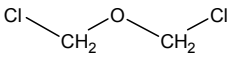
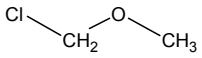
BIS(CHLOROMETHYL) ETHER AND TECHNICAL-GRADE CHLOROMETHYL METHYL ETHER

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

First Listed in the *First Annual Report on Carcinogens*



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 in humans (IARC 1982, 1987). Numerous epidemiological studies and case reports from around the world have demonstrated that workers exposed to BCME and/or CMME have an increased risk for lung cancer. Among heavily exposed workers, the relative risks are ten fold or greater. Risks increase with duration and cumulative exposure. Histological evaluation indicates that exposure results primarily in lung cancer of the small-cell type. Maximal relative risks appear to occur 15 to 20 years after first exposure, and latency is shortened among workers with heavier exposure.

An IARC Working Group reported that there is sufficient evidence of carcinogenicity of BCME and technical-grade CMME in experimental animals (IARC 1974, 1979, 1982, 1987). The evaluation of technical-grade CMME alone is complicated by the presence of 1 to 8% BCME as a contaminant. Technical-grade CMME produced local sarcomas in mice after subcutaneous administration and was an initiator of mouse skin tumors after topical application. It produced a low incidence of tumors of the respiratory tract in rats and hamsters after exposure by inhalation. When administered by subcutaneous injection, BCME induced pulmonary tumors and local fibrosarcomas in mice of both sexes and fibromas and fibrosarcomas in female rats. The compound is also an initiator of skin tumors in mice. When administered by inhalation, BCME induced lung tumors in mice and squamous cell carcinomas of the lung and esthesioneuroepitheliomas of the nasal cavity in rats. When applied topically, BCME induced papillomas, most of which progressed to squamous cell carcinomas, in female mice (IARC 1974, 1979).

PROPERTIES

BCME and CMME are flammable, volatile, colorless liquids that are miscible with ethanol and many other organic solvents. In aqueous solutions, they are rapidly hydrolyzed to form hydrochloric acid and formaldehyde. BCME has a suffocating odor and CMME has an irritating odor. BCME can form whenever formaldehyde, water, and hydrogen chloride vapors are mixed at room temperature, even in low concentrations. When heated to decomposition, these chemicals emit toxic fumes of hydrochloric acid and other chlorinated compounds. Vapors may form explosive mixtures with air (IARC 1974, HSDB 2001a, b).

USE

BCME and CMME are primarily used as chemical intermediates and alkylating agents. BCME is used as a laboratory reagent, to manufacture plastics, ion-exchange resins, and polymers, and as a monitoring indicator for chloromethyl ether (HSDB 2001a). BCME was once used for crosslinking of cellulose, surface treatment of vulcanized rubber to increase adhesion, and in the manufacture of flame-retardant fabrics (ATSDR 1989). CMME is used as an industrial solvent, to manufacture dodecylbenzyl chloride, water repellants, ion exchange resins, and polymers, and as a chloromethylation reagent (HSDB 2001b).

PRODUCTION

Chem Sources (2001) identified five U.S. suppliers of BCME and nine suppliers of CMME. The 1979 TSCA Inventory identified four domestic producers of CMME, with a total of 31 million lb produced in 1977, and one producer of BCME with a volume of 550,000 lb. Although significant quantities of BCME and CMME were previously manufactured in this country, use of these chemicals was curtailed in 1976 (HSDB 2001b). Three U.S. manufacturers of CMME were identified (HSDB 2001b). BCME is no longer produced as a commercial product in the United States; however, small quantities may be produced or repackaged as a chemical intermediate or laboratory chemical (ATSDR 1989, HSDB 2001a). BCME is produced as a contaminant during the manufacture of CMME, usually at levels of 0.5 to 5% (ATSDR 1989). Technical grades of CMME are contaminated with 1 to 8% BCME (IARC 1974). No data on imports or exports were available for these compounds.

EXPOSURE

The primary routes of potential human exposure to BCME and technical-grade CMME are inhalation and dermal contact. Because BCME is used very little in this country and because it is rapidly degraded in the environment, the probability of human exposure is very low. It has not been detected in ambient air or water (ATSDR 1989). EPA's Toxic Chemical Release Inventory (TRI) listed three industrial facilities that produced, processed, or otherwise used BCME in 1999 and five for CMME. These facilities released 157 lb of BCME and 1,540 lb of CMME to the environment in 1999. Historical TRI data showed that environmental releases of BCME and CMME ranged from 0 to 576 lb/yr and 1,000 to 4,214 lb/yr, respectively, between 1988 and 1999 (TRI99 2001).

Occupational exposure to CMME is minimized because most industrial operations working with the chemical are conducted in closed process vessels. The most likely means of exposure to BCME is inhalation of vapors in the workplace during the production and use of chemicals in which it may occur as a contaminant or may be formed inadvertently (ATSDR 1989). The risk of potential occupational exposure to the chemicals is greatest for workers such as chemical plant workers, ion-exchange resin makers, laboratory workers, and polymer makers. The National Occupational Exposure Survey (1981-1983) indicated that 14 workers, including 5 women, were potentially exposed to BCME (NIOSH 1984). This estimate was based only on observations of the actual use of the compound.

REGULATIONS

EPA regulates bis(chloromethyl) ether and chloromethyl methyl ether under the Clean Water Act (CWA), Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), Resource Conservation and Recovery Act (RCRA), Superfund Amendments and Reauthorization Act (SARA), and Toxic Substances Control Act (TSCA). Reportable quantities (RQs) of 10 lb (4.54 kg) have been established for both compounds under CERCLA. They are considered hazardous constituents of waste regulated under RCRA, and listed as extremely hazardous substances under the Emergency Planning and Community Right to Know Act (EPCRA). Bis(chloromethyl) ether, however, was deleted from the hazardous substance list of the CWA because of its extremely short half-life in water and the absence of data indicating it is a water pollution problem. Both compounds are subject to reporting under SARA.

The possible presence of bis(chloromethyl) ether in dental restorative materials is noted by the FDA; exposure is considered incidental.

NIOSH has set the recommended exposure limit (REL) to bis(chloromethyl) ether and chloromethyl methyl ether at the lowest feasible concentration. OSHA issued an emergency temporary standard covering both chemicals in 1973, and a final standard in 1974; this standard prohibits operations in open vessels and requires exhaust fans, protective clothing and devices, and warning signs and labels. OSHA also regulates occupational exposure to bis(chloromethyl) ether and chloromethyl methyl ether as potential carcinogens. It further regulates the two chemicals under the Hazard Communication Standard and as chemical hazards in laboratories. Regulations are summarized in Volume II, Table 39.

REFERENCES

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