Bis(2-chloro-1-methylethyl) ether; CASRN 108-60-1

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 <u>IRIS assessment</u> <u>development process</u>. 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 <u>guidance documents located</u> on the IRIS website.

STATUS OF DATA FOR Bis(2-chloro-1-methylethyl) ether

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	10/01/1989
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	not evaluated	

File First On-Line 10/01/1989

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Bis(2-chloro-1-methylethyl) ether CASRN — 108-60-1 Last Revised — 10/01/1989

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
Decrease in hemoglobin and possible erythro- cyte destruction	NOAEL: 400 ppm (35.8 mg/kg/day)	1000	1	4E-2 mg/kg/day
104-Week Mouse Study Oral Exposure (diet)	LOAEL: 2000 ppm (198 mg/kg/day)			
Mitsumori et al., 1979				

*Conversion Factors: Determined by principal investigators

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

Mistsumori, K., T. Usui, K. Takahashi and Y. Shirasu. 1979. Twenty-four month chronic toxicity studies of dichlorodiisopropyl ether in mice. Nippon NoYaku Gakkaishi. 4(3): 323-335.

Bis(2-chloro-1-methylethyl) ether (98.5% pure) was incorporated into the diets of SPF-ICR mice (56 males and 56 females/group) at levels of 0, 80, 400, 2000, or 10,000 ppm for up to 104 weeks. Comprehensive hematological, blood biochemical, and urinalysis determinations were performed on 7 mice/sex/group at 13, 26, and 52 weeks; on 6/sex/group at 78 weeks; and the remaining mice at 104 weeks. Hemosiderin deposition in the spleen was seen in the males on the 10,000 ppm diet (HDT) and in females receiving both the 2000 and 10,000 ppm diet. Decreases in hemoglobin concentration and red blood cell counts were also observed. These findings indicate a treatment-related increase in erythrocyte destruction. A NOAEL of 2000 ppm for males and 400 ppm for females was indicated. These doses were determined by the investigators to be equivalent to 198 and 35.8 mg/kg/day for males and females, respectively. The females were considered more sensitive to the effects of bis(2-chloro-1-methylethyl) ether in the diet and the NOAEL of 400 ppm (35.8 mg/kg/day) was considered appropriate.

All other available studies on bis(2-chloro-1-methylethyl) ether were conducted using an isopropyl isomer mixture containing only 70% of the bis(2-chloro-1-methylethyl) ether. Accordingly, none of these studies were included with this summary.

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

UF — The 1000-fold uncertainty factors accounts for both interspecies and interhuman variability in the toxicity of this chemical in lieu of specific data. An additional uncertainty factor of 10 was indicated to account for data gaps in the studies on bis(2-chloro-1-methylethyl) ether.

MF — None

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

None.

I.A.5. Confidence in the Oral RfD

Study — Medium Database — Low RfD — Low

Confidence in the principal study is medium because an acceptable number of animals of each sex was used, four doses were given, and many test parameters were measured. Confidence in the database is low because no supporting studies were available. Accordingly, confidence in the RfD is low.

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

Source Document — U.S. EPA, 1989

Other EPA Documentation — None

Agency Work Group Review — 12/18/1985, 08/13/1987, 07/20/1989

Verification Date — 07/20/1989

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 bis(2-chloro-1-methylethyl) ether 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 <u>hotline.iris@epa.gov</u> 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 <u>hotline.iris@epa.gov</u> (internet address).

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

Substance Name — Bis(2-chloro-1-methylethyl) ether CASRN — 108-60-1

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Bis(2-chloro-1-methylethyl) ether CASRN — 108-60-1

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 — Bis(2-chloro-1-methylethyl) ether CASRN — 108-60-1

VI.A. Oral RfD References

Mitsumori, K., T. Usui, K. Takahashi and Y. Shirasu. 1979. Twenty-four month chronic toxicity studies of dichlorodiisopropyl ether in mice. J. Pesticide Sci. 4: 323-335.

U.S. EPA. 1989. Drinking Water Health Advisory for Bis-(2-chloroisopropyl) ether, Office of Drinking Water, Washington, DC. (Draft)

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Bis(2-chloro-1-methylethyl) ether CASRN — 108-60-1

Date	Section	Description
10/01/1989	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 — Bis(2-chloro-1-methylethyl) ether CASRN — 108-60-1 Last Revised — 10/01/1989

- 108-60-1
- 2,2'-Oxybis(1-chloropropane)
- BCMEE
- beta, beta'-dichlorodiisopropyl ether
- Bis(1-chloroisopropyl) ether
- Bis(1-chloro-2-propyl) ether
- Bis(beta-chloroisopropyl) ether
- Bis(2-chloroisopropyl) ether [this synonym is also used with CASRN 39638-32-9]
- DCIP (nematocide)
- Dichlorodiisopropyl ether
- 2,2'-Dichlorodiisopropyl ether [this synonym is also used with CASRN 39638-32-9]
- Dichloroisopropyl ether [this synonym is also used with CASRN 39638-32-9]
- 2,2'-Dichloroisopropyl ether [this synonym is also used with CASRN 39638-32-9]
- Ether, bis(2-chloro-1-methylethyl)
- HSDB 503
- NCI-C50044
- Nemamort
- Nemamorte
- Propane, 2,2'-oxybis(1-chloro-
- RCRA waste number U027