

## Chloromethyl methyl ether (CMME); CASRN 107-30-2

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 CMME

**File First On-Line 09/30/1987**

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	yes	09/30/1987*

\* A comprehensive review of toxicological studies was completed (07/28/05) - please see section II.D.2. for more information.

## I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Chloromethyl methyl ether (CMME)  
CASRN — 107-30-2

Not available at this time.

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

Substance Name — Chloromethyl methyl ether (CMME)  
CASRN — 107-30-2

Not available at this time.

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## **II. Carcinogenicity Assessment for Lifetime Exposure**

Substance Name — Chloromethyl methyl ether (CMME)  
CASRN — 107-30-2  
Last Revised — 09/30/1987

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 — A; human carcinogen

Basis — The observation of an increased incidence of respiratory cancer in exposed workers and the observation of respiratory tumors in mice, rats, and hamsters exposed by inhalation forms the basis for this classification.

## II.A.2. Human Carcinogenicity Data

Sufficient. Commercial grade CMME is always contaminated with 1 to 8% bis(chloromethyl)ether (BCME), a known human carcinogen. CMME has an extremely short half-life in aqueous solution (estimated to be less than one-half second), but may be converted to BCME through hydrolysis (Nelson, 1976).

Numerous case reports (Bettendorf, 1976; Reznik et al., 1977) and epidemiologic studies (Figuroa et al., 1973; DeFonso and Kelton, 1976; Lemen et al., 1976; Nelson, 1976; Weiss et al., 1980) have reported respiratory cancer associated with exposure to CMME. There are four studies of workers exposed to technical grade CMME with 1 to 8% of BCME as a contaminant. All studies observed statistically significant excesses in the incidence of lung carcinomas, predominantly of the oat-cell type. The age range in the study populations was 35 to 54 years, with a latency period of 8 to 16 years. In a retrospective cohort mortality study of 1827 workers exposed to CMME for up to 19 years and 8870 controls, 26 cases of respiratory cancer were reported (9.3 expected, SMR=278) (Pasternack et al., 1977). This increased incidence was statistically significant. Exposure was not quantifiable. A statistically significant dose-response relationship was observed for duration and intensity of exposure (Pasternack, 1977; Albert et al., 1975). The observed number of lung carcinomas was higher than expected in the workers exposed to CMME contaminated with BCME (technical grade CMME) by comparison to unexposed workers, but was lower than the observed numbers in workers who were exposed to BCME alone. Hence the observed lung carcinomas in the CMME-exposed workers may be due to the contaminant BCME, which is a known human carcinogen. Therefore, despite the limitations of these studies, the human evidence for the carcinogenicity of technical grade CMME is considered to be sufficient.

## II.A.3. Animal Carcinogenicity Data

Leong (1971) administered 2 ppm CMME by inhalation to 50 A/Heston strain male mice for 6 hours/day, 5 days/week for 101 days. An increased incidence of lung adenomas with increasing proportions of BCME was seen compared with controls but was not statistically significant. Newborn ICR Swiss mice injected with 125 uL/kg CMME subcutaneously had an increased incidence of pulmonary tumors, but the increase was not statistically significant (Gargus et al., 1969).

Laskin et al. (1975) reported two respiratory carcinomas in 74 male Sprague-Dawley rats and two in 90 male Syrian golden hamsters with lifetime exposures to 1 ppm CMME for 6 hours/day, 5 days/week. CMME administered by subcutaneous injection (1/week for 30 days) to 20 female Sprague-Dawley rats, and female ICR/Ha Swiss mice produced encapsulated nodules and injection site sarcomas (Van Duuren et al., 1969, 1971, 1972). Dermal application of CMME to

mice has not resulted in tumors (Van Duuren et al., 1969; IARC, 1974). CMME has been shown to initiate skin tumorigenesis in initiation/promotion assays with phorbol ester in mice (IARC, 1974).

BCME has been found to be a skin carcinogen and to induce respiratory tract tumors in rodents when administered by inhalation (Van Duuren et al., 1968; Leong et al., 1971; Drew et al., 1975; Kuschner et al., 1975).

#### **II.A.4. Supporting Data for Carcinogenicity**

CMME is mutagenic to *E. coli* and *S. typhimurium* in the absence of exogenous metabolism (Mukai and Troll, 1969; Mukai and Hawryluk, 1973). Cytogenetic analysis of peripheral lymphocytes in workers exposed to CMME and BCME showed 6.7% aberrant cells compared with 2% in controls (Zudova and Landa, 1977).

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

Not available. Risk is likely to be no more than that of BCME, a contaminant of CMME.

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

Not available.

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

##### **II.D.1. EPA Documentation**

Source Document — U.S. EPA, 1980, 1977

The 1980 Ambient Water Quality Criteria for Chloroalkyl Ethers has received internal and external review.

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

Agency Work Group Review — 05/13/1987

Verification Date — 05/13/1987

A comprehensive review of toxicological studies published through July 2005 was conducted. No new health effects data were identified that would be directly useful in the revision of the existing carcinogenicity assessment for Chloromethyl methyl ether and a change in the assessment is not warranted at this time. For more information, IRIS users may contact the IRIS Hotline at [hotline.iris@epa.gov](mailto: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](mailto:hotline.iris@epa.gov) (internet address).

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**III. [reserved]**

**IV. [reserved]**

**V. [reserved]**

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## **VI. Bibliography**

Substance Name — Chloromethyl methyl ether (CMME)  
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### **VI.A. Oral RfD References**

None

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### **VI.B. Inhalation RfC References**

None

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### **VI.C. Carcinogenicity Assessment References**

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## VII. Revision History

Substance Name — Chloromethyl methyl ether (CMME)

CASRN — 107-30-2

Date	Section	Description
10/28/2003	II.D.2.	Screening-Level Literature Review Findings message has been added.
08/15/2005	II.D.2.	Screening-Level Literature Review Findings message has been removed and replaced by comprehensive literature review conclusions.

## VIII. Synonyms

Substance Name — Chloromethyl methyl ether (CMME)

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Last Revised — 09/30/1987

- 107-30-2
- Chlordimethylether
- Chlorodimethyl ether
- Chloromethoxymethane
- Chloromethyl Methyl Ether
- CMME
- Dimethylchloroether
- Ether, chloromethyl methyl
- ETHER, DIMETHYL CHLORO
- ETHER METHYLIQUE MONOCHLORE
- HSDB 908
- Methane, chloromethoxy-
- Methoxychloromethane
- Methoxymethyl chloride
- Methyl Chloromethyl Ether
- METHYL CHLOROMETHYL ETHER, ANHYDROUS
- Monochlorodimethyl ether
- MONOCHLOROMETHYL METHYL ETHER
- RCRA WASTE NUMBER U046
- UN 1239