



# *Canadian Environmental Protection Act*

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## Priority Substances List Assessment Report

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# **Bis(2-Chloroethyl) Ether**



Government  
of Canada

Gouvernement  
du Canada

Environment  
Canada

Environnement  
Canada

Health  
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PRIORITY SUBSTANCES LIST  
ASSESSMENT REPORT

Bis(2-CHLOROETHYL) ETHER

Government of Canada  
Environment Canada  
Health and Welfare Canada

Also available in French under the title:  
*Loi canadienne sur la protection de l'environnement*  
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## **Synopsis**

Data gathered under the authority of Section 16 of CEPA indicated that bis(2-chloroethyl) ether (BCEE) is not currently used or produced in Canada. This organic compound can be formed as a by-product in some industrial processes and was reported at measurable concentrations in in-plant industrial effluents at two industrial facilities in southern Ontario. However, no data were found concerning concentrations of BCEE in the ambient environment in Canada.

Since BCEE is manufactured and used in the United States, the highest concentration identified for surface waters in that country was used to represent a worst-case scenario in Canada for the purpose of this assessment. This concentration is approximately five orders of magnitude lower than the concentration found to induce adverse effects in the guppy, the most sensitive aquatic species identified among existing toxicity studies.

Exposure of terrestrial organisms to BCEE is considered to be negligible because of the extremely low rate of release and short persistence of this substance in the atmosphere. For the same reasons, BCEE is not considered to be associated with depletion of stratospheric ozone or with global warming, and is not expected to contribute significantly to ground level ozone formation.

Owing to the lack of available information on concentrations of BCEE in several environmental media to which humans are exposed, it is not possible to quantitatively estimate the total daily intake of BCEE by the general population in Canada. Available data on the toxicity of BCEE in humans are extremely limited. None of the long-term studies in experimental animals is considered to be of sufficient quality to provide useful quantitative information on either the potential of BCEE to cause cancer or the toxicological effects produced by long-term exposure to this substance. Information on the developmental and reproductive effects of BCEE in experimental animals has not been identified.

**Based on these considerations, the federal Minister of the Environment and the federal Minister of National Health and Welfare have concluded that bis(2-chloroethyl) ether is not entering the environment in a quantity or concentration or under conditions that constitute a danger to the environment or to the environment upon which human life depends. However, there are insufficient data to determine whether BCEE constitutes a danger in Canada to human life or health.**

## 1.0 Introduction

The *Canadian Environmental Protection Act* (CEPA) requires the federal Minister of the Environment and the federal Minister of National Health and Welfare to prepare and publish a Priority Substances List that identifies substances, including chemicals, groups of chemicals, effluents, and wastes that may be harmful to the environment or constitute a danger to human health. The Act requires both Ministers to assess these substances and determine whether they are "toxic" as defined under Section 11 of the Act which states:

"...a substance is toxic if it is entering or may enter the environment in a quantity or concentration or under conditions

- (a) having or that may have an immediate or long-term harmful effect on the environment;
- (b) constituting or that may constitute a danger to the environment on which human life depends; or
- (c) constituting or that may constitute a danger in Canada to human life or health."

Substances that are assessed as "toxic" as defined under Section 11 may be placed on Schedule I of the Act. Consideration can then be given for possible development of regulations, guidelines, or codes of practice to control any aspect of these substances' life cycle, from the research and development stage through manufacture, use, storage, transport, and ultimate disposal.

The assessment of whether bis(2-chloroethyl) ether (BCEE) is "toxic", as defined under CEPA, was based on the determination of whether it **enters** or is likely to enter the Canadian environment in a concentration or quantities or under conditions that could lead to **exposure** of humans or other biota to levels that could cause harmful **effects**.

Data relevant to the assessment of whether BCEE is "toxic" under CEPA were identified through evaluation of existing review documents (ATSDR, 1989; Durkin *et al.*, 1975; Clement Associates Inc., 1989; U.S. EPA, 1980; 1987a; 1987b; 1990) supplemented with information from published reference texts and literature identified through on-line searches of databases conducted between April and November, 1991. These databases included: AQUIRE, AQUALINE, AQUAREF, BIOSIS Previews, CAS ONLINE, CAB, CCINFO, Chemical Evaluation Search and Retrieval System (CESARS), Chemical Hazard Response Information System (CHRIS), Cooperative Documents Project (CODOC), Environment Canada Departmental Library Catalogue (ELIAS), ENVIROLINE, Federal Register, Hazardous Substances Data Bank (HSDB), Integrated Risk Information System (IRIS), MICROLOG, Pollution Abstracts, Registry of Toxic Effects of Chemical Substances (RTECS), TOXLINE, TOXLIT, TRI (TOXNET). Reviews of the environmental fate and effects, and effects of BCEE on human health were prepared under contract by Monenco Consultants Ltd., and

Cambridge Environmental Inc. (Croy *et al.*, 1991), respectively. In addition, a number of officials within federal and provincial governments were asked to provide any available (unpublished) monitoring data on the levels of BCEE in the Canadian environment, including drinking water. Data relevant to the assessment of the effects of BCEE on the environment obtained after June, 1992 have not been included. Similarly, data relevant to the assessment of the effects of BCEE on human health obtained after February 1992 were not considered for inclusion.

Review articles were consulted where appropriate. However, all original studies that form the basis for determining whether BCEE is "toxic" under CEPA have been critically evaluated by the following Environment Canada staff (entry, and environmental exposure and effects) and Health and Welfare Canada staff (human exposure and effects on human health):

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In this report, a synopsis concerning BCEE that will appear in the *Canada Gazette* is presented. Section 2.0 is an extended summary of the technical information that is critical to the assessment. The assessment of whether BCEE is "toxic" is presented in Section 3.0. A Supporting Document that presents the technical information in greater detail has also been prepared.

As part of the review and approvals process established by Environment Canada, the environmental sections of this Assessment Report were peer reviewed by the following scientists: Dr. Derek Muir (Fisheries and Oceans Canada, Winnipeg, Manitoba) and Dr. Keith Solomon (Centre for Toxicology, Guelph, Ontario). Sections related to the effects on human health were approved by the Standards and Guidelines Rulings Committee of the Bureau of Chemical Hazards of Health and Welfare Canada. The entire Assessment Report was reviewed and approved by the Environment Canada/Health and Welfare Canada CEPA Management Committee.

Copies of this Assessment Report and the unpublished Supporting Document are available upon request from:

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## 2.0 Summary of Information Critical to Assessment of "Toxic"

### 2.1 Identity, Properties, Production, and Uses

Bis(2-chloroethyl) ether (BCEE) is a  $\beta$ -chloroalkyl ether (U.S. EPA, 1980) with the Chemical Abstracts Service (CAS) registry number of 111-44-4, the molecular formula  $C_4H_8Cl_2O$ , and the structural formula  $(ClCH_2CH_2)_2O$ . Synonyms for BCEE include dichloroethyl ether, dichloroethyl oxide, and bis( $\beta$ -chloroethyl) ether. This organic compound is a colourless, volatile liquid with a "chlorinated solvent-like" odour (Sittig, 1981). At ambient temperature, BCEE has a vapour pressure of 0.095 kPa (Verschueren, 1983), a low n-octanol/water partition coefficient [ $\log K_{ow}$ ] ranging from 1.0 (Sittig, 1981) to 1.58 (Hawley, 1981), and a high water solubility ranging from 10 200 (Verschueren, 1983) to 17 400 mg/L (Hake and Rowe, 1963). The log organic carbon/water partition coefficient ( $K_{oc}$ ) values reported in the literature range from 0.80 (Ellington *et al.*, 1991) to 1.14 (Mabey *et al.*, 1982). Analytical methods used to quantify BCEE in environmental media include gas chromatography/mass spectrometry and gas chromatography with electron capture detection (Dressman *et al.*, 1977; Quaghebeur *et al.*, 1986).

Information provided in response to a Notice published under Section 16(1) of CEPA indicated that there was no commercial activity involving more than one kilogram of BCEE in Canada in 1990 or 1991 (Environment Canada, 1992). However, BCEE was reportedly used in Canada between 1984 and 1986 as either a fragrance, perfume, deodorizer, or flavouring agent (Canada Gazette, 1991).

In the United States, BCEE is reported to be used as an intermediate reactant in the synthesis of the methylthiocarbamic acid fungicide commonly known as metam-sodium. Bis(2-chloroethyl) ether is believed to be present in trace amounts in the final product. Metam-sodium is registered in Canada under the *Pest Control Products Act*. This fungicide is imported for use in Canada but it is not manufactured in Canada.

### 2.2 Entry into the Environment

Bis(2-chloroethyl) ether does not occur naturally in the environment. Any amount detected in the environment, therefore, is of anthropogenic origin (U.S. EPA, 1980).

Bis(2-chloroethyl) ether enters the Canadian environment as a by-product from chlorination of waste streams containing ethylene or propylene. Under the Municipal and Industrial Strategy for Abatement (MISA) program of the Ontario Ministry of the Environment (MOE), BCEE was detected in in-plant effluent at one organic chemical manufacturing plant in southern Ontario (MOE, 1991a). Also under the MISA program, levels of BCEE have been detected in samples at an iron and steel plant in southern Ontario (MOE, 1991b). The exact mechanism that results in the formation of BCEE at the latter site is not known.

As noted in Subsection 2.1, BCEE may be present as a contaminant in a fungicide that is imported into Canada. In 1990, however, it was estimated, based on the quantities



imported and the known level of contamination, that less than 100 grams of BCEE would have been released to the Canadian environment from this source (Agriculture Canada - Environment Canada, 1992).

Bis(2-chloroethyl) ether has also been detected in 2 of 275 samples of raw sewage in Toronto, Ontario, and in one sample of secondary effluent. These levels were above the detection limit (15 µg/L) but could not be accurately quantified because of limitations related to analytical quality control (MOE, 1988). Bis(2-chloroethyl) ether was not detected in primary and tertiary effluents.

In the United States, a total of 2700 kg/yr was estimated to be released into the environment in 1989. Seventy percent of this amount was reported to be emitted to the air, while the remaining 30% was released in water (U.S. EPA, 1990; Toxic Release Inventory Database).

## 2.3 Exposure-related Information

### 2.3.1 Fate

The U.S. EPA (1992) estimated the half-life for the reaction of BCEE with hydroxyl radicals in the atmosphere to be approximately 2.8 days. A half-life of 13.44 h has been reported for the indirect photolysis of BCEE in the gaseous phase (U.S. EPA, 1987a). In view of its high solubility in water, rainfall would likely result in removal of BCEE from the atmosphere (Durkin *et al.*, 1975).

A hydrolysis half-life of 20 to 22 years was estimated for BCEE at a temperature of 20 °C (Mabey *et al.*, 1982; Milano *et al.*, 1989). Based on the low-to-moderate Henry's Law constant (1.3 Pa · m<sup>3</sup>/mole), BCEE would tend to remain in water. Using the approach of Mackay and Wolkoff (1973), Durkin *et al.* (1975) calculated the half-life with respect to volatilization of BCEE from a body of water to be 5.78 days at 25 °C. Similarly, a half-life of 3.4 days (from water) was calculated by the U.S. EPA (1987a). Hence, the removal of BCEE from surface waters will likely occur within a week although it will persist in bottom waters.

Biodegradation of BCEE in aquatic systems is not well understood. In the only study identified, Tabak *et al.* (1981) reported that BCEE was completely biodegraded within 7 days in aqueous medium inoculated with sewage sludge.

Based on its  $K_{OC}$  and water solubility, BCEE is not expected to adsorb to soil or sediment and is therefore considered to be mobile in these media (U.S. EPA, 1987a). Wilson *et al.* (1981) reported that BCEE leached readily through sandy soil.

The biodegradation of BCEE is not well understood although this process may play some role in the fate of this substance in soil. Kincannon and Lin (1986) reported a half-life of BCEE in soil of approximately 16.7 days, based on the results of a 97-day soil column study in which the degradation of BCEE mixed with hexachloroethane (as a constituent of a hazardous waste sludge) was quantitated. The U.S. EPA (1987a)

reported that, because of its vapour pressure, BCEE should volatilize relatively rapidly from dry surfaces. In the only study identified dealing with soil volatilization [a 7-day microcosm study by Piwoni *et al.* (1986)], the soil was kept moist and an insignificant amount (3%) of applied BCEE was calculated to have volatilized.

For biota, Barrows *et al.* (1978) reported a bioconcentration factor (BCF) of 11 and a biological half-life of between 4 and 7 days for bluegill sunfish (*Lepomis macrochirus*) based on the results of a study in which the fish were exposed to BCEE (under flow-through conditions) for 14 days at a mean water concentration of 10 µg/L.

### **2.3.2 Concentrations**

No information was identified on levels of BCEE in the ambient Canadian environment or in foodstuffs. Bis(2-chloroethyl) ether was not detected in 50 samples of Toronto drinking water and eight samples of bottled spring water in 1990 (detection limits of 0.000 03 and 0.001 µg/L, respectively) (Kendall, 1990). In Alberta, BCEE has not been detected in drinking water (detection limit of 1 µg/L) since 1986, although it was present in trace amounts in one sample obtained in 1989 (Alberta Ministry of the Environment, 1991).

The Ontario Ministry of the Environment, under the MISA program, reported the presence of BCEE (from 1989 to 1990) in an in-plant effluent stream at one industrial site producing propylene oxide in Sarnia, Ontario (detection limit 4.4 µg/L). The mean concentration of BCEE at this site was 375 µg/L, with levels ranging from 6.1 to 1057 µg/L (MOE, 1991a). The mean concentration of BCEE in the in-plant effluent in 1991 was reported to be 46 µg/L; levels ranged from 15 to 376 µg/L. These effluent streams are diluted with cooling water before being discharged to the environment and, although levels of BCEE at the outflow pipe were not monitored, they were probably below the limit of detection. At another facility in Alberta involved in similar industrial activity, levels of BCEE at the point of discharge to the environment were below the detection limit of 10 µg/L (NAQUADAT, 1991).

Bis(2-chloroethyl) ether was also reported in five of 12 monthly samples of an in-plant effluent stream from an iron and steel manufacturing facility in southern Ontario, as part of the MISA program. Concentrations of BCEE in four of the samples were reported to be 18 µg/L while the fifth contained 9 µg/L (detection limit 4.4 µg/L) (MOE, 1991b).

The highest concentrations of BCEE in the United States were reported for industrial effluents (8 to 170 µg/L) and landfill leachates (12 400 µg/L) (DeWalle and Chian, 1981). The highest concentration reported for selected surface waters was 1.4 µg/L (Pellizzari *et al.*, 1979). Also in the United States, BCEE was found in some municipal drinking waters at concentrations up to 0.6 µg/L (estimated mean <0.1 µg/L) (Manwaring *et al.*, 1977). The limits of detection were not reported in these studies.

## 2.4 Effects-related Information

### 2.4.1 Experimental Animals and In Vitro

Bis(2-chloroethyl) ether is acutely toxic following inhalation, oral, or dermal exposure. Carpenter *et al.* (1949) calculated values of the LC<sub>50</sub> of 1000 ppm (5850 mg/m<sup>3</sup>) and 20 ppm (117 mg/m<sup>3</sup>) following the exposure of rats to BCEE for 0.75 and 4 hours, respectively (Smyth and Carpenter, 1948; Carpenter *et al.*, 1949). The LD<sub>50</sub> for the oral administration of BCEE to experimental animals ranges from 75 to 136 mg/kg body weight (b.w.) (Smyth and Carpenter, 1948; Spector, 1956; cited in Durkin *et al.*, 1975).

Data on short-term toxicity are restricted principally to the results of two (limited) range finding studies in mice. One study involved a route not relevant to that by which humans are exposed in the general environment (Theiss *et al.*, 1977; Innes *et al.*, 1969), and one subchronic unpublished study in which animals were only exposed (via inhalation) to a single concentration of BCEE [Dow Chemical, 1958 (cited in Durkin *et al.*, 1975 and ATSDR, 1989)].

Studies on the chronic effects of exposure to BCEE have been restricted to those in which the principal focus was carcinogenesis. The carcinogenicity of BCEE has been investigated in two bioassays in experimental animals following oral administration (Innes *et al.*, 1969; Weisburger *et al.*, 1981). In one of these investigations on mice (Innes *et al.*, 1969), there was evidence of an increase in liver tumor incidence. These studies were limited, however, by small group sizes (Innes *et al.*, 1969; Weisburger *et al.*, 1981); single doses of BCEE (Innes *et al.*, 1969); inadequate reporting of tumor pathology (Innes *et al.*, 1969; Weisburger *et al.*, 1981) or incidence (Weisburger *et al.*, 1981); short periods of exposure (Innes *et al.*, 1969); and inadequate assessment of effects other than tumor induction (Innes *et al.*, 1969; Weisburger *et al.*, 1981).

In the study conducted by Weisburger *et al.* (1981), small groups of male and female Charles River CD rats were administered (by gavage) 25 or 50 mg/kg (b.w.) BCEE twice a week for 78 weeks, after which time the treatment was discontinued and the animals observed for a further 26-week period. These authors reported (although no quantitative data were provided) that there was a "substantial difference" between the mean weight of the BCEE-exposed females and corresponding controls, and "a reduction" in the mean weight of the high-dose male rats.

Other investigations on the carcinogenicity of BCEE have been restricted to limited bioassays of pulmonary tumor induction in mice receiving the compound intraperitoneally (Theiss *et al.*, 1977); tumor induction at the site of (subcutaneous) injection (Van Duuren *et al.*, 1972); and tumor-initiating potential on mouse skin (Van Duuren *et al.*, 1972). The results of these limited studies have been largely negative, i.e., no increase in tumour incidence was observed.

The genotoxicity of BCEE has been assessed in a moderate number of investigations (principally mutagenicity in bacterial assays) for which the results have

been equivocal; BCEE has been reported to be mutagenic in some bacterial assays but not in others. Jorgenson *et al.* (1977) performed heritable translocation assays in mice fed BCEE (by gavage) and concluded that BCEE was not likely to be mutagenic, although no experimental details were reported.

No information was identified regarding the reproductive, developmental, neurological, or immunological toxicity of BCEE.

#### 2.4.2 *Humans*

Information on effects in humans is restricted to case reports in a few individuals and one clinical study. Schrenk *et al.* (1933) reported that the "brief" (time not stated) exposure (by inhalation) of male volunteers to BCEE at concentrations ranging from 550 to 1000 ppm (3218 to 5850 mg/m<sup>3</sup>) caused extreme irritation to the eyes (lacrimation) and nasal passages, and that such exposure was considered intolerable. Epidemiological data on the effects of chronic exposure to BCEE on human health were not identified.

#### 2.4.3 *Ecotoxicology*

For aquatic species, the 7-day LC<sub>50</sub> for the guppy (*Poecilia reticulata*) was reported to be 56.9 mg/L (Konemann, 1981). Buccafusco *et al.* (1981) reported a 96-hour LC<sub>50</sub> of 600 mg/L for the bluegill sunfish (*Lepomis macrochirus*). LeBlanc (1980) reported a 48-hour LC<sub>50</sub> of 240 mg/L for *Daphnia magna*. In all three of the above studies, organisms were exposed to nominal concentrations of BCEE in closed containers, under static, or static with renewal, conditions.

For microbes, anaerobic microbial activity was not inhibited when exposed to BCEE at concentrations up to 100 mg/L in a nutrient buffer solution (Johnson and Young, 1983). Cho *et al.* (1989) reported an LC<sub>50</sub> and an LC<sub>10</sub> of 2160 and 600 µg/L, respectively, for microbes indigenous to industrial waste stabilization ponds and that require a supply of organic material for food.

No relevant data were available to assess toxicity to wildlife.

No information was found on the effects of BCEE on the ozone layer or global warming; however, in view of its relatively short atmospheric lifetime, effects on these environmental parameters would not be anticipated.

### 3.0 Assessment of "Toxic" Under CEPA

#### 3.1 CEPA 11 (a) Environment

No commercial activity involving more than one kilogram of BCEE took place in Canada during 1990 to 1991. No data were found concerning concentrations of BCEE in the ambient environment in Canada. However, BCEE can be formed as a by-product in some industrial processes resulting in its release in industrial effluents. Levels in final discharges to the environment were not measured, but they are believed to be below the detection limit (4.4 µg/L) because of in-plant dilutions.

Bis(2-chloroethyl) ether is highly soluble in water and tends to remain in the water, although some volatilization from soil and water to the atmosphere occurs. Due to lack of adsorption, BCEE is mobile in soils, especially those low in organic carbon content, and therefore, has the potential to reach groundwater. Bis(2-chloroethyl) ether does not bioaccumulate or biomagnify to any significant extent. Exposure of terrestrial organisms to BCEE is considered to be negligible because of its extremely low rate of release and short persistence in the atmosphere.

For aquatic biota, a 7-day LC<sub>50</sub> of 56.9 mg/L (nominal concentration) for the guppy (*Poecilia reticulata*) was reported. The lowest LC<sub>50</sub> reported for acute toxicity (48-hour) was 240 mg/L (nominal concentration) for *Daphnia magna*. Bis(2-chloroethyl) ether is manufactured and used in the United States, and the highest concentration reported for surface waters in that country, 1.4 µg/L, was used as a surrogate for the worst-case scenario in the ambient environment in Canada. This concentration is approximately 40 000 times lower than the reported 7-day LC<sub>50</sub> for the guppy (*Poecilia reticulata*).

**Therefore, on the basis of available data, BCEE is not considered to be "toxic" as defined under Paragraph 11 (a) of the *Canadian Environmental Protection Act*.**

#### 3.2 CEPA 11 (b) Environment on which Human Life Depends

The short persistence of BCEE in the atmosphere and the extremely low levels of release preclude this substance from contributing to ozone layer depletion, global warming, or photochemical smog formation.

**Therefore, on the basis of available data, BCEE is not considered to be "toxic" as defined under Paragraph 11 (b) of the *Canadian Environmental Protection Act*.**

### **3.3 CEPA 11 (c) Human Life or Health**

Owing to the lack of available information on concentrations of BCEE in several environmental media to which humans are exposed, it is not possible to quantitatively estimate the total daily intake of BCEE by the general population in Canada. It is also not appropriate to estimate intake on the basis of fugacity modelling, owing to the lack of commercial activity reported for this compound.

Available data on the toxicity of BCEE to humans are extremely limited. None of the long-term (subchronic or chronic/carcinogenicity) studies in experimental animals is considered to be of sufficient quality to provide useful quantitative information concerning the carcinogenic potential of BCEE, or the toxicological effects produced by long-term exposure to this substance. Moreover, studies of the developmental and reproductive effects of BCEE in experimental animals have not been identified.

**Therefore, there are insufficient data to assess whether BCEE is "toxic", as defined under Paragraph 11(c) of the *Canadian Environmental Protection Act*.**

### **3.4 Conclusion**

**On the basis of available data, BCEE is not considered to be "toxic" as defined under Paragraphs 11(a) and 11(b) of the *Canadian Environmental Protection Act*. It has been concluded that available data are insufficient to assess whether BCEE is "toxic", as defined under Paragraph 11(c) of *Canadian Environmental Protection Act*.**

#### **4.0 Recommendations for Research**

In order to carry out a more comprehensive assessment of the effects of BCEE on human health and the environment, the following additional information would be required:

1. measurement of levels of BCEE in air, water (to characterize the frequency of release and loadings of BCEE in industrial effluents), and food;
2. toxicity data from well designed subchronic and chronic studies, and information on the developmental and reproductive toxicity in mammalian species; and
3. relevant data on toxicity in aquatic and terrestrial organisms present in the Canadian environment.

In view of the small amounts (if any) of BCEE entering the country, the priority for this research is considered to be low at this time.

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