — High

Confidence in the DePass et al. (1986a) study is rated high because it was a well-conducted lifetime study in two species by a relevant route and defined a NOAEL and LOAEL. Confidence in the database is also high because it contains another chronic rat study and a monkey study that

support the NOEL and LOAEL from the DePass et al. (1986a) study. It also contains data which indicate that the RfD is protective of teratogenic and reproductive effects. Confidence in the RfD is therefore high.

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

Source Document — U.S. EPA, 1986

ECAO-CIN internal review and limited Agency Review. The Carcinogen Assessment Group, the Office of Pesticide Programs, and the Office of Toxic Substances are currently reviewing the document.

Other EPA Documentation — None

Agency Work Group Review — 03/19/1987

Verification Date — 03/19/1987

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 Ethylene glycol conducted in August 2003 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 — Ethylene glycol
CASRN — 107-21-1

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Ethylene glycol
CASRN — 107-21-1

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 — Ethylene glycol
CASRN — 107-21-1

VI.A. Oral RfD References

Blood, F.R. 1965. Chronic toxicity of ethylene glycol in the rat. Food Cosmet. Toxicol. 3: 229-234.

Blood, F.R., G.A. Elliott and M.S. Wright. 1962. Chronic toxicity of ethylene glycol in the monkey. Toxicol. Appl. Pharmacol. 4: 489-491.

DePass, L.R., R.H. Garman, M.D. Woodside, et al. 1986a. Chronic toxicity and oncogenicity studies of ethylene glycol in rats and mice. Fund. Appl. Toxicol. 7: 547-565.

DePass, L.R., M.D. Woodside, R.R. Maronpot and C.S. Weil. 1986b. Three-generation reproduction and dominant lethal mutagenesis studies of ethylene glycol in the rat. Fund. Appl. Toxicol. 7: 566-572.

Lamb, J.C., R.R. Maronpot, D.K. Gulati, V.S. Russell, L. Hommel-Barnes and P.S. Sabharwal. 1985. Reproductive and development toxicity of ethylene glycol in the mouse. Toxicol. Appl. Pharmacol. 81(1): 100-112.

Maronpot, R.R., J.P. Zelenak, E.V. Weaver and N.J. Smith. 1983. Teratogenicity study of ethylene glycol in rats. Drug. Chem. Toxicol. 6(6): 579-594.

Price, C.J., C.A. Kimmel, R.W. Tyl and M.C. Marr. 1985. The developmental toxicity of ethylene glycol in rats and mice. Toxicol. Appl. Pharmacol. 81(1): 113-127.

U.S. EPA. 1986. Health Effects Assessment for Ethylene Glycol. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Emergency and Remedial Response, Washington, DC.

VI.B. Inhalation RfD References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Ethylene glycol
CASRN — 107-21-1

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

VIII. Synonyms

Substance Name — Ethylene glycol
CASRN — 107-21-1
Last Revised — 09/30/1987

- 107-21-1
- ATHYLENGLYKOL
- 1,2-DIHYDROXYETHANE
- DOWTHERM SR 1
- 1,2-ETHANDIOL
- 1,2-ETHANEDIOL
- ETHYLENE ALCOHOL
- ETHYLENE DIHYDRATE
- Ethylene glycol
- GLYCOL
- GLYCOL ALCOHOL
- LUTROL-9
- M.E.G.
- MACROGOL 400 BPC
- MONOETHYLENE GLYCOL
- NCI-C00920
- NORKOOL
- TESCOL
- UCAR 17