Screening Assessment

Phenol, 2,2'-methylenebis[6-(1,1-dimethylethyl)-4-methyl-
(MBMBP)

Chemical Abstracts Service Registry Number
119-47-1

Environment Canada
Health Canada

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Synopsis

Under the *Canadian Environmental Protection Act, 1999* (CEPA 1999), the Ministers of the Environment and of Health have conducted a screening assessment of Phenol, 2,2'-methylenebis[6-(1,1-dimethylethyl)-4-methyl- (MBMBP), Chemical Abstracts Service Registry Number 119-47-1, which was selected as one of 123 substances on the Domestic Substances List for a pilot project for screening assessments.

MBMBP is used in industry as an antioxidant (in acrylonitrile–butadiene–styrene copolymer, polypropylene, polyacetal, rubber, latex and adhesives) and as a stabilizer (in styrenic and olefin polymers and polyoxymethylene homopolymers and copolymers). Results from the *Notice with Respect to Certain Substances on the Domestic Substances List (DSL)* conducted under the authority of section 71 of CEPA 1999 for the year 2000 indicated that MBMBP was not manufactured in Canada, although 10 to 100 tonnes of MBMBP were imported into Canada.

Based on its sources and use patterns, MBMBP is expected to be released mostly to water. Current Canadian releases to the aquatic environment could occur as a result of losses arising during the processing of plastics containing MBMBP. There are no natural sources of MBMBP in the environment. Data concerning measured levels of MBMBP in air, water, soil and sediment in Canada were not found.

When released to water, MBMBP partitions to water and sediment. In water, MBMBP undergoes slow biodegradation. MBMBP should not bioaccumulate to a high degree in the tissues of freshwater organisms, as the highest experimental bioconcentration factor identified was 125. MBMBP is therefore considered to be persistent in water but not bioaccumulative, according to the criteria specified in the *Persistence and Bioaccumulation Regulations* under CEPA 1999. No experimental data were found on the half-lives of MBMBP in soil or sediment. MBMBP is quickly removed from the troposphere, with an estimated atmospheric half-life of less than 7 hours.

According to experimental results, MBMBP has the potential to harm aquatic organisms. No experimental toxicity data were found for sediment-dwelling organisms. There is also a lack of data on the toxicity of MBMBP to terrestrial organisms. A risk quotient analysis, integrating potential exposure with known adverse environmental effects, was performed for aquatic and soil media. The predicted exposure concentration of MBMBP in surface water (based on conservative environmental modelling of current potential releases) was lower than the adverse effect threshold predicted for sensitive aquatic organisms. The predicted exposure concentration of MBMBP in soil (based on conservative environmental modelling of MBMBP-amended sewage treatment plant sludge) was lower than the adverse effect threshold predicted for sensitive soil-dwelling organisms.

Based on the available information and the weight of evidence, it is concluded that MBMBP is not entering the environment in a quantity or concentration or under

conditions that have or may have an immediate or long-term effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends. Therefore, it is concluded that MBMBP does not meet the criteria set out in paragraphs 64*(a)* and 64*(b)* of the *Canadian Environmental Protection Act, 1999*.

Comparison of a conservative critical effect level (i.e., 6 mg/kg-bw per day) for slight changes in biochemical parameters in a 90-day study in dogs with the highest of the upper-bounding estimates of exposure for all age groups in the population living in the vicinity of a point source (i.e., 0.037 µg/kg-bw per day) for the 0- to 6-month age group (based on conservative modelling of potential releases to the environment) resulted in a margin of exposure of approximately 160 000. This margin is considered adequate to address elements of uncertainty associated with limitations of the database for population exposure and health effects (including intraspecies and interspecies variations in sensitivity, as well as the biological adversity or severity of the effects deemed critical), in which confidence is low and moderate, respectively.

Although no information was identified on the presence of MBMBP in consumer products, the nature of the physical and chemical properties is such that consumer products are not expected to contribute significantly to the exposure of the general population in Canada.

The outcome of this screening health assessment is that MBMBP does not meet the criterion set out under paragraph 64*(c)* of CEPA 1999—i.e., it is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health. This determination is based on the adequacy of the sufficiently health-protective margin between a conservatively selected lowest effect level and upper-bounding estimates of exposure of individuals in the general population.

Based on the information available for environmental and human health considerations, it is concluded that MBMBP does not meet any of the criteria set out in section 64 of the *Canadian Environmental Protection Act, 1999*.

Introduction

Screening assessments focus on information critical to determining whether a substance meets the criteria for defining a chemical as toxic as set out in section 64 of the *Canadian Environmental Protection Act, 1999* (CEPA 1999) (Canada 1999). Screening assessments examine scientific information and develop conclusions by incorporating a weight-of-evidence approach and precaution.

A screening assessment was undertaken on Phenol, 2,2'-methylenebis[6-(1,1-dimethylethyl)-4- (MBMBP; CAS RN 119-47-1) on the basis that this compound was included in the Domestic Substances List (DSL) pilot project for screening assessment as a substance likely to be prioritized because it met the criteria for persistence and/or bioaccumulation and inherent toxicity to non-human organisms.

This screening assessment includes consideration of information on chemical properties, hazards, uses and exposure. Data relevant to the screening assessment of this substance were identified in original literature, review and assessment documents, stakeholder research reports, and from recent literature searches, up to January 2004 for ecological sections of the document and July 2003 for human health sections of the document. In addition, an industry survey was conducted in 2000 through a *Canada Gazette* notice issued under authority of section 71 of CEPA 1999. This survey collected data on the Canadian manufacture and import of the DSL pilot project substances (Canada 2001). Key studies were critically evaluated.

The approach taken in the ecological screening assessment is to examine various supporting information and develop conclusions based on a weight-of-evidence approach as required under section 76.1 of CEPA 1999. The screening assessment does not present an exhaustive or critical review of all available data. Rather, it presents the critical studies and lines of evidence pertinent to the conclusion.

Evaluation of risk to human health involves consideration of data relevant to estimation of exposure (non-occupational) of the general population, as well as information on health hazards. Decisions for human health are based on the nature of the critical effect and/or margins between conservative effect levels and estimates of exposure, taking into account confidence in the completeness of the identified databases on both exposure and effects, within a screening context. The screening assessment does not represent an exhaustive or critical review of all available data. Rather, it presents a summary of the critical information upon which the conclusion is based.

This screening assessment was prepared by staff in the Existing Substances programs at Health Canada and Environment Canada. The substance matter in this report pertaining to ecological aspects has been subjected to external review. The State of the Science

Report for a Screening Health Assessment was reviewed externally by V.C. Armstrong (Consultant), P. Price (The Lifeline Group Inc), and staff of Toxicology Advice and Consulting Limited and Toxicology Excellence in Risk Assessment. While external comments were taken into consideration, the final content and outcome of the screening risk assessment remain the responsibility of Health Canada and Environment Canada. Additionally, the draft of this screening assessment was subject to a 60-day public comment period from June 23, 2007, to August 22, 2007. The State of the Science Report for a Screening Health Assessment has been posted on the Health Canada website since January 30, 2006, and the draft ecological screening assessment has been posted on the Environment Canada website since July 2006.

Information on ecological screening assessments under CEPA 1999 is available at http://www.ec.gc.ca/substances/ese.

The critical information and considerations upon which the assessment is based are summarized below.

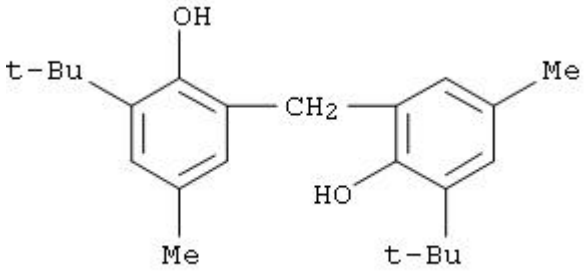
Substance Identity

Substance name

For the purposes of this document, this substance will be referred to as MBMBP, an acronym derived from the Philippine Inventory of Chemicals and Chemical Substances inventory name for this substance.

Table 1. Substance identity for MBMBP

Chemical Abstracts Service Registry Number (CAS RN)	**119-47-1**
DSL name	**Phenol, 2,2'-methylenebis[6-(1,1-dimethylethyl)-4-methyl-**
National Chemical Inventories (NCI) names[1]	*Phenol, 2,2'-methylenebis[6-(1,1-dimethylethyl)-4-methyl-* (TSCA, PICCS, ASIA-PAC, NZIoC) *6,6'-di-tert-butyl-2,2'-methylenedi-p-cresol* (EINECS) *6,6'-di-tert-butyl-4,4'-dimethyl-2,2'-methylenediphenol* (ENCS) *2,2'-methylene bis[6-(1,1-dimethylethyl)-4-methylphenol]* (ECL) *2,2'-methylene-bis-(4-methyl-6-tert-butylphenol)* (PICCS)
Other names	*2,2'-bis(4-methyl-6-tert-butylphenol)methane; 2,2'-methylene-bis(4-methyl-6-t-butylphenol); 2,2'-methylenebis(4-methyl-6-tert-butylphenol); 2,2'-methylenebis(6-tert-butyl-4-methylphenol); 2,2'-methylenebis[6-(1,1-dimethylethyl)-4-methyl)phenol; 2,2'-methylenebis[6-tert-butyl-p-cresol]; 3,3'-di-tert-butyl-2,2'-dihydroxy-5,5'-dimethyldiphenylmethane; 6,6'-methylenebis(2-tert-butyl-4-methylphenol)*
Chemical group (DSL Stream)	Discrete organics
Major chemical class or use	Phenols
Major chemical sub-class	Aromatic phenols
Chemical formula	$C_{23}H_{32}O_2$

Chemical structure	
SMILES[2]	Oc(c(cc(c1)C)Cc(c(O)c(cc2C)C(C)(C)C)c2)c1C(C)(C)C
Molecular mass	340.51 g/mol

[1] National Chemical Inventories (NCI). 2006: ASIA-PAC (Asia-Pacific Substances Lists); ECL (Korean Existing Chemicals List); EINECS (European Inventory of Existing Commercial Chemical Substances); ENCS (Japanese Existing and New Chemical Substances); NZIoC (New Zealand Inventory of Chemicals); PICCS (Philippine Inventory of Chemicals and Chemical Substances); and TSCA (Toxic Substances Control Act Chemical Substance Inventory).

[2] Simplified Molecular Line Input Entry System.

Physical and Chemical Properties

Experimental and modelled data are available for MBMBP.

Table 2 contains experimental and modelled physical and chemical properties for the neutral form of MBMBP that are relevant to its environmental fate.

Table 2. Physical and chemical properties of the neutral form of MBMBP

Property	Value	Measured/ Predicted	Reference
Physical state (at 20°C and 101.325 kPa)	Solid	–	–
Melting point (°C)	130–131	measured	Beilstein database 2000
	118–128	not stated	HSDB 1998
Boiling point (°C) (at 0.07 hPa)	187	measured	European Chemicals Bureau 1995
Vapour pressure (Pa)	4.7×10^{-11}	predicted	Sumitomo Chemical Co Ltd. 2000
	3.31×10^{-7} (2.48×10^{-9} mmHg)	predicted	EPIWIN 3.11
Water solubility (mg/L)	0.02	not stated	CITI 1992
Log K_{ow} (Octanol-water partition coefficient) (dimensionless)	6.25	measured	OECD 2001
K_{oc} (Organic carbon-water partition coefficient) (dimensionless)	1.5×10^{5}	predicted	OECD 2001
Log K_{oc}	6.63	predicted	EPIWIN 3.11
pKa (Acid dissociation constant) (dimensionless)	11.92 and 12.93	predicted	CompuDrug Chemistry Ltd. 1995
Henry's Law constant ($Pa \cdot m^3/mol$) *	8.0×10^{-7}	predicted	OECD 2001
Constant for reaction with OH^- radicals in air (cm^3/molecules-sec)	40.86×10^{-12}	predicted	Kwok and Atkinson 1995

***** Converted from $atm \cdot m^3/mol$ (units reported in OECD 2001)

Sources

MBMBP is produced by the reaction of 2-*tert*-butyl-*p*-cresol with formaldehyde through a carbonyl condensation.

Although MBMBP is considered a high production volume substance globally (OECD 2004), a survey conducted pursuant to section 71 of CEPA 1999 indicated that during the year 2000, between 10 and 100 tonnes of MBMBP at a concentration higher than 1% were imported into Canada. In addition, companies reported either importing or manufacturing MBMBP at a concentration lower than 1% and in a quantity meeting the reporting threshold of 100 kg. MBMBP was not reported as being manufactured at a concentration higher than 1% in Canada (Canada 2001).

Uses

The principal uses of MBMBP are as an antioxidant in acrylonitrile-butadiene-styrene copolymer, polypropylene, polyacetal, rubber, latex and adhesives; and as a stabilizer in styrenic and olefin polymers and polyoxymethylene homopolymers and copolymers (HSDB 1998, 1999).

No data have been identified to indicate the levels of MBMBP present in consumer products. However, given the physical and chemical properties of MBMBP, consumer products are not expected to contribute significantly to the exposure of the general Canadian population to this substance.

Releases to the Environment

The direct release of MBMBP to surface water could occur in sewage treatment plant (STP) effluent at STPs that receive influent from processing facilities. Releases to air are expected to be negligible because MBMBP's vapour pressure is very low. Releases to soil could occur from the application of STP sludge that contains MBMBP. MBMBP could partition to sediment from surface water that contains MBMBP. Information about releases was requested in the survey conducted pursuant to section 71 of CEPA 1999, but no releases were reported (Canada 2001).

Environmental Fate

The Level III fugacity model (CEMC 2002) has been used to predict the environmental fate of MBMBP. If released to water, most (74.3%) of the substance would tend to partition to the sediment phase, while release only to soil or only to air would result in partitioning mostly (>90%) into the soil.

Persistence and Bioaccumulation Potential

Environmental Persistence

Experimental results indicate that MBMBP is persistent in water (CITI 1992). Predicted results indicate that MBMBP is not persistent in air (EPIsuite 2001). No experimental data were found for half-lives in soil or sediment.

Potential for Bioaccumulation

According to experimental results (OECD 2001), MBMBP is not likely to be bioaccumulative. The highest reported bioconcentration factor in this study was 125, significantly below the criterion of 5000 for bioaccumulation as specified in the *Persistence and Bioaccumulation Regulations* under CEPA 1999 (Canada 2000). Caution should be exercised in the interpretation of these results, however, because the study used a solubilizer to achieve MBMBP concentrations above its aqueous solubility limit, so the actual bioconcentration factor might be higher than reported.

Potential to Cause Ecological Harm

Data concerning measured levels of MBMBP in air, water, soil and sediment in Canada were not found. The Screening Information Data Set initial assessment report (OECD 2001) reports that no quantitative monitoring data are available globally, including Canada. No data could be found for concentrations of MBMBP in wildlife in Canada or worldwide.

Environmental concentrations were calculated based on potential losses during plastic processing. Processing plant effluents were assumed to be treated by municipal sewage treatment plants (STPs) before discharge to the environment. The local concentration in STP effluent is calculated using ChemSim, a modelling program developed for Environment Canada that predicts aquatic concentrations downstream from point sources of a substance's release (Canadian Hydraulics Centre 2003). In order to run ChemSim, inputs, including the loading rate, are required. In this case, the loading rate is the mass of MBMBP in STP effluent released in one day. To calculate the loading rate, the following conservative assumptions were made:

- The upper range of the quantity of MBMBP imported in 2000 is 100 tonnes (100 000 kg). For the conservative exposure scenario, we have assumed that this quantity is imported by one distributor who sells to one customer who
  - uses the total quantity of MBMBP as a plastic additive;
  - uses the total quantity at one processing facility in one calendar year; and
  - discharges processing plant effluent into a municipal sewage treatment system.

- For calculating the amount of MBMBP released from the processing facility into the municipal sewage system, the Organisation for Economic Co-operation and Development (OECD) emission release scenario for plastic additives was used, with a release percentage of 0.65% (OECD 2003c). For determining the number of operating days (300 per year), the European Union Technical Guidance Document was used (European Chemicals Bureau 2003).
- The 92.2% removal rate for MBMBP at the STP was calculated using the STP fugacity model within the EPI Suite of models, version 3.10 (EPIsuite 2001).

The ChemSim model run assumed a standard river in Southern Ontario with a flow rate of 5 m^3/s and predicted a maximum concentration of MBMBP of 7.46×10^{-3} mg/L, 50 m from the point of impingement (release). Further assumptions required to run ChemSim (pertaining to river flow and channel geometry) are listed in the ChemSim report for this substance (Environment Canada 2004). The predicted environmental concentration for the aquatic medium (PEC_{aq}) is therefore 7.46×10^{-3} mg/L.

Most of the MBMBP in STP influent is removed (92.2%) and ends up in the sewage sludge. Since application of sewage sludge to agricultural land is a possibility, we have considered an exposure scenario involving sewage sludge–amended soil. No data on MBMBP concentrations in Canadian sewage sludge or soil were found. For the conservative soil exposure scenario, we calculate a concentration of MBMBP in sewage sludge to be 257 mg/kg dry weight, based on standard calculations, adapted to MBMBP, for estimating the concentration of a substance in sewage sludge (Droste 1997). Using this MBMBP concentration in sewage sludge and assuming that MBMBP-containing sludge is applied to the land for 10 years (OMOE 1996) and that no or little biodegradation of the MBMBP occurs, this would result in a soil concentration of 1.64 mg/kg dry weight. The predicted environmental concentration for soil (PEC_{soil}) is therefore 1.64 mg/kg dry weight.

Experimental toxicity data exist for effects in aquatic organisms (green algae, water flea and fish; OECD 2001). There is some uncertainty connected to these data, because the toxicity values are all above the water solubility limit. The critical toxicity value (CTV) selected is the lowest acceptable chronic value of 0.89 mg/L, the lowest-observed-effect concentration (LOEC) for immobility in *Daphnia magna* (water flea). No toxicity data were found for effects on soil- or sediment-dwelling organisms, terrestrial plants, or wildlife.

A- In the Aquatic Compartment

The conservative exposure scenario considered the release of MBMBP to the aquatic medium following industrial processing of the imported substance entirely at one site and the subsequent treatment and release from an STP. The PEC for the aquatic medium is 0.00746 mg/L.

The CTV for this assessment is the lowest acceptable chronic value (21-day LOEC) of 0.89 mg/L for immobility in *Daphnia magna*. The CTV is then divided by an application factor of 10 to account for uncertainty in extrapolating from laboratory to field conditions and for intraspecies and interspecies variations in sensitivity, giving a predicted no-effect concentration (PNEC) of 0.089 mg/L.

Therefore, the quotient for risk to aquatic species is calculated as follows:

$$\text{Risk quotient} = \frac{PEC_{aq}}{PNEC_{aq}} = \frac{0.00746 \text{ mg/L}}{0.089 \text{ mg/L}} = 0.0838$$

As this calculated risk quotient is much less than 1, it is predicted that MBMBP is unlikely to have harmful effects on pelagic organisms.

B – In Other Environmental Compartments

The soil CTV for MBMBP is 2670 mg/kg dry weight, which is the LOEC calculated using an equilibrium partitioning approach. The PNEC is determined by dividing the CTV by an application factor of 10 to account for extrapolation from laboratory to field conditions and intraspecies and interspecies variations in sensitivity. Therefore, the PNEC for soil-dwelling organisms is 267 mg/kg dry weight.

A risk quotient can thus be calculated as follows:

$$\text{Risk quotient} = \frac{PEC_{soil}}{PNEC_{soil}} = \frac{1.64 \text{ mg/kg dry weight soil}}{267 \text{ mg/kg dry weight soil}} = 0.00614$$

Since this quotient is significantly less than 1, it is predicted that MBMBP is unlikely to have harmful effects on soil-dwelling invertebrate organisms exposed to sewage sludge–amended agricultural land.

Uncertainties in Evaluation of Ecological Risk

Exposure Characterization

There is some uncertainty associated with the exposure characterization. There is a lack of monitoring data for MBMBP; environmental concentrations had to therefore be estimated using models. The use of models to predict actual concentrations based on current releases introduces uncertainties that are not easily quantifiable. Model selection, model inputs, release scenarios, site-specific information and meteorology are all factors that will affect the predicted exposure values.

Because of a lack of current information, conservative scenarios had to be developed. These scenarios also included some assumptions, such as the percentage of MBMBP released in STP effluent. Additionally, some sources, such as small companies that did not meet the reporting threshold of the section 71 survey, may not be included in the assessment and may account for a certain volume of MBMBP released to the environment. Current monitoring data from sites where MBMBP could be released, as well as from sites located far from point sources, would be very useful to support the assumptions in this assessment. However, given the available information, the scenarios developed are considered conservative (e.g., high release amounts were assumed for these sources). Even if the uncertainty about each actual exposure value is high, the confidence in the resulting conclusion is good.

Effects Characterization

Some uncertainty is associated with the PNEC determination. Due to MBMBP's low water solubility, homogeneous solutions could be reached in the toxicity studies only by using the maximum allowable dispersant (castor oil) concentration. Although effects were observed, concentrations of MBMBP in the environment are unlikely to reach the toxicity thresholds reported in the studies. Nevertheless, the studies were robustly summarized, and toxicity data can be used to select a conservative toxicity value for the assessment of risk to aquatic organisms.

There are no experimental toxicity data for soil-dwelling organisms. Equilibrium partitioning was used to estimate the toxicity of MBMBP to soil-dwelling organisms based on data for aquatic species. Also, the soil exposure concentration was estimated using conservative assumptions, such as lack of biodegradation.

Potential to Cause Harm to Human Health

Exposure Assessment

Quantitative data upon which to base upper-bounding estimates of intake of MBMBP were not available for any environmental media in Canada or elsewhere. Estimated environmental concentrations were modelled for air, water and soil based on the

information provided in the section 71 survey (Canada 2001).Children aged 0.5–4 years appear to be the subgroup (of the general population) most highly exposed to MBMBP in Canada. Their maximum upper-bounding daily intake is 3.4×10^{-4} µg/kg-bw per day—an estimate based on modelled environmental concentrations (see Appendix 1). Elevated exposure from drinking water may occur in populations close to point-source releases of MBMBP to surface water. Due to the absence of monitoring data, upper-bounding estimates of daily intake associated with potential point-source releases of MBMBP to surface water were estimated based on conservative modelled concentrations in drinking water.[1] Estimated intakes ranged from 7.1×10^{-3} µg/kg-bw per day (12–19 years) to a maximum of 3.7×10^{-2} µg/kg-bw per day for the 0–6 months age group.

Confidence in the exposure database is considered to be very low to low, as it is based solely on modelled concentrations of MBMBP in air, soil and water, and there is no indication of whether MBMBP is present in food. In view of MBMBP's high octanol-water partition coefficient, exposures through food and breast milk could occur. However, given the low concentrations predicted in water and soil and the fate of MBMBP in the environment, it is unlikely that exposures through foodstuffs and breast milk would exceed the conservative estimate presented here. MBMBP may also be present in residual amounts in consumer products, but no data were available as a basis for quantifying this exposure, although it is expected to contribute minimally to total intake compared with soil.

Health Effects Assessment

Based on a screening-level evaluation of available toxicological data on MBMBP (see Appendix 2), the lowest lowest-observed-effect level (LOEL) identified was 6 mg/kg-bw per day in dogs exposed to MBMBP via the diet for 90 days (ACC 1965b). At this dose, there was a significant difference in plasma alkaline phosphatase activity from pre-exposure levels to those measured at weeks 12 and 17 in dogs exposed to MBMBP compared with controls. Histopathological changes in the liver were also observed at the higher exposure levels (i.e., 10 mg/kg-bw per day or more). Results of the one limited chronic bioassay and the results of quantitative structure-activity relationship and structure-activity relationship modelling do not indicate that MBMBP is carcinogenic; similarly, the available limited data and model predictions do not suggest that the substance has a high potential for genotoxicity.

[1] For the point-source release scenario, it was assumed that 0.65% of the maximum estimated quantity of MBMBP imported into Canada was released into wastewater at one location (OECD 2003b) and that the plant operated 300 days/year (European Communities 2003). Removal of MBMBP during wastewater treatment was modelled (EPIsuite 2003) and subtracted from the amount released, and it was assumed that there was no further biodegradation in the environment (i.e., half-lives were assumed to be negligible). Modelling indicated that water concentrations were estimated to be 0.35 µg/L. For formula-fed infants, the concentration of MBMBP in the water used to reconstitute formula accounts for the intake of MBMBP from food. No measured data were identified.

The confidence in the database on health effects is considered to be moderate, based on the number of available toxicity studies addressing acute, repeated-dose and long-term genetic, reproductive and developmental toxicity endpoints.

Characterization of Risk to Human Health and Uncertainties

Comparison of a conservative critical effect level (i.e., 6 mg/kg-bw per day) for slight changes in biochemical parameters in a 90-day study in dogs with the highest of the upper-bounding estimates of exposure for all age groups in the population living in the vicinity of a point source (i.e., 0.037 μg/kg-bw per day) for the 0- to 6-month age group (based on conservative modelling of potential releases to the environment) resulted in a margin of exposure of approximately 160 000.

Based on the level of confidence in the available database and the conservative nature of this evaluation, including the use of an upper-bounding exposure estimate based on modelled predictions and lowest reported effect level, the margin between estimated exposure levels of MBMBP and those causing health effects in experimental animals is considered adequate to address elements of uncertainty associated with limitations of the database for population exposure and health effects (including intraspecies and interspecies variations in sensitivity, as well as the biological adversity or severity of the effects deemed critical), in which confidence is low and moderate, respectively.

Conclusion

Based on available information, it is concluded that MBMBP is not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends. In addition, it is concluded that MBMBP is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

It is therefore concluded that MBMBP does not meet the criteria in section 64 of the *Canadian Environmental Protection Act, 1999*. Additionally, MBMBP meets the criteria for persistence but does not meet the criteria for bioaccumulation set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000)

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Appendix 1: Upper-bounding estimates of daily intake of MBMBP by the general population in Canada

Route of exposure	Estimated intake (µg/kg-bw per day) of MBMBP by various age groups						
	0–6 months[1, 2, 3]		0.5–4 years[4]	5–11 years[5]	12–19 years[6]	20–59 years[7]	60+ years[8]
	formula fed	not formula fed					
Air[9]	7.2×10^{-9}		1.5×10^{-8}	1.2×10^{-8}	6.8×10^{-9}	5.8×10^{-9}	5.1×10^{-9}
Drinking water[10]	6.4×10^{-6}	2.4×10^{-6}	2.7×10^{-6}	2.1×10^{-6}	1.2×10^{-6}	1.3×10^{-6}	1.3×10^{-6}
Food and beverages[11]		NA[12]	NA	NA	NA	NA	NA
Soil[13]	2.1×10^{-4}		3.4×10^{-4}	1.1×10^{-4}	2.6×10^{-5}	2.2×10^{-5}	2.2×10^{-5}
Total intake	2.2×10^{-4}	2.1×10^{-4}	3.4×10^{-4}	1.1×10^{-4}	2.8×10^{-5}	2.3×10^{-5}	2.3×10^{-5}

[1] No data were identified on concentrations of MBMBP in breast milk.

[2] Assumed to weigh 7.5 kg, to breathe 2.1 m^3 of air per day, to drink 0.8 L of water per day (formula fed) or 0.3 L/day (not formula fed), and to ingest 30 mg of soil per day (Health Canada 1998).

[3] For exclusively formula-fed infants, intake from water is synonymous with intake from food. The concentration of MBMBP in water used to reconstitute formula was based on modelling. No data on concentrations of MBMBP in formula were identified for Canada. For non-formula fed infants approximately 50% are introduced to solid foods by 4 months of age and 90% by 6 months of age (NHW 1990; cited in Health Canada 1998).

[4] Assumed to weigh 15.5 kg, to breathe 9.3 m^3 of air per day, to drink 0.7 L of water per day and to ingest 100 mg of soil per day (Health Canada 1998).

[5] Assumed to weigh 31.0 kg, to breathe 14.5 m^3 of air per day, to drink 1.1 L of water per day and to ingest 65 mg of soil per day (Health Canada 1998).

[6] Assumed to weigh 59.4 kg, to breathe 15.8 m^3 of air per day, to drink 1.2 L of water per day and to ingest 30 mg of soil per day (Health Canada 1998).

[7] Assumed to weigh 70.9 kg, to breathe 16.2 m^3 of air per day, to drink 1.5 L of water per day and to ingest 30 mg of soil per day (Health Canada 1998).

[8] Assumed to weigh 72.0 kg, to breathe 14.3 m^3 of air per day, to drink 1.6 L of water per day and to ingest 30 mg of soil per day (Health Canada 1998).

[9] Modelling using ChemCAN 4.0 (Mackay et al. 1996) indicated that the highest concentration of MBMBP in ambient air was 2.56×10^{-8} µg/m^3. Ambient air was assumed to be representative of exposure to indoor air since there is no indication of additional sources of MBMBP in indoor environments. No measured data were identified.

[10] It was assumed that 0.65% of the maximum estimated quantity of MBMBP imported into Canada was released via wastewater (OECD 2003b) and that 92.97% of those emissions would be removed during wastewater treatment prior to release into the environment (EPIsuite 2003). It was also assumed that there was no further biodegradation following the release of MBMBP to the environment (i.e., half lives were assumed to be negligible). Modelling using ChemCAN 4.0 (Mackay et al. 1996) indicated that the highest concentration of MBMBP in water was 6.0×10^{-5} µg/L. For formula-fed infants, the concentration of MBMBP in the water used to reconstitute formula accounts for the intake of MBMBP from food. No measured data were identified.

[11] No measured data were identified.

[12] NA = not available

[13] It was assumed that 1.0% of the maximum estimated quantity of MBMBP imported into Canada was released via solid waste that is sent to landfill and released to soil. It was also assumed that there was

no biodegradation in the environment (i.e., half lives were assumed to be negligible). Modelling using ChemCAN 4.0 (Mackay et al. 1996) indicated that the highest concentration of MBMBP in soil was 52.2 µg/kg. No measured data were identified.

Appendix 2: Summary of health effects information for MBMBP

Endpoint	Lowest effect levels[1]/Results
Acute toxicity	Lowest **oral LD_{50}** (mouse) = 3200 mg/kg-bw (Ashland Oil Inc. 1992) [Additional studies: Hagan 1952; Stasenkova et al. 1977; Sumitomo Chemical Co Ltd. 1977a; ACC 1988; Bayer AG 1988; Takagi et al. 1994; HSDB 1998] Lowest **dermal LD_{50}** (rabbit) >10 000 mg/kg-bw (ACC 1988)
Short-term repeated-dose toxicity	Lowest **oral (gavage) LOEL** (rat) = 50 mg/kg-bw per day: prolongation of prothrombin time, increased liver weight, degeneration of spermatids and vacuolation of Sertoli cells (28- and 53-day studies) (MHW 1996, 1999) [Additional studies: Hagan 1952; Takahashi and Hiraga 1981a, 1981b; Ashland Oil Inc. 1992]
Subchronic toxicity	Lowest **oral (diet) LOEL** (dog) = 6 mg/kg-bw per day: change in alkaline phosphatase activity (90-day study) (ACC 1965b) [Additional studies: ACC 1965a; Takagi et al. 1994]
Chronic toxicity/ carcinogenicity	Lowest **non-neoplastic oral (diet) LOEL** (rat) = 12.7 mg/kg-bw per day: increased relative liver weight (18-month study); no increases in tumour incidence observed in rats exposed to up to 42.3 mg/kg-bw per day for 18 months (Takagi et al. 1994)
Genotoxicity and related endpoints: *in vitro*	**Negative**: Mutagenicity in *Salmonella typhimurium* TA98, TA100, TA1535 and TA1537 and *Escherichia coli* (Sumitomo Chemical Co Ltd. 1977b; Yamaguchi et al. 1991; MHW 1996), chromosomal aberrations in Chinese hamster lung cells (MHW 1996), DNA damage in *Bacillus subtilis* (Sumitomo Chemical Co Ltd. 1977b) **Positive**: Cell transformation in BALB/c3T3 cells and promotion in Chinese hamster V79 lung fibroblasts (Tsuchiya et al. 1995)
Developmental toxicity	Lowest **oral (gavage) LOEL** (fetal rat) = 375 mg/kg-bw per day: increase in fetal deaths; **LOEL** (maternal) = 187 mg/kg-bw per day: decreased body weight gain (exposure during gestation days 7–17) (Tanaka et al. 1990) [Additional studies: Telford et al. 1962; MHW 1999]

Endpoint	**Lowest effect levels[1]/Results**
Reproductive toxicity	Lowest **oral (diet) LOEL** (male rat) = 42.3 mg/kg-bw per day: decreased absolute and relative testis weights, testis tubule atrophy and decreased spermatogenesis (18-month study) (Takagi et al. 1994) [Additional studies: MHW 1996, 1999]

[1] LD_{50} = median lethal dose; LOEL = lowest-observed-effect level.