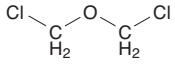
Bis(chloromethyl) Ether and Technical-Grade Chloromethyl Methyl Ether

CAS Nos. 542-88-1 and 107-30-2

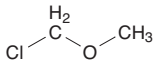
Known to be human carcinogens

First listed in the *First Annual Report on Carcinogens* (1980)

Also known as BCME and CMME



Bis(chloromethyl) ether



Chloromethyl methyl ether

Carcinogenicity

Bis(chloromethyl) ether (BCME) and technical-grade chloromethyl methyl ether (CMME) are *known to be human carcinogens* based on sufficient evidence of carcinogenicity from studies in humans.

Cancer Studies in Humans

Numerous epidemiological studies and case reports from various geographical locations have demonstrated that occupational exposure to BCME or CMME causes lung cancer (predominantly small-cell carcinoma). The risk of lung cancer was shown to increase with increasing exposure duration or cumulative exposure. Among the most heavily exposed workers, the risk of lung cancer was increased at least tenfold, and the time between exposure and diagnosis of disease was shorter. The studies were of workers exposed either to BCME or to CMME; however, because BCME is a contaminant of technical-grade CMME (at levels of 1% to 7%), workers exposed to CMME probably were also exposed to BCME. The International Agency for Research on Cancer concluded that there was sufficient evidence for the carcinogenicity of BCME and technical-grade CMME in humans (IARC 1974, 1987).

Cancer Studies in Experimental Animals

Exposure to BCME by inhalation caused lung tumors in rats and mice and nasal-cavity tumors in rats. Administration of BCME by subcutaneous injection caused lung tumors in mice of both sexes and connective-tissue tumors (fibroma and/or fibrosarcoma) at the injection site in mice of both sexes and in female rats. Dermal exposure of female mice to BCME caused benign skin tumors (papilloma), most of which progressed to skin cancer (squamous-cell carcinoma). Evaluation of technical-grade CMME is complicated by the presence of BCME as a contaminant. Exposure to technical-grade CMME by inhalation caused a low incidence of respiratory-tract tumors in rats and hamsters, and subcutaneous administration caused tumors at the injection site (sarcoma) in mice. IARC (1987) concluded that there was sufficient evidence for the carcinogenicity of BCME and technical-grade CMME in experimental animals.

Studies on Mechanisms of Carcinogenesis

BCME caused mutations in bacteria. It also caused unscheduled DNA synthesis in cultured human cells but did not cause chromosomal aberrations in bone-marrow cells of rats exposed *in vivo*. CMME caused mutations in bacteria and enhanced virus-induced transformation of mammalian cells. The incidence of chromosomal aberrations was increased slightly in white blood cells from workers exposed to BCME or CMME (IARC 1987).

Properties

BCME is a chloroalkyl ether compound that exists at room temperature as a colorless liquid with a suffocating odor. It is only slightly soluble in water, but it is miscible with ethanol, ethyl ether, and many organic solvents. The compound is unstable in moist air and hydrolyzes rapidly in water (Akron 2009). Physical and chemical properties of BCME are listed in the following table. No physical or chemical properties were identified for technical-grade CMME.

Property	Information (BCME)
Molecular weight	115.0
Specific gravity	1.323 at 15°C/4°C
Melting point	–41.5°C
Boiling point	106°C
Log K_{ow}	1.04
Water solubility	1.020 g/L at 25°C
Vapor pressure	29.4 mm Hg at 25°C
Vapor density relative to air	4

Source: HSDB 2009.

Use

BCME and CMME are used primarily as chemical intermediates and alkylating agents. BCME is used as a laboratory reagent, in the manufacture of plastics, ion-exchange resins, and polymers, and as a monitoring indicator for chloromethyl ether (HSDB 2009). BCME formerly was used for cross-linking of cellulose, for surface treatment of vulcanized rubber to increase adhesion, and in the manufacture of flame-retardant fabrics (ATSDR 1989). CMME is used as an alkylating agent and industrial solvent in the manufacture of dodecylbenzyl chloride, water repellents, ion-exchange resins, and polymers, and as a chloromethylation reagent (HSDB 2009).

Production

BCME and CMME previously were manufactured in the United States, but use of these chemicals had been widely curtailed by 1976 (HSDB 2009). In 1977, U.S. production of BCME was 45,400 kg (100,000 lb), and that of CMME was 4.6 million kilograms (10 million pounds). In 1982, BCME was no longer produced in the United States, and only 2,270 kg (5,000 lb) of CMME was produced. There were three U.S. manufacturers of CMME in 1969, one in 1973, and none in 2009 (IARC 1974a,b, HSDB 2009, SRI 2009). Although BCME is no longer produced commercially in the United States, small quantities may be produced or repackaged as a chemical intermediate or laboratory chemical (ATSDR 1989, HSDB 2009). In 2009, BCME was available from five U.S. suppliers and CMME from nine U.S. suppliers (ChemSources 2009). No data on U.S. imports or exports of BCME or CMME were found.

Exposure

The primary routes of potential human exposure to BCME and technical-grade CMME are inhalation and dermal contact. Because BCME is little used in the United States and because it is rapidly degraded in the environment, the probability of human exposure is very low. BCME has not been detected in ambient air or water (ATSDR 1989). According to the U.S. Environmental Protection Agency's Toxics Release Inventory, almost all environmental releases of BCME and CMME have been to the air. Reported annual releases of BCME to air ranged from 255 to 574 lb in the early 1990s, but since 1995, annual releases to air have not exceeded 7 lb, and no releases to air were reported in 1995, 1996, 1998, 2000, or 2009. Releases of CMME to air since 1988 (the earliest year for which reports were available) have fluctuated between 1,000 lb in 1988 and 4,155 lb in 1997. In 2009, one facility reported releases of 3,600 lb of CMME to air (TRI 2009).

The primary route of occupational exposure to BCME or CMME is inhalation of vapors; however, the potential for exposure is low, because these chemicals are no longer produced or sold in large quan-

tities, and most industrial operations involving them take place in closed-process vessels. The most likely means of exposure to BCME is during the production or use of chemicals in which it may occur as a contaminant or may be formed inadvertently. The potential for occupational exposure to BCME or CMME is greatest for chemical plant workers, ion-exchange resin makers, laboratory workers, and polymer makers (ATSDR 1989). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 14 workers (all laboratory workers), including 5 women, potentially were exposed to BCME. No estimate of potential exposure to CMME was reported (NIOSH 1990).

Regulations

Environmental Protection Agency (EPA)

Clean Air Act

National Emission Standards for Hazardous Air Pollutants: BCME and CMME are listed as hazardous air pollutants.

Prevention of Accidental Release: Threshold quantity (TQ) = 1,000 lb for BCME and 5,000 lb for CMME.

Clean Water Act

Water Quality Criteria: Based on fish or shellfish and water consumption = 0.00015 µg/L for BCME; based on fish or shellfish consumption only = 0.017 µg/L for BCME.

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable quantity (RQ) = 10 lb for BCME and CMME.

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: BCME and CMME are listed substances subject to reporting requirements.
Threshold planning quantity (TPQ) = 100 lb for BCME and CMME.
Reportable quantity (RQ) = 10 lb for BCME and CMME.

Resource Conservation and Recovery Act

Listed Hazardous Waste: Waste codes for which the listing is based wholly or partly on the presence of BCME = P016, K017; on the presence of CCME = U046.
BCME and CMME are listed as hazardous constituents of waste.

Mine Safety and Health Administration (MSHA, Dept. of Labor)

To control airborne exposure, neither BCME nor CMME shall be used or stored except by competent persons under laboratory conditions approved by a nationally recognized agency acceptable to the Secretary.

Occupational Safety and Health Administration (OSHA, Dept. of Labor)

BCME and CMME are listed as potential occupational carcinogens: Engineering controls, work practices, and personal protective equipment are required.
BCME and CMME are considered highly hazardous chemicals: Threshold quantity (TQ) = 100 lb for BCME; = 500 lb for CMME.

Guidelines

American Conference of Governmental Industrial Hygienists (ACGIH)

Threshold limit value – time-weighted average (TLV-TWA) = 0.001 ppm for BCME; = exposure to CCME by all routes should be as low as possible.

National Institute for Occupational Safety and Health (NIOSH, CDC, HHS)

BCME and CMME are listed as potential occupational carcinogens.

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