



Canadian Environmental Protection Act

Priority Substances List
Assessment Report No. 5

Methyl tertiary-butyl Ether



Government
of Canada

Gouvernement
du Canada

Environment
Canada

Environnement
Canada

Health
Canada

Santé
Canada



**PRIORITY SUBSTANCES LIST
ASSESSMENT REPORT No. 5**

METHYL *tertiary*-BUTYL 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
Liste des substances d'intérêt prioritaire
Rapport d'évaluation n°. 5
Oxyde de tert-butyle et de méthyle

CANADIAN CATALOGUING IN PUBLICATION DATA

Main entry under title:

Priority substances list, assessment report no. 5,
methyl tertiary-butyl ether

At head of title: Canadian Environmental
Protection Act.

Issued also in French under title: Liste des
substances d'intérêt prioritaire, rapport
d'évaluation n^o 5, oxyde de tert-butyle
et de méthyle.

Includes bibliographical references.

ISBN 0-662-19941-3

DSS cat. n. EN40-215/5E

1. Butyl methyl ether. 2. Butyl methyl ether --
Toxicity testing. 3. Environmental monitoring --
Canada. I. Canada. Environment Canada.
II. Canada. Health and Welfare Canada.

TD196.B87P74 1992 363.73'84 C92 - 099764 - 3

TABLE OF CONTENTS

Overview of Findings	v
1.0 Introduction.....	1
2.0 Summary of Critical Supporting Data.....	4
2.1 Identity and Physical/Chemical Properties of Substance.....	4
2.2 Production and Uses.....	4
2.3 Sources and Releases	5
2.4 Environmental Fate and Concentrations	5
2.4.1 <i>Fate</i>	5
2.4.2 <i>Concentrations</i>	5
2.5 Toxicokinetics and Metabolism.....	6
2.6 Mammalian Toxicology.....	7
2.7 Effects on Humans	8
2.8 Effects on the Environment.....	8
3.0 Assessment of "Toxic" Under CEPA	9
3.1 Entry.....	9
3.2 Exposure.....	9
3.3 Effects.....	10
3.3.1 <i>Human health</i>	10
3.3.2 <i>Environment</i>	12
3.4 Conclusions	12
3.4.1 <i>Effects on the environment (Paragraph 11 (a))</i>	12
3.4.2 <i>Effects on the environment on which human life depends (Paragraph 11 (b))</i>	12
3.4.3 <i>Effects on human health (Paragraph 11 (c))</i>	13
3.4.4 <i>General conclusions</i>	13
4.0 Recommendations for Research and Evaluation.....	14
5.0 References.....	15

Overview of Findings

Methyl *tertiary*-butyl ether (MTBE) is used in Canada as an octane enhancer in gasoline. Methyl *tertiary*-butyl ether can enter the environment at any stage in the production, storage, and transport of undiluted MTBE or MTBE-blended gasoline. Although data on concentrations of MTBE in the environment are not available, modelling of the fate of MTBE has provided predictions for concentrations of MTBE in the various media to which humans and other organisms may be exposed.

The highest concentrations of MTBE predicted in surface water in Canada are at least eight orders of magnitude lower than the concentration that induces adverse effects in fathead minnow, the most sensitive aquatic species identified. The effect levels reported in inhalation studies conducted on laboratory mammals are considered relevant to wild mammals. The highest predicted atmospheric concentration is at least seven orders of magnitude lower than the lowest reported effect level in a subchronic inhalation study in mammals.

Because of its low rate of release, its short persistence in the atmosphere, and the resulting low concentrations of MTBE in the atmosphere, MTBE is not associated with depletion of stratospheric ozone or with global warming, and is not expected to contribute significantly to the formation of ground-level ozone.

Based on predicted concentrations of MTBE in ambient air and water and limited information on concentrations in shellfish, the total average daily intakes of MTBE have been estimated for various age groups in the general population. These estimates are much less (by approximately 45 000 times) than the intake to which it is believed that a person can be exposed over a lifetime without deleterious effect, *i.e.*, the Tolerable Daily Intake derived on the basis of data from bioassays in animal species.

Based on these considerations, the federal Minister of the Environment and the federal Minister of Health and Welfare have concluded that the predicted concentrations of MTBE in the environment in Canada do not constitute a danger to the environment or to the environment on which human life depends, or to human life or health. Therefore, MTBE is not considered to be "toxic" as defined under Section 11 of the *Canadian Environmental Protection Act*.

1.0 Introduction

The *Canadian Environmental Protection Act* (CEPA) requires the federal Minister of the Environment and the federal Minister of 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 also requires both Ministers to assess these substances and determine whether they are "toxic" as defined in 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" according to Section 11 may be placed on Schedule I of the Act. Consideration can then be given to developing 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 methyl *tertiary*-butyl ether (MTBE) is "toxic", as defined in 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 at levels that could cause adverse **effects**.

Data relevant to the assessment of the entry, environmental exposure, and environmental effects of MTBE were obtained from searches of electronic databases between 1989 and 1991. These databases included: BIOSIS Previews, Chemical Evaluation Search and Retrieval System (CESARS), Chemical Abstracts, Environment Canada Departmental Library Catalogue (ELIAS), FATERATE, Federal Register, International Register of Potentially Toxic Chemicals (IRPTC), National Technical Information Service (NTIS), Pollution Abstracts, Registry of Toxic Effects of Chemical Substances (RTECS), SOLUB, TOXLINE, and the Toxic Releases Inventory Data Base. Additional information was obtained from members of the Canadian Petroleum Products Institute (CPPI) and other representatives of the petroleum industry and from C.S. Liu of Alberta Environment. Trade information, including production, import, storage, and use data, was obtained from industry through a mandatory request for information under CEPA, Section 16. Although much of the research on MTBE has been conducted

outside Canada, available Canadian data on sources, use patterns, fate, and effects of MTBE on the Canadian environment were emphasized.

To identify data relevant to the estimation of exposure of the general human population to MTBE, several commercial databases were searched from the early 1970s to July 1991. These included: Environmental Bibliography, ENVIROLINE, Pollution Abstracts, ELIAS, SQUAREF, BIOSIS Previews, MICROLOG, Cooperative Documents Project (CODOC), Integrated Risk Information System (IRIS), and Chemical Hazard Response Information System (CHRIS).

To identify toxicological data relevant to the assessment of effects on human health, on-line literature searches were conducted in June 1991 on the following databases: Hazardous Substances Data Bank, RTECS, TOXLINE, TOXLIT, Federal Register, and NTIS. Additional relevant information was obtained from the Canadian Petroleum Products Institute, the MTBE Health Effects Testing Task Force (a committee of American producers and users of MTBE overseeing toxicological testing of MTBE), and the United States Environmental Protection Agency (U.S. EPA). Non-validated studies of Industrial Bio-Test Laboratories Inc. have been cited in this report but are not used in assessing whether MTBE is "toxic" under CEPA.

Data relevant to the assessment of whether MTBE is "toxic" to human health obtained after the completion of the human health-related sections of this report (*i.e.*, October 1991) were not considered for inclusion. Similarly, data relevant to the assessment of whether MTBE is "toxic" to the environment obtained after April 1992 have not been considered.

Review articles were consulted where appropriate. However, all original studies that form the basis for determining whether MTBE 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):

Environment Canada

A. Bobra
D. Caldbick
R. Chénier
M. Hanlon
K. Lloyd
C. B. Prakash

Health and Welfare Canada

G. Long
M.E. Meek
S. Savard

In this report, an overview of findings concerning MTBE 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. This information is presented in greater detail in a Supporting Document that is available upon request. The assessment of whether MTBE is "toxic" under CEPA is presented in Section 3.0.

The human health-related sections of the Supporting Document and/or Assessment Report were reviewed externally by S. Ridlon, Chairman of the MTBE Health Effects Testing Task Force, and British Industrial Biological Research Association (BIBRA) Toxicology International. These sections were then approved by the Standards and Guidelines Rulings Committee of the Bureau of Chemical Hazards of Health and Welfare Canada. Environmental components of the Supporting Document were reviewed externally by G. Grappolini, Petro-Canada Products, on behalf of the Canadian Petroleum Products Institute, and by C. S. Liu from Alberta Environment. The final Assessment Report was reviewed and approved by the Environment Canada/Health and Welfare Canada CEPA Management Committee.

Copies of this assessment report and of the unpublished supporting document are available upon request from:

Commercial Chemicals Branch
Environment Canada
14th Floor, Place Vincent Massey
351 St. Joseph Boulevard
Hull, Quebec
K1A 0H3

Environmental Health Centre
Health and Welfare Canada
Room 104
Tunney's Pasture
Ottawa, Ontario
K1A 0L2

2.0 Summary of Critical Supporting Data

2.1 Identity and Physical/Chemical Properties of Substance

Methyl *tertiary*-butyl ether (CAS Registry Number 1634-04-4) is an aliphatic ether with structural formula $\text{CH}_3\text{OC}(\text{CH}_3)_3$. It is a volatile, clear, flammable, colourless liquid at room temperature, and has a terpene-like odour. Methyl *tertiary*-butyl ether is miscible in gasoline and soluble in water, alcohol, and ether. It has a relatively high vapour pressure (3.35×10^4 Pa at 25°C) (Ambrose *et al.*, 1976), a high water solubility (4.8×10^4 mg/L at 20°C) (Merck & Co., Inc., 1989) and a low log octanol/water partition coefficient (1.3) (Veith *et al.*, 1983).

Methyl *tertiary*-butyl ether is produced by reacting isobutylene with methanol over an acid catalyst. Common analytical methods used to quantify MTBE include gas chromatography with mass spectrometry, flame ionization, or an oxygen specific response flame ionization detector.

2.2 Production and Uses

The first plant ever to produce MTBE in Canada began operating in 1992 in an industrialized area of Edmonton, Alberta. The plant is to produce an estimated 500 000 tonnes of MTBE per year, most of which is intended for export to the United States. The MTBE will be shipped by rail from Edmonton to Kitimat, British Columbia and from there it will be shipped by ocean tanker (Solsberg, 1991).

From 1986 to 1990, Canada imported between 7000 and 25 000 tonnes/year of MTBE for the purpose of blending as an octane enhancer in unleaded gasoline. Most of the imports entered Ontario and Quebec, and smaller amounts went to Alberta and British Columbia. Over the next five years, it is estimated that importation will increase to approximately 38 000 tonnes/year. Assuming that Canada's overall consumption of gasoline will not change appreciably over the next four years, it is estimated that MTBE-blended gasolines will continue to account for approximately 2% of the total unleaded gasoline in Canada, as it has during the past five years. The average concentrations of MTBE in these blended gasolines range from 6.5 to 9.6% by volume (Environment Canada, 1991).

Worldwide production of MTBE has increased dramatically since 1979, when it was approved in the United States and other countries for use in gasoline. In western Europe, unleaded gasoline can contain 10 to 15% MTBE by volume. In the United States, concentrations of up to 15% MTBE by volume in unleaded gasoline have been approved by the U.S. EPA. Methyl *tertiary*-butyl ether is currently among the 50 highest production volume chemicals in the United States. Total production of MTBE in the United States was estimated to be 3 200 000 tonnes/year (Chemical Market Reporter, 1990). World production capacity in 1989 was 7 425 000 tonnes and is projected to rise to 19 413 000 tonnes/year by 1994. The growing demand for MTBE as a gasoline-blending component results from the expanded market for high octane unleaded

gasolines, and the increased pressure to reduce evaporative emissions, carbon monoxide (CO) emissions, and the aromatic contents of gasoline (Prakash, 1989).

2.3 Sources and Releases

Methyl *tertiary*-butyl ether can enter the environment at any stage in the production, storage, and transport of undiluted MTBE or MTBE-blended gasoline. The largest environmental releases are through fugitive emissions from chemical manufacturing plants, gasoline terminals, service stations, and from spills (U.S. EPA, 1986). No data are available on releases of MTBE from engine combustion of MTBE-blended gasoline. Canadian data on environmental releases are not available. Releases of MTBE from ten plants in the United States have been estimated to range from 0.003 to 0.07% of the total MTBE used or produced, with an average of 97% of released MTBE being emitted into air, 1.7% into water, and 1.3% into soil (TOXNET-TRI, 1991). Assuming that 0.07% of all the projected production of MTBE at the Edmonton plant would be released into the environment in similar proportions, this would result in annual releases of 340 tonnes of MTBE into the air, 6 tonnes into water, and 5 tonnes into soil.

2.4 Environmental Fate and Concentrations

2.4.1 Fate

Mechanisms affecting the environmental fate of MTBE include photo-oxidation (Japar *et al.*, 1990; 1991), volatilization (Thomas, 1982), and biodegradation (Fujiwara *et al.*, 1984). In the environment, MTBE should be found primarily in the atmosphere and in water because of its relatively high vapour pressure, high water solubility, and low octanol/water partition coefficient.

Based on measured rate constants for reactions with hydroxyl radicals in air, the photo-oxidation half-life for MTBE has been estimated to be between 20.7 and 265 hours (Atkinson, 1985; Wallington *et al.*, 1988). The atmospheric oxidation of MTBE produces *tertiary*-butyl formate (major product), 2-methoxy-2-methyl propanal, and other minor products (Japar *et al.*, 1991). In water, biodegradation appears to be the only degradation process of any significance. The half-life of MTBE was estimated to be between 28 and 180 days for aerobic biodegradation in surface waters and between 112 and 720 days for anaerobic biodegradation in deep water or groundwater (Fujiwara *et al.*, 1984). Based on physical/chemical properties, the half-life for volatilization of MTBE from surface waters to the atmosphere was estimated to be 9 hours (U.S. EPA, 1986).

2.4.2 Concentrations

No information was found in the literature on MTBE concentrations in air, surface waters, groundwater, soil, or sediment in Canada. In a study carried out in Nova Scotia for the detection of organic and inorganic contaminants in shellfish, MTBE was not detected (detection limit of 0.01 µg/g) in 21 samples that were assayed (Environment Canada, 1989).

Concentrations of MTBE in ground-level air at three refineries in the United States were less than $30 \mu\text{g}/\text{m}^3$ (API, 1989). Trace quantities of MTBE ($5 \text{ ng}/\text{L}$) were detected in estuarine water and sediment samples adjacent to motorways and centres of heavy urban road traffic in the United Kingdom (Bianchi and Varney, 1989).

There have been several incidents of MTBE being detected in groundwater in areas where underground storage tanks containing MTBE-blended gasoline have leaked. In some of these incidents in the United States, MTBE concentrations ranged from $1.96 \mu\text{g}/\text{L}$ to $236 \text{ mg}/\text{L}$ (Garrett, 1987). When present in groundwater at high concentrations, MTBE can act as a cosolvent and enhance the mobility of other gasoline components (Rao *et al.*, 1990; Garrett *et al.*, 1986).

Bioconcentration of MTBE in aquatic biota is not significant. Whole body, steady-state bioconcentration factors (BCF) of 1.1 and 1.08 have been reported for carp, *Cyprinus carpio* (Fujiwara *et al.*, 1984). Fish exposed for 28 days and then transferred to clean water eliminated almost all of the MTBE residues within 3 days (Fujiwara *et al.*, 1984). Concentrations in fish would therefore be expected to be close to the concentrations in water.

Because of the lack of data on the behaviour of MTBE in the Canadian environment, estimates of fate and concentrations of MTBE in the environment were generated using the Level III Fugacity Computer Model of Mackay and Paterson (1991) developed for southern Ontario. Based on estimates for import into southern Ontario (Environment Canada, 1991) and data on releases in the United States (TOXNET-TRI, 1991), it was assumed that MTBE would be released into the environment at rates of $119 \text{ mol}/\text{hour}$ into air, $3.6 \text{ mol}/\text{hour}$ into water, and $0.6 \text{ mol}/\text{hour}$ into soil. Modelling indicated that at steady-state, 56.2% MTBE would be found in the air, 43.3% in surface water, $<0.01\%$ in sediment, and 0.5% in soil. This would result in steady-state concentrations of $1.5 \text{ ng}/\text{m}^3$ in air, $0.12 \text{ ng}/\text{L}$ in water, $0.28 \text{ ng}/\text{kg}$ (dry weight) in soil, and $0.068 \text{ ng}/\text{kg}$ (dry weight) in sediment.

A release of 1% of the total estimated 1992 Canadian production of 500 000 tonnes/year would result in emissions and concentrations approximately 50 times greater than those estimated in the previous paragraph. The 1% release was chosen to represent a worst-case scenario, corresponding to approximately ten times the estimated maximum United States emission rate from chemical plants.

2.5 Toxicokinetics and Metabolism

Methyl tertiary-butyl ether appears to be rapidly and completely absorbed from the gastrointestinal tract of rats, whereas absorption following dermal exposure is limited (Bio-Research Laboratories Ltd., 1990a). Following oral, inhalation, dermal, or intravenous exposure in experimental animals, MTBE is rapidly eliminated unchanged, or as metabolites, principally tertiary-butanol in expired air and tertiary-butanol, 2-methyl- 1,2-propanediol and *alpha*-hydroxyisobutyric acid in urine (Savolainen *et al.*, 1985; Exxon Biomedical Sciences, Inc., 1988; Bio-Research Laboratories, Ltd. 1990a; 1990b; 1990c; 1990d).

Available data indicate that accumulation of MTBE and/or metabolites following repeated exposure by inhalation is unlikely (Bio-Research Laboratories Ltd., 1990c) and that the metabolism of MTBE to tertiary-butanol may be saturated at high doses (Bio-Research Laboratories Ltd., 1990a; 1990b; 1990d). Methyl *tertiary*-butyl ether and its metabolite tertiary-butanol have been detected in the blood, urine, fatty tissue, and mothers' milk of patients undergoing gallstone treatment by transhepatic gallbladder litholysis using MTBE (Leuschner *et al.*, 1991).

2.6 Mammalian Toxicology

The acute toxicity of MTBE is low following inhalation, oral, or dermal administration. The oral (gavage) LD₅₀ in male and female albino rats is approximately 3.8 g/kg b.w. (Industrial Bio-Test Laboratories, Inc., 1969; ARCO Chemical Co., 1980). Reported LC_{50s} in rats for 4-hour inhalation exposures to MTBE are 85 g/m³ (Industrial Bio-Test Laboratories, Inc., 1969) and 120 g/m³ (ARCO Chemical Co., 1980). Methyl *tertiary*-butyl ether did not induce dermal sensitization in guinea pigs (ARCO Chemical Co., 1980).

Short-term repeated dose toxicity studies for MTBE are limited to a two-week inhalation study in small groups of rats and monkeys (Industrial Bio-Test Laboratories, Inc., 1970a; 1970b), a nine-day inhalation study in rats (Bio/dynamics Inc., 1984) and a 14-day study in which the compound was administered orally by gavage to rats (Robinson *et al.*, 1990). At high concentrations (> 1020 ppm; > 3731 mg/m³), inhalation of MTBE induced clinical signs of eye irritation and chronic inflammatory changes in the nasal mucosa and trachea (Bio/dynamics Inc., 1984) and profound anaesthesia following ingestion of 1428 mg/kg b.w. (Robinson *et al.*, 1990). Decreases in body weight gain have also been observed following ingestion of lower doses (714 mg/kg b.w.) (Robinson *et al.*, 1990).

Subchronic toxicity studies are limited to one oral and three inhalation studies in rats. In an inhalation study conducted by Greenough *et al.* (1980), anaesthesia was the only adverse effect observed in rats at concentrations as low as 250 ppm (915 mg/m³). However, this effect was not observed at higher concentrations in a more recent investigation in another strain of rats.

In the most extensive bioassay, Dodd and Kintigh (1989) reported a "no-observed-adverse-effect-level (NOAEL)" of 797 ppm (2915 mg/m³), based on neurobehavioural effects observed at concentrations of 3920 ppm (14 339 mg/m³) and above. Increases in the relative weights of the liver and kidney in male rats were observed at this concentration (797 ppm), which might more appropriately have been considered a lowest-observed-effect-level (LOEL).

Data on the chronic toxicity and potential carcinogenicity of MTBE have not been identified. However, an oncogenicity study in CD-1 mice and F344 rats is under way and is expected to be completed in late 1992 (Kneiss, 1991).

In four inhalation studies conducted to date, MTBE has not induced developmental effects in rats, rabbits, or mice at doses below those that were toxic to the mother (Conaway *et al.*, 1985; Tyl, 1989; Biles *et al.*, 1987). Adverse effects on reproduction in the absence of parental toxicity have not been observed in one- and two-generation studies in rats (Biles *et al.*, 1987; Neepser-Bradley, 1991).

Methyl *tertiary*-butyl ether has been assayed in several *in vitro* and *in vivo* genotoxicity tests covering a range of genetic endpoints. Although there is no convincing evidence that MTBE is genotoxic in studies conducted to date, definitive conclusions cannot be reached because of the limitations of several of the available investigations.

2.7 Effects on Humans

Available data on the toxicity of MTBE to humans are restricted to case reports of adverse effects following its use as a treatment for gallstones. In general, only mild effects have been reported, including a faint odour on the breath, nausea, vomiting, drowsiness, and mild inflammatory changes in the gallbladder following repeated treatment with several millilitres of MTBE (Allen *et al.*, 1985; Sauerbruch *et al.*, 1985; Murray *et al.*, 1988; Thistle *et al.*, 1989; Van Sonnenberg *et al.*, 1991). Ponchon *et al.* (1988), however, noted the potential for adverse effects from treatment with MTBE, describing a case in which leakage of 15 mL of MTBE resulted in coma and acute renal failure.

2.8 Effects on the Environment

Few data are available on the toxicity of MTBE to aquatic biota. Data on acute toxicity are available for one species of invertebrate, four species of fish, and one species of amphibian. The experimental data ranged from a 96-hour LC₅₀ of 672 mg/L for the fathead minnow, *Pimephales promelas* (Geiger *et al.*, 1988), to a 96-hour LC₅₀ of > 10 000 mg/L for a copepod, *Nitocra spinipes* (Tarkpea and Svanberg, 1982).

No data are available for toxicity to wild mammals, birds, terrestrial plants, or soil biota. The toxicity of MTBE to wild mammals can be assessed by extrapolation from the results of toxicity studies conducted using laboratory mammals (see Section 2.6).

Methyl *tertiary*-butyl ether is not considered to be a greenhouse gas or to contribute to stratospheric ozone depletion, since its low rate of release to the atmosphere and its short atmospheric half-life (less than 12 days) result in very low atmospheric concentrations. Because MTBE is a volatile organic compound, it could contribute to the formation of ground-level ozone. The extent of its contribution is not known, but it is believed to be relatively small given the low concentrations of MTBE in air compared to those of other volatile organic compounds (CCME, 1990).

3.0 Assessment of "Toxic" Under CEPA

As described in the Introduction, the following assessment will consider the entry of MTBE to the environment, the exposure to humans and other biota, and potential harmful effects to humans and other biota.

3.1 Entry

From 1986 to 1990, Canada imported between 7000 and 25 000 tonnes/year of MTBE for the purpose of gasoline blending. Approximately 2% of the unleaded gasoline in Canada is blended with MTBE, which accounts for about 6.5 to 9.6% by volume of the resulting blend. It is expected that 500 000 tonnes/year will be produced in Canada starting in 1992, with most of this production being exported. Methyl *tertiary*-butyl ether can enter the environment at any stage in the production, storage, use, and transport of MTBE or MTBE-blended gasoline.

The largest environmental releases are likely to occur as fugitive emissions from chemical manufacturing plants, gasoline terminals, service stations, and spills. Therefore, although data are not available on the absolute amounts of MTBE entering the Canadian environment and on the resulting environmental concentrations, it is concluded that MTBE enters the Canadian environment.

3.2 Exposure

No data are available on environmental concentrations in Canada. Based on steady-state fugacity modelling, environmental concentrations in southern Ontario are estimated to be 1.5 ng/m³ in air and 0.12 ng/L in water. Under a worst-case scenario, it was assumed that approximately 1% of the predicted Canadian MTBE production could be emitted to the environment, resulting in environmental concentrations of 75 ng/m³ in air and 6 ng/L in water.

Human exposure to MTBE is difficult to estimate because of the lack of data on concentrations of MTBE in ambient and indoor air, drinking water, or in food in Canada, the United States, and other countries. Based on fugacity modelling, it is estimated that inhalation in air would be the principal route of exposure {e.g., 35 ng/day based on a predicted concentration of 1.5 ng/m³ and an assumed inhalation volume of air for adults of 23 m³ daily (EHD, 1988)}. Intake in drinking water would be considerably less {0.18 ng/day based on a predicted concentration of 0.12 ng/L and an assumed volume ingested of 1.5 L daily for adults (EHD, 1988)}. Based on data available concerning the physical/chemical properties of MTBE and the limited information on concentrations in shellfish, intake in food is expected to be negligible compared to that inhaled.

It is recognized that there may be additional exposure (including dermal) of the general population to MTBE at self-serve gasoline stations. Available data, however, are insufficient to estimate exposure from this source and absorption following dermal exposure appears to be limited.

It is estimated, therefore, that the average daily intake of MTBE for Canadian adults would not exceed 35 ng/day (<0.5 ng/(kg b.w.·day) for a 70 kg man) (EHD, 1988). For 5- to 11-year-olds, the age group with greatest predicted exposure on a body weight basis, estimated intake is 0.67 ng/(kg b.w.·day) { assuming average body weight of 27 kg, inhalation volume of 12 m³/day, drinking water intake of 0.3 L/day (EHD, 1988), and predicted concentrations of MTBE of 1.5 ng/m³ in air and 0.12 ng/L in water }.

These estimated intakes are based on mean predicted concentrations in the general environment. Elevated levels, for example, present in groundwater in areas where underground storage tanks containing MTBE-blended gasoline have leaked, were not considered relevant to estimation of exposure for the general population.

3.3 Effects

3.3.1 Human health

Limited data are available on the toxicity of MTBE to human health. Epidemiological studies of exposed populations are not available and information on chronic toxicity or carcinogenicity in experimental animals has not been identified. An oncogenicity study is in progress, however, and should be completed within the next few years. Although there is no convincing evidence that MTBE is genotoxic from *in vitro* and *in vivo* studies covering a range of genetic endpoints, it is not possible to draw definitive conclusions due to the limitations of several of the available investigations. Methyl *tertiary*-butyl ether has been classified, therefore, in Group V (inadequate data to assess) of the classification scheme developed for use in the derivation of the "Guidelines for Canadian Drinking Water Quality" (EHD, 1989). In studies conducted to date, MTBE has also not induced adverse reproductive effects in rats or developmental effects in rabbits, rats, or mice at doses below those that were maternally toxic.

For compounds classified in Group V, a Tolerable Daily Intake (TDI) is derived on the basis of a no- or lowest-observed (adverse) effect level (NO(A)EL or LO(A)EL) in humans or animals divided by an uncertainty factor. With the exception of the one- and two-generation studies designed to specifically investigate reproductive and developmental effects (Biles *et al.*, 1987; Neeper-Bradley, 1991), the longest term studies of the effects of MTBE are sub-chronic investigations. Those in which an adequate range of endpoints has been examined are restricted to one oral (Robinson *et al.*, 1990) and two inhalation studies (Greenough *et al.*, 1980; Dodd and Kintigh, 1989) in rats. The inhalation studies are the most relevant to this assessment since, based upon concentrations in air and water predicted by fugacity modelling and a limited amount of information on MTBE levels in shellfish in Canada, air is expected to be the principal medium of exposure to MTBE for the general population. In an inhalation study conducted by Greenough *et al.* (1980), anaesthesia was the only adverse effect observed in rats at concentrations as low as 250 ppm (915 mg/m³). However, this effect was not observed at higher concentrations in a more recent, extensive investigation on another strain of rats (Dodd and Kintigh, 1989). This was the most extensive subchronic study in which there was assessment of neurobehavioural effects and histopathological examination of the nervous system, in addition to traditional endpoints in groups exposed

examination of the nervous system, in addition to traditional endpoints in groups exposed to three concentrations and controls. The "NOAEL" in this study was considered to be 797 ppm (2915 mg/m³) based on neurobehavioural effects, including increased body temperature in female rats, decreased hind limb grip in males, and increased motor activity in females observed at the next highest concentration. However, increases in the relative weights of the liver and kidney in males were recorded at 797 ppm (2915 mg/m³). It might be more appropriate, therefore, to consider this concentration as a LOEL. On the basis of this "NOAEL", a Tolerable Daily Intake (TDI) is conservatively (owing to the paucity of available data), derived as follows:

$$\begin{aligned} \text{TDI} &= \frac{2915 \text{ mg/m}^3 \times (6/24) \times (5/7) \times 0.144 \text{ m}^3/\text{d}}{10\,000 \times 0.25 \text{ kg}} \\ &= \frac{75.5 \text{ mg/ (kg b.w.}\cdot\text{day)}}{2500} \\ &= 0.030 \text{ mg / (kg b.w.}\cdot\text{day)} \text{ which is: } 30 \text{ }\mu\text{g / (kg b.w.}\cdot\text{day)} \\ &\quad \text{or } 30\,000 \text{ ng/ (kg b.w.}\cdot\text{day)} \end{aligned}$$

where:

- 2915 mg/m³ = the "NOAEL" in the most extensive sub-chronic study by the most appropriate route of exposure (*i.e.*, inhalation) conducted to date (Dodd and Kintigh, 1989)
- 6/24 and 5/7 = conversion of dosing for 6 hours/day, 5 days/week to continuous exposure
- 0.144 m³/day = assumed inhaled air volume of adult rats (Altman and Dittmer, 1972)
- 0.25 kg = assumed body weight of adult rats (NIOSH, 1985)
- 10 000 = uncertainty factor (x 10 for intraspecies variation; x 10 for interspecies variation; x 10 for less than chronic study; x10 for lack of data on carcinogenicity and chronic toxicity and minimal effects - increases in liver and kidney weights in males - observed at the "NOAEL" in the critical study)

In the two-generation reproductive toxicity study conducted by Neeper-Bradley (1991), clinical signs and transient reductions in body weight were observed in F₀ and F₁ animals exposed to 3000 ppm (10 974 mg/m³). Based on these results, the NOEL was considered to be 400 ppm (1463 mg/m³), which is slightly less than the "NOAEL" from the subchronic study (Dodd and Kintigh, 1989) used here in the derivation of the TDI. However, the assessment of neurobehavioural effects and histopathological examination

3.3.2 *Environment*

Very few data are available on the toxicity of MTBE to aquatic biota. The most sensitive species identified was the fathead minnow, with a 96-hour LC₅₀ of 672 mg/L.

No data are available for toxicity of MTBE to wild mammals, birds, terrestrial plants, or soil biota. The effect levels reported in inhalation studies conducted on laboratory animals are considered relevant to wild mammals. The lowest reported effect level was 797 ppm (2915 mg/m³) for rats under conditions of subchronic (13-week) exposure by inhalation.

3.4 **Conclusions**

Methyl *tertiary*-butyl ether is used in Canada for gasoline blending and is produced for export. Both sources can lead to entry of MTBE into the Canadian environment. This entry results in concentrations of MTBE that may be estimated for the various media to which humans and other organisms are exposed.

3.4.1 *Effects on the environment (Paragraph 11 (a))*

The concentration of MTBE in surface water predicted under a worst-case scenario (6 ng/L) is 1.12×10^8 times lower than the 96-hour LC₅₀ for the fathead minnow (672 mg/L).

The highest predicted airborne concentration of MTBE (75 ng/m³) is 3.9×10^7 times lower than the lowest reported effect level in a subchronic inhalation study in rats (2915 mg/m³).

Given the low predicted concentrations of MTBE in the environment and the lack of bioaccumulation, concentrations in food for wildlife are expected to be at least several orders of magnitude lower than those causing acute toxicity. In addition, given the low toxicity of MTBE to aquatic organisms, wildlife food sources are not expected to be at risk due to environmental concentrations of MTBE.

Therefore, on the basis of available data, MTBE is not considered to be "toxic" as defined under Paragraph 11 (a) of CEPA.

3.4.2 *Effects on the environment on which human life depends (Paragraph 11 (b))*

Due to its low rate of release and its short persistence in the atmosphere, MTBE is not expected to be involved in global warming or in the depletion of stratospheric ozone. The contribution of MTBE to the formation of ozone in the lower atmosphere is believed to be relatively small because of its low predicted atmospheric concentrations.

Therefore, on the basis of available data, MTBE is not considered to be "toxic" as defined under Paragraph 11 (b) of CEPA.

3.4.3 *Effects on human health (Paragraph 11 (c))*

It is difficult to estimate exposure of the Canadian population owing to the lack of data on concentrations of MTBE in ambient and indoor air, drinking water, or food. Based on fugacity modelling and limited information on concentrations in shellfish, it is estimated that the average daily intake of MTBE for the age group of the Canadian population most exposed on a body weight basis (*i.e.*, 5- to 11-year-olds) is 0.67 ng/(kg b.w.·day). Although not based on actual data on concentrations in air, water or food, this estimated average daily intake is considerably less (by approximately 45 000 times) than the Tolerable Daily Intake previously derived.

Therefore, on the basis of available data, MTBE is not considered to be "toxic" as defined under Paragraph 11 (c) of CEPA.

3.4.4 *General conclusions*

Therefore, on the basis of available data, MTBE is not considered to be "toxic" as defined under Paragraphs 11 (a), (b) and (c) of CEPA.

4.0 Recommendations for Research and Evaluation

1. Given the almost total absence of data on environmental concentrations in Canada, concentrations of MTBE in air, water, groundwater, soil, and biota should be monitored in areas adjacent to major sources, including MTBE production and storage facilities, service stations, and areas of high vehicle traffic. This research is considered to be of medium priority.
2. Long-term toxicity tests should be undertaken using aquatic and terrestrial organisms. This research is considered to be of low priority.
3. When available, the results of the ongoing carcinogenicity bioassay and data on concentrations of MTBE in ambient air in Canada should be assessed with respect to their implications for a possible designation of "toxic" under the Act. This assessment is considered to be of high priority.

5.0 References

- Allen, M.J., T.J Borody, T.B. Bugliosi, G.R. May, N.F. LaBusso and J.L. Thistle, "Rapid Dissolution of Gallstones by Methyl *tert*-butyl Ether", *N. Engl. J. Med.*, 312, 217-220 (1985).
- Altman, P. and D.S. Dittmer (ed.), *Biology Data Book*, 2nd edition, Federation of American Societies for Experimental Biology, Bethesda, Maryland (1972).
- Ambrose, D., J.H. Ellemdler, C.H.S. Sprake and R. Townsend, "Thermodynamic Properties of Organic Oxygen Compounds. XLIII. Vapour Pressures of Some Ethers", *J. Chem. Thermodynamics*, 8, 165-178 (1976).
- API (American Petroleum Institute), "Monitoring near Refineries for Airborne Chemicals on the SARA Title III Section 313 List. Volume 1. Validated Ambient Air Concentrations Around Three Refineries", API Publication 841-44841, American Petroleum Institute, Washington (January, 1989).
- ARCO Chemical Company, "Methyl *Tertiary* Butyl Ether: Acute Toxicological Studies", ARCO Chemical Company, Newton Square, Pennsylvania (July, 1980).
- Atkinson, R., "Kinetics and Mechanism of the Gas-phase Reactions of the Hydroxyl Radical with Organic Compounds Under Atmospheric Conditions", *Chem. Rev.*, 86(1), 69-201(1985).
- Bianchi, A. and M.S. Varney, "Analysis of Methyl *tert*-butyl Ether and 1,2-Dihaloethanes in Estuarine Water and Sediments Using Purge and Trap Gas Chromatography", *J. High Resolut. Chromatogr.*, 12(3), 184-186 (1989).
- Biles, R., R. Schroeder and C. Holdsworth, "Methyl *tertiary*-butyl Ether Inhalation in Rats: A Single Generation Reproduction Study", *Toxicol. Ind. Health*, 3 (4), 519-534 (1987).
- Bio/dynamics Inc., "A Nine Day Inhalation Toxicity Study of Methyl t-Butyl Ether in the Rat". Final Report. Project No. 80-7452. East Millstone, New Jersey. NTIS Publication No. NTIS/OTS0513214 (1984).
- Bio-Research Laboratories Ltd., "Mass Balance of Radioactivity and Metabolism of Methyl *tert*-Butyl Ether (MTBE) in Male and Female Fischer 344 Rats after Intravenous, Oral and Dermal Administration of ¹⁴C-MTBE". Report No. 38843, Senneville, Quebec (1990a).
- Bio-Research Laboratories Ltd., "Pharmacokinetics of Methyl *tert*-Butyl Ether (MTBE) and *tert*-Butyl Alcohol (TBA) in Male and Female Fischer-344 Rats after Administration of MTBE by the Intravenous, Oral and Dermal Routes". Report No. 38842. Senneville, Quebec (1990b).

- Bio-Research Laboratories Ltd., "Disposition of Radioactivity and Metabolism of Methyl *tert*-butyl Ether (MTBE) in Male and Female Fischer 344 Rats after Nose-Only Inhalation Exposure to ¹⁴C-MTBE". Report No. 38845. Senneville, Quebec (1990c).
- Bio-Research Laboratories Ltd., "Pharmacokinetics of Methyl *tert*-Butyl Ether (MTBE) and *tert*-Butyl Alcohol (TBA) in Male and Female Fischer-344 Rats after Single and Repeat Inhalation Nose-Only Exposures to MTBE". Report No. 3844. Senneville, Quebec (1990d).
- CCME, "Management Plan for Nitrogen Oxides (NO_x) and Volatile Organic Compounds (VOCs). Phase I", Canadian Council of Ministers of the Environment, CCME-EPC/TRE-31E (1990).
- Chemical Market Reporter, "MTBE: Stage Two?", *Chem. Market Rep.*, 32, pp. 7 (March 19, 1990).
- Conaway, C., R. Schroeder, and N. Snyder, "Teratology Evaluation of Methyl *tertiary*butyl Ether in Rats and Mice", *J. Toxicol. Environ. Health*, 16(6), 797-809 (1985).
- Dodd, D. and W. Kintigh, "Methyl *Tertiary* Butyl Ether (MTBE): Repeated (13-Week) Vapor Inhalation Study in Rats with Neurotoxicity Evaluation". Union Carbide, Bushy Run Research Center. Project Report 52-507. Export, Pennsylvania. NTIS Publication No. NTIS/OTS0528043 (1989).
- [An abstract of this study has been published as: Gill, M., Dodd, D., Garman, R., Neptun, D., Ridlon, S. and Jernigan, J., "Methyl *tertiary*-butyl Ether (MTBE): 13-week Vapor Inhalation Study in Rats with Neurotoxicity Evaluation", *The Toxicologist*, 10(1), 304 (1990)]
- EHD (Environmental Health Directorate), "Derivation of Maximum Acceptable Concentrations and Aesthetic Objectives for Chemicals in Drinking Water", In: *Guidelines for Canadian Drinking Water Quality - Supporting Documentation*", Health and Welfare Canada, Bureau of Chemical Hazards (1989).
- EHD (Environmental Health Directorate), "Reference Values for Canadian Populations", draft report. Prepared by Environmental Health Directorate Working Group on Reference Values, Health and Welfare Canada (1988).
- Environment Canada, "Analysis of Shellfish for Organic and Inorganic Contaminants". Prepared for Environment Canada, Conservation and Protection, Dartmouth, Nova Scotia, Unpublished Report No. AN 893118 (March, 1989).
- Environment Canada, "MTBE Use Pattern Report", Results of the CEPA Section 16(1) Notice to Industry Conducted by the Commercial Chemicals Branch, March 20. Environment Canada, Commercial Chemicals Branch, Ottawa (1991).

- Exxon Biomedical Sciences, Inc., "Pharmacokinetic Studies on Methyl *Tertiary* Butyl Ether (MtBE)". Final Report. Project Numbers 208450B, 208450C, 208450D, 208450E. East Millstone, New Jersey (1988).
- Fujiwara, Y., T. Kinoshita, H. Sato and I. Kojima, "Biodegradation and Bioconcentration of Alkyl Ethers", *Yukagaku*, 33(2), 111-114 (1984).
- Garret, P., M. Moreau and J.D. Lowry, "MTBE as a Ground Water Contaminant", Proceedings of the *NWWA/API (National Well Water Association /American Petroleum Institute) Conference on Petroleum Hydrocarbons and Organic Chemicals in Ground Water*, November 12-14, 1986, Houston, Texas, 227-238 (1986).
- Garrett, P., "Oxygenates as Ground Water Contaminants", Paper Presented at the 1987 *Conference on Alcohols and Octane*, San Antonio, Texas, April 1-2 (1987).
- Geiger, D.L., D.J. Call and L.T. Brooke, "Acute Toxicities of Organic Chemicals to Fathead Minnows (*Pimephales promelas*)". Center for Lake Superior Environmental Studies, University of Wisconsin-Superior, Volume 4 (1988).
- Greenough, R., P. McDonald, P. Robinson, J. Cowie, W. Maule, F. Macnaughtan and A. Rushton, "Methyl *Tertiary* Butyl Ether (Driveron) Three Month Inhalation Toxicity in Rats". Inveresk Research International. Report No. 1596. Edinburgh. NTIS Publication No. NTIS/OTS 0513483 (1980).
- Industrial Bio-Test Laboratories, Inc., "Report to Sun Oil Company. Acute Toxicity Studies on X-801-25", IBT No. A6809. Northbrook, Illinois (1969).
- Industrial Bio-Test Laboratories, Inc., "Report to Sun Oil Company. Two-Week Subacute Vapor Inhalation Toxicity Study With 7-70A in Rhesus Monkeys", P.O. No. 11-108-10-001122. IBT No. N8971. Northbrook, Illinois. NTIS Publication No. NTIS/OTS0513071 (1970a).
- Industrial Bio-Test Laboratories, Inc., "Report to Sun Oil Company. Two-Week Subacute Vapor Inhalation Toxicity Study With 7-70A in Albino Rats". P.O. No.11-108-10-001122. IBT No. N8970. Northbrook, Illinois (1970b).
- Japar, S.M., T.J. Wallington, J.F.O. Richert and J.C. Ball, "The Atmospheric Chemistry of Oxygenated Fuel Additives: t-Butyl Alcohol and t-Butyl Ether", presented at the 83rd *Annual Meeting of the Air and Waste Management Association*, Pittsburgh, Pennsylvania, June 24-29 1990, presentation 90-96.5 (1990).
- Japar, S.M., T.J. Wallington, S.J. Rudy and T.Y. Chong, "Ozone-forming Potential of a Series of Oxygenated Organic Compounds", *Environ. Sci. Technol.* 25, 415-420 (1991).

- Kneiss, J., "An Overview of the MTBE Toxicology Testing Program", presented at the National Conference on Octane Markets and Reformulated Gasoline, March 19-21, 1991, San Antonio, Texas (1991).
- Leuschner, U., A. Hellstern, K. Schmidt, H. Fischer, S. Guldutuna, K. Hubner and M. Leuschner, "Gallstone Dissolution with Methyl *tert*-butyl Ether in 120 Patients -Efficacy and Safety", *Dig. Dis. Sci.*, 36 (2), 193-199 (1991).
- Mackay, D. and S. Paterson, "Evaluating the Multimedia Fate of Organic Chemicals: A Level III Fugacity Model", *Environ. Sci. Technol.*, 25,427-436 (1991).
- Merck & Co., Inc., *The Merck Index*, 11th edition, Merck & Co., Inc., Rahway, New Jersey (1989).
- Murray, W., G. Laferla and G. Fullarton, "Choledocholithiasis *in vivo* Stone Dissolution Using Methyl *tertiary* Butyl Ether (MTBE)", *Gut*, 29 (2), 143-145 (1988).
- Neeper-Bradley, T., "Two-Generation Reproduction Study of Inhaled Methyl Tertiary Butyl Ether in CD (Sprague-Dawley) Rats", Union Carbide, Bushy Run Research Center. Laboratory Project ID 53-594. Export, Pennsylvania (1991).
- NIOSH, "Registry of Toxic Effects of Chemical Substances. 1983-84 Cumulative Supplement to the 1981-82 edition." U.S. Department of Health and Human Services, National Institute for Occupational Safety and Health (1985).
- Ponchon, T., J. Baroud, B. Pujol, P. Valette and D. Perrot, "Renal Failure During Dissolution of Gallstones by Methyl *tert*-butyl Ether", *Lancet II* (8605), 276-277 (1988).
- Prakash, C.B., "Motor Vehicle Emissions From Gasoline Containing MTBE", Unpublished Report Number IP-97, Environment Canada, Industrial Programs Branch, Ottawa (June, 1989).
- Rao, P.S.C., L.S. Lee, and R. Pinal, "Cosolvency and Sorption of Hydrophobic Organic Chemicals", *Environ. Sci. Technol.* 24, 647-654 (1990).
- Robinson, M., R. Bruner and G. Olson, "Fourteen- and Ninety-day Oral Toxicity Studies of Methyl *tertiary*-butyl Ether in Sprague-Dawley Rats", *J. Am. Coll. Toxicol.*, 9 (5), 525-540 (1990).
- Sauerbruch, T., J. Holl, W. Kruis, M. Delius and G. Paumgartner, "Dissolution of Gallstones by Methyl *tert*-butyl Ether", *N. Engl. J. Med.*, 313 (6), 385-386 (1985).
- Savolainen, H., P. Pfaffli and E. Elovaara, "Biochemical Effects of Methyl *tertiary*-butyl Ether in Extended Vapour Exposure of Rats", *Arch. Toxicol.*, 57(4), 285-288 (1985).

- Solsberg, L., "Environmental Impact Assessment Report, MTBE TRANS-SHIPMENT PROJECT", compiled by Counterspil Research Inc., Vancouver, B.C. (1991).
- Tarkpea, M. and O. Svanberg, "The Acute Toxicity of Motor Fuels to Brackish Water Organisms", *Mar. Pollut. Bull.*, 13(4), 125-127 (1982).
- Thistle, J.L., G.R. May, C.E. Bender, H.J. Williams, A.J. LeRoy, P.E. Nelson, C.J. Peine, B.T. Petersen and J.E. McCulloch, "Dissolution of Cholesterol Gall Bladder Stones by Methyl *tert*-butyl Ether Administered by Percutaneous Transhepatic Catheter", *N. Engl. J. Med.*, 320, 633-639 (1989).
- Thomas, R.G., "Volatilization", In: *Handbook of Chemical Properties Estimation Methods*, Lyman, Reehl and Rosenblatt (eds.). McGraw-Hill, New York (1982).
- TOXNET-TRI, Toxic Release Inventory Data Base (TRI) on-line (August, 1991).
- Tyl, R., "Developmental Toxicity Study of Inhaled Methyl *Tertiary* Butyl Ether in New Zealand White Rabbits". Union Carbide, Bushy Run Research Center. Project Report 51-628. Export, Pennsylvania. NTIS Publication No. NTIS/OTS0528041 (1989).
- [An abstract of this study has been published as: Neeper-Bradley, T., R. Tyl, L. Fisher, D. Tarasi, D. Fait and D. Dodd, "Developmental Toxicity Study in Inhaled Methyl *tertiary* Butyl Ether (MTBE) in New Zealand White Rabbits and CD-1 Mice", *The Toxicologist*, 10(1), 41(1990)]
- U.S. EPA, "Nineteenth Report of the Interagency Testing Committee to the Administrator: Receipt and Request for Comments Regarding Priority List of Chemicals", *Fed. Reg.*, 51(220), 41417-41432 (1986).
- Van Sonnenberg, E., S. Zakko, A. Hofmann, H. D'Agostino, H. Jinich, D. Hoyt, K. Miyai, G. Ramsby and A. Moossa, "Human Gallbladder Morphology After Gallstone Dissolution with Methyl *tert*-butyl Ether", *Gastroenterology*, 100 (6), 1718-1723 (1991).
- Veith, G.D., D.J. Call and L.T. Brooke, "Structure-toxicity Relationships for the Fathead Minnow, *Pimephales promelas*: Narcotic Industrial Chemicals", *Can. J. Fish. Aquat. Sci.*, 40(6), 743-748 (1983).
- Wallington, T. J., P. Dagaut, R. Liu and M.J. Kurylo, "Gas-phase Reactions of Hydroxyl Radicals with the Fuel Additives Methyl *tert*-butyl Ether and *tert*-butyl Alcohol over the Temperature Range 240-440 K", *Environ. Sci. Technol.*, 22(7), 842-844 (1988).