Ethyl ether; CASRN 60-29-7

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 Ethyl ether

File First On-Line 09/01/1990

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	09/01/1990
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 — Ethyl ether
CASRN — 60-29-7
Last Revised — 09/01/1990

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
Depressed body weights **Rat Oral Subchronic Study** **U.S. EPA, 1986**	NOAEL: 500 mg/kg/day LOAEL: 2000 mg/kg/day	3000	1	2E-1 mg/kg/day

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

U.S. EPA. 1986. Rat oral subchronic study with ethyl ether. Prepared by American Biogenics Corporation for the Office of Solid Waste, Washington, DC.

Four groups of male and female rats (30/sex/group) were gavaged daily with 0, 500, 2000, and 3500 mg/kg/day of ethyl ether for 13 weeks. Six weeks after the initiation of dosing, an interim sacrifice of 10 rats/sex was performed. The remaining animals continued in the experiment until the day of the final sacrifice. Data generated from this study included body weight changes; food consumption; ophthalmological examinations; clinical, biochemical, and gross morphological changes; and histopathology of target organs. An evaluation of data revealed marked toxicity of ethyl ether at the high dose (3500 mg/kg/day), including mortality, decreased food intake, and body weight loss. Body weight loss was observed in both sexes at the two highest doses; only females showed a significant reduction at the high dosage. Histopathological evaluations of tissues revealed no effects related to the administration of ethyl ether. Based on data available from this study, 500 mg/kg/day is considered a NOAEL and 2000 mg/kg/day a LOAEL (significant body weight depression in male rats).

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

UF — An uncertainty factor of 3000 reflects 10 to extrapolate from subchronic to chronic data, 10 for interspecies extrapolation, 10 to account for intraspecies variability, and an additional factor of 3 for lack of toxicity data in a second species and reproductive/developmental studies.

MF — None

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

Additional information regarding orally administered ethyl ether is essentially limited to acute toxicity data. Reported intentional consumption can result in symptoms similar to those associated with alcoholism (Moeschlin, 1965). Ether anesthesia of pregnant mice and rats has been reported to produce some embryotoxic and teratogenic effects; however, the authors did not consider ether anesthesia as "highly teratogenic" (Schwetz and Becker, 1970).

Other criteria for ethyl ether exposure include a TLV of 400 ppm (1210 mg/cu.m) (ACGIH, 1984), an OSHA standard of 400 ppm, and a NIOSH recommended IDLH of 19,000 ppm in the atmosphere (Mackinson, 1980).

I.A.5. Confidence in the Oral RfD

Study — Medium
Database — Low
RfD — Low

The oral subchronic study was based on a well-designed experimental protocol, provided adequate toxicological endpoints, identified both a LOAEL and a NOAEL, and is considered of medium confidence. The database does not provide pertinent information on toxicity data in a second species, on reproductive or developmental studies, however, and is considered of low confidence. Low confidence in the RfD follows.

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, 1986

Agency Work Group Review — 06/11/1986, 03/19/1987, 09/19/1989, 10/19/1989, 11/15/1989

Verification Date — 11/15/1989

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 Ethyl ether conducted in November 2001 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 — Ethyl ether
CASRN — 60-29-7

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Ethyl ether
CASRN — 60-29-7

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 — Ethyl ether
CASRN — 60-29-7

VI.A. Oral RfD References

ACGIH (American Conference of Governmental Industrial Hygienists). 1984. TLVs - Threshold Limit Values for Chemical Substances and Physical Agents in the Environment with Intended Changes for 1984-1985. Cincinnati, OH. p. 19.

Mackison, F.W. 1980. NIOSH/OSHA Pocket Guide to Chemical Hazard. U.S. Government Printing Office, Washington, DC. DHEW (NIOSH) Publ. No. 78-210.

Moeschlin, S. 1965. Poisoning: Diagnosis and Treatment. Grune and Stratton, New York. p. 294.

Schwetz, B.A. and B.A. Becker. 1970. Embryotoxicity and fetal malformations of rats and mice due to maternally administered ether. Toxicol. Appl. Pharmacol. 17: 275.

U.S. EPA. 1986. Rat oral subchronic study with ethyl ether. Prepared by American Biogenics Corporation for the Office of Solid Waste, Washington, DC.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Ethyl ether
CASRN — 60-29-7

Date	Section	Description
09/01/1990	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 — Ethyl ether
CASRN — 60-29-7
Last Revised — 09/01/1990

- 60-29-7
- AETHER
- ANAESTHETIC ETHER
- ANESTHESIA ETHER
- ANESTHETIC ETHER
- DIAETHYLAETHER [GERMAN]
- DIETHYL ETHER
- DIETHYL OXIDE
- DWUETYLOWY ETER [POLISH]
- ETER DIETILICO [SPANISH]
- ETERE ETILICO [ITALIAN]
- ETHANE, 1,1'-OXYBIS-
- ETHER
- ETHER DIETHYLIQUE [FRENCH]
- ETHER, ETHYL
- ETHER ETHYLIQUE [FRENCH]
- ETHOXYETHANE
- ETHYL ETHER
- ETHYL OXIDE
- HSDB 70
- NSC 100036
- 3-OXAPENTANE
- 1,1'-OXYBISETHANE
- OXYDE D'ETHYLE [FRENCH]

- RCRA WASTE NUMBER U117
- SOLVENT ETHER
- UN 1155