Substance Profile for The Challenge
Benzene, 1,3-bis(1-isocyanato-1-methylethyl)-
(Tetramethyl-m-xylylene diisocyanate)
CAS No. 2778-42-9

Introduction

The *Canadian Environmental Protection Act, 1999* (CEPA 1999) required the Minister of Health and Minister of the Environment to categorize the approximately 23 000 substances on the Domestic Substances List (DSL). Categorization involved identifying those substances on the DSL that are a) considered to be persistent (P) and/or bioaccumulative (B), based on criteria set out in the *Persistence and Bioaccumulation Regulations* (Government of Canada, 2000), and "inherently toxic" (iT) to humans or other organisms, or b) that present, to individuals in Canada, the greatest potential for exposure (GPE).

Further to this activity, the Act requires the Minister of the Environment and the Minister of Health to conduct screening assessments of substances that meet the categorization criteria. A screening assessment involves a scientific evaluation of available information for a substance to determine whether the substance meets the criteria set out in section 64 of CEPA 1999. Based on the results of a screening assessment, the Ministers can propose taking no further action with respect to the substance, adding the substance to the Priority Substances List (PSL) for further assessment or recommending the addition of the substance to the List of Toxic Substances in Schedule 1 of CEPA 1999 and, where applicable, the implementation of virtual elimination of releases to the environment.

A number of substances have been identified by the Ministers as high priorities for action based on the information obtained through the categorization process. This includes substances:

- that were found to meet all of the ecological categorization criteria, including persistence, bioaccumulation potential and inherent toxicity to aquatic organisms (PBiT), and that are known to be in commerce, or of commercial interest, in Canada, and/or
- that were found either to meet the categorization criteria for GPE or to present an intermediate potential for exposure (IPE), and were identified as posing a high hazard to human health based on available evidence on carcinogenicity, mutagenicity, developmental toxicity or reproductive toxicity.

Based on a consideration of the ecological and/or human health concerns associated with these substances, and the requirement under section 76.1 of CEPA 1999 for the Ministers to apply a weight of evidence approach and the precautionary principle when conducting

and interpreting the results of an assessment, sufficient data are currently available to conclude whether substances meet the criteria under section 64 of CEPA 1999.

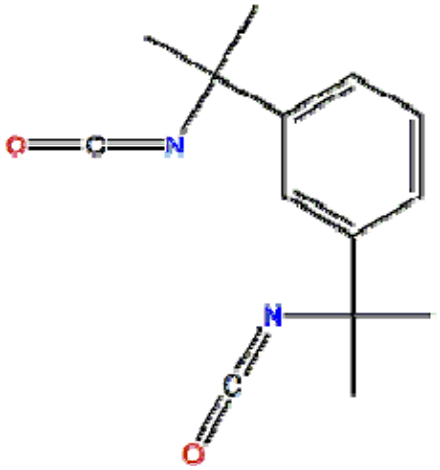
As such, the Ministers have issued a Challenge to industry and other interested stakeholders through publication in Canada Gazette Part I December 9, 2006 to submit, within the timelines stated in the Challenge section of this document, specific information that may be used to inform risk assessment and to develop and benchmark best practices for risk management and product stewardship.

The substance Benzene, 1,3-bis(1-isocyanato-1-methylethyl)- was identified as a high priority for action as it was found to be persistent, bioaccumulative and inherently toxic to aquatic organisms and is believed to have commercial interest in Canada. The technical human health and ecological information that formed the basis for concern associated with this substance is contained in Appendices I and II, respectively.

Substance Identity

For the purposes of this document, this substance will be referred to as tetramethyl-m-xylylene diisocyanate which has been derived from the inventory name Benzene, 1,3-bis(1-isocyanato-1-methylethyl)-.

CAS Registry Number	2778-42-9
Inventory names	Benzene, 1,3-bis(1-isocyanato-1-methylethyl)-; 1,3-Bis(1-isocyanato-1-methylethyl)benzene;
Other names	a,a,a',a'-Tetramethyl-m-phenylenedimethylene diisocyanate;a,a,a',a'-Tetramethyl-m-xylylene diisocyanate; 1,3-Bis(a-isocyanatoisopropyl)benzene; Isocyanic acid, a,a,a',a'-tetramethyl-m-xylylene ester; Isocyanic acid, m-phenylenediisopropylidene ester; m-Bis(1-isocyanato-1-methylethyl)benzene; m-TMXDI; Tetramethyl-m-xylylene diisocyanate;1,3-Bis(1-isocyanato-1-methylethyl)benzene
Chemical group	Discrete organics
Chemical sub-group	Isocyanate
Chemical formula	$C_{14}H_{16}N_2O_2$

Chemical structure	
SMILES	O=C=NC(c1cc(ccc1)C(N=C=O)(C)C)(C)C
Molecular mass	244.30 g/mol

No reports of manufacture in or import into Canada of this substance at or above the reporting threshold of 100 kg in the 2005 calendar year were received in response to a Notice published under section 71 of CEPA 1999 (Environment Canada 2006a). However, the Declaration of Non-Engagement form associated with this Notice (EC Survey 2006b) further invited any companies to identify themselves as stakeholders if they had an interest in a listed substance. Two stakeholder(s) identified themselves as having an interest in this substance.

The use identified during nomination of the DSL for the years 1984-86 was “Organic Chemicals, Industrial”.

THE CHALLENGE

Respecting direction under section 76.1 of CEPA 1999, and in the absence of additional relevant information as a result of this Challenge, the Ministers are predisposed to conclude, based on a screening assessment, that this substance satisfies the definition of toxic under section 64 of CEPA 1999. As such, the Ministers are prepared to then recommend to the Governor in Council that this substance be added to the List of Toxic Substances in Schedule 1 of CEPA 1999, with the intent of initiating the development of risk management measures taking into account socio-economic considerations.

If it is determined that the substance meets the virtual elimination criteria in subsection 77(4) of CEPA 1999, then subsequent risk management activities will be based on the objective of eliminating the release of any measurable quantity of the substance to the environment. In the absence of further information on existing management practices for a substance, actions would be proposed based on the assumption of worst-case practices. The management actions being considered for such substances at this time include prohibition through regulations, of the manufacture, use, sale, offer for sale and import of this substance, except for those activities controlled under the *Pest Control Products Act* and/or the *Food and Drugs Act.*

Exceptionally, should no information be identified to indicate that this substance is in commerce in Canada, the Ministers will conclude, based on a screening assessment, that this substance does not satisfy the definition of toxic under section 64 of CEPA 1999. However, given the properties of this substance, there is concern that new activities for the substance that have not been identified or assessed under CEPA 1999 could lead to the substance meeting the criteria set out in section 64 of the Act. Therefore it would be recommended that this substance be subject to the Significant New Activity provisions specified under subsection 81(3) of the Act, to ensure that any new manufacture, import or use of this substance in quantities greater than 100 kg/year is notified, and that ecological and human health risk assessments are conducted as specified in section 83 of the Act prior to the substance being introduced into Canada.

Section 71 Notice

Under the Challenge, information deemed necessary for improved decision making may be gathered by the Minister of Environment using section 71 of CEPA 1999. This information may be used for the purpose of assessing whether a substance is toxic or is capable of becoming toxic as defined under section 64 of CEPA 1999, or for the purpose of assessing whether to control, or the manner in which to control a substance.

The information mandated through the notices may relate to, among other things; quantity of the substance imported, manufactured, used, or released, concentrations, suppliers, customers, as well as types of uses of the substance.

Copies of the section 71 notice and guidance on how to comply with it are available from the Government of Canada Chemicals Portal (www.chemicalsubstanceschimiques.gc.ca), or from the contact provided below.

Opportunity to Submit Additional Information to Inform Screening Assessment

The Ministers of Health and Environment are inviting the submission of additional information for consideration during screening assessment of this substance. Data of the types described in the following paragraphs are considered most relevant, although other submitted information will be considered.

Data on the persistence, bioaccumulation, and potential for toxicity of the substance to organisms in different environmental media – Through the categorization exercise, available experimental data were collected up to December 2005. Where acceptable experimental data were not available, Quantitative Structure Activity Relationships (QSARs) or read across data were used to fill the data gaps. Since experimental data are preferred, interested parties have an opportunity to provide new or additional relevant experimental study information on the persistence, bioaccumulation, and potential for toxicity of this substance to organisms in different environmental media (air, water, sediment, soil). Efforts should focus on providing data for the endpoints for which quality experimental data does not already exist, as demonstrated by the information summarized in Appendix II of this document. As submitted data will be evaluated for completeness and robustness, it is recommended that stakeholders follow the guidance for test protocols and alternative approaches for test data, as described in Section 8 of the "Guidelines for the Notification and Testing of New Substances: Chemicals & Polymers".[1]

Data on the toxicity of the substance to human health - Through the categorization exercise, the high health priorities for action were those substances identified by various agencies as representing a high health hazard on the basis of potential to induce cancer, and/or adversely affect reproduction and development, two critical determinants of the health of Canadians of all ages. The hazard classifications used were those developed by national or international agencies in which large numbers of substances have been classified for endpoint-specific hazard based on original review and critical evaluation of data, assessments of weight of evidence and extensive peer review. Interested parties have an opportunity to provide new or additional relevant experimental study information on the toxicity of the substance to human health which could inform the screening assessment.

[1] "Guidelines for the Notification and Testing of New Substances: Chemicals & Polymers (version 2005)", Government of Canada, Available from http://www.ec.gc.ca/substances/nsb/eng/cp_guidance_e.shtml

Responses to this part of the challenge for this substance should be received at the address provided below by November 13, 2007.

Opportunity to Submit Additional Information on Current Uses and Existing Control Measures to Inform the Risk Management Approach for this Substance

The Ministers of Health and Environment are inviting the submission of additional information that is deemed beneficial by interested stakeholders, relating to the extent and nature of the management/stewardship of substances listed under the Challenge.

Organizations that may be interested in submitting additional information in response to this invitation include those that manufacture, import, export or use this substance whether alone, in a mixture or in a product, including manufactured items.

Additional information is being invited in the following areas:

- Import, manufacture and use quantities
- Substance and product use details
- Releases to the environment and spill management
- Current and potential risk management and product stewardship actions
- Existing legislative or regulatory programs controlling/managing the substance
- Information to support the development of a regulatory impact assessment.

A questionnaire is available which provides a detailed template as an example for the submission of this information. Guidance on how to respond to the challenge questionnaire is also available. Interested stakeholders are invited to provide available additional information, recognizing that not all questions in the questionnaire may be relevant to a particular substance, use, or industrial sector.

Copies of the questionnaire and associated guidance are available from the Government of Canada Chemicals Portal (www.chemicalsubstanceschimiques.gc.ca)**,** or from the contact provided below.

Responses to this part of the challenge for this substance should be received at the address provided below by November 13, 2007.

Request for Documents and Submission of Information

Documents and instructions may be requested from the following contact. Information in response to the above Challenge must be submitted to this address:

DSL Surveys Coordinator
Place Vincent Massey, 20th Floor
351 Saint Joseph Boulevard
Gatineau QC K1A 0H3
Tel: 1-888-228-0530/819-956-9313
Fax: 1-800-410-4314 / 819-953-4936
Email: DSL.surveyco@ec.gc.ca

Appendix I
Human Health Information to Support the Challenge for Tetramethyl-m-xylylene diisocyanate CAS No. 2778-42-9

Introduction

Under the *Canadian Environmental Protection Act, 1999* (CEPA, 1999), Health Canada undertook to categorize substances on the Domestic Substances List (DSL) to identify those representing the greatest potential for human exposure (GPE) and those among a subset of substances considered persistent (P) and/or bioaccumulative (B) by Environment Canada that are also considered to be "inherently toxic" to humans.

In order to efficiently identify substances that represent the highest priorities for screening assessment from a human health perspective, Health Canada developed and applied a Simple Exposure Tool (SimET) to the DSL to identify those substances that meet the criteria for GPE, Intermediate Potential for Exposure (IPE) or Low Potential for Exposure (LPE), and a Simple Hazard Tool (SimHaz) to identify those substances that pose a high or low hazard.

Tetramethyl-m-xylylene diisocyanate (CAS No. 2778-42-9) is considered to meet the criteria for LPE under SimET and does not meet the criteria for high hazard under SimHaz. This document summarizes the currently available information on which the SimET and SimHaz results are based.

Exposure Information from Health Related Components of DSL Categorization

SimET was developed and used to identify substances on the DSL considered to represent GPE. This approach was based on three lines of evidence: 1) the quantity in commerce in Canada, 2) the number of companies involved in commercial activities in Canada (i.e., number of notifiers), and 3) the consideration by experts of the potential for human exposure based on various use codes. The proposed approach was released for public comment in November 2003 and also enabled designation of substances as presenting an IPE or LPE, based on criteria for quantity and nature of use (Health Canada, 2003)

Results of the Application of SimET

Tetramethyl-m-xylylene diisocyanate has been determined to be LPE based on a consideration of the DSL nomination information listed below.

Nomination Information for DSL

Quantity in Commerce

The quantity reported to be manufactured, imported or in commerce in Canada during the calendar year 1986 was 100 kg

Number of Notifiers

The number of notifiers for the calendar years 1984-1986 was fewer than 4.

Use Codes and Description

The following DSL use codes have been identified for the substance:

76 Organic Chemicals, Industrial

Hazard Information from Health Related Components of DSL Categorization

Simple Hazard Tool (SimHaz)

SimHaz is a tool that has been used to identify, among all of the approximately 23 000 substances on the DSL, those considered to present either high or low hazard to human health based on formalized weight of evidence criteria and/or peer review/consensus of experts. This tool has been developed through extensive compilation of hazard classifications of Health Canada and other agencies and consideration of their robustness based on availability of transparent documentation of both process and criteria (Health Canada, 2005)

Results of the Application of SimHaz

Tetramethyl-m-xylylene diisocyanate has not been classified for hazard by any of the agencies considered under the SimHaz tool and therefore does not meet the criteria for high hazard under SimHaz.

Uncertainties

SimET and SimHaz have been developed as robust tools for effectively identifying substances from the DSL considered to be human health priorities for further consideration. It is recognized that they do not include a number of elements normally considered in a human health risk assessment such as a comprehensive characterization of exposure and hazard, a comparison of exposure metrics to hazard metrics and a detailed analysis of uncertainties.

References

Health Canada. 2003. Proposal for Priority Setting for Existing Substances on the Domestic Substances List under the Canadian Environmental Protection Act, 1999: Greatest Potential for Human Exposure. http://www.hc-sc.gc.ca/ewh-semt/alt_formats/hecs-sesc/pdf/pubs/contaminants/existsub/exposure/greatest_potential_human_exposure-risque_exposition_humaine_e.pdf

Health Canada. 2005. Proposed Integrated Framework for the Health-Related Components of Categorization of the Domestic Substances List under CEPA 1999 http://www.hc-sc.gc.ca/ewh-semt/alt_formats/hecs-sesc/pdf/contaminants/existsub/framework-int-cadre_e.pdf

Appendix II
Ecological Information
to Support The Challenge for
Tetramethyl-m-xylylene diisocyanate
CAS No. 2778-42-9

Introduction

The information in this document will form the basis of a screening assessment under section 74 of CEPA, 1999. Data relevant to an ecological screening assessment were identified in original literature, review documents, commercial and government databases prior to December 2005. Properties and characteristics may also have been estimated using Quantitative Structure Activity Relationship (QSAR) models. In addition, an industry survey was conducted for the year *2005* through a Canada Gazette Notice issued pursuant to section 71 of CEPA 1999 (Environment Canada, 2006a). This Notice requested data on the Canadian manufacture and import for the 2005 survey of the substance.

Physical and Chemical Properties

Table 1 contains experimental and modelled physical-chemical properties of tetramethyl-m-xylylene diisocyanate which are relevant to its environmental fate.

Table 1. Physical and chemical properties for Tetramethyl-m-xylylene diisocyanate.

Property	Type	Value	Temperature (C°)	Reference
Melting point	Experimental	-10°C		Cytec, 2005
Boiling point	Experimental	290°C		Cytec, 2005
Vapour pressure	Experimental	3.2E-3 mm Hg/ 0. 43Pa	25°	SRC Physprop, 2003
Henry's Law Constant	Modelled	3.26E-1 Pa-m^3/mole	25°	HENRYWIN
Log Kow (Octanol-water partition coefficient)	Modelled	4.74	25°C	KOWWIN
Water solubility	Experimental	5.833 mg/L	25°C	Cytec, 2005
	Modelled	2.29 mg/L	25°C	WSKOWWIN

Log Koc (Organic carbon partition coefficient)	Modelled	5.05		PCKOCWIN v1.66

Manufacture, Importation, and Uses

Manufacture and Importation

In Canada, no manufacture or import of tetramethyl-m-xylylene diisocyanate was reported in response to a CEPA section 71 survey notice for the 2005 calendar year. However, 1 Canadian and 1 American company identified themselves as having a stakeholder interest in the substance (Environment Canada, 2006a).

Elsewhere, tetramethyl-m-xylylene diisocyanate has been identified as a OECD HPV chemical (1997), as a US HPV (Sponsor Cytec Industries), and a LPV chemical in the European Union. Two companies are cited as producers/importers in the European Union LPV chemical

Uses

No uses were identified as a result of the S.71 notice (Environment Canada 2006). Previously, however, "Organic Chemicals, Industrial" was identified as the one use for this substance on the DSL in 1984-86.

However, a number of uses have been identified through the US HPV program. Tetramethyl-m-xylylene diisocyanate is a versatile aliphatic isocyanate finding broad end-use applicability. Tetramethyl-m-xylylene diisocyanate is used as an industrial intermediate that is incorporated into various polymers to improve performance. This chemical imparts improved physical properties to polyurethane products, affording higher strength and improved adhesion, appearance, and flexibility, resulting in more durable products. Application areas for the polymers incorporating tetramethyl-m-xylylene diisocyanate include specialty coatings, aqueous dispersions, automotive coatings, wood coatings, inks, sealants, adhesives, thermoplastic urethanes, and lacquers. Common commercial products that may have been made using tetramethyl-m-xylylene diisocyanate include, fabric and leather finishes, adhesives, automotive paints, printing inks, sealants, and wood coatings. Tetramethyl-m-xylylene diisocyanate is FDA approved for use in food-packaging under specific listings in the Code of Federal Regulations (CFR) Title 21-Food and Drugs Chapter I-Food and Drug Administration, Department of Health and Human Services (Cytec, 2005).

The substance may be in the Canadian environment because of its many potential uses in consumer products. However, amounts may be limited as it is often reacted into polymers, making it difficult for it to be released from products.

Releases, Fate and Presence in the Environment

Releases

Since there were no reports of import or manufacture at or above the reporting threshold of 100 kg in 2006, releases of this substance to the Canadian environment are presumed to be very low. According to Cytec Industries (2005), tetramethyl-m-xylylene diisocyanate is not expected to be widely dispersed in the environment as a result of its usage patterns, as it is anticipated that the substance is not used directly but rather reacted into the polymers in which they are added (Cytec, 2005).

The substance tetramethyl-m-xylylene diisocyanate is not known to be naturally produced in the environment.

Fate

The high log Kow and Koc values indicate that this substance will likely partition primarily to soil under most release scenarios, with smaller fractions predicted to partition to water and sediment. Indeed, the results of the Level III Fugacity modelling indicate that if the chemical is released equally to the three major environmental compartments (air, water, and soil), that soil, water and sediment (where the chemical has been indicated to persist: see Table 3), will account for 99% of media partitioning (Table 2).

Table 2. Results of the Level III fugacity modelling (EPIWIN V 3.12)

	Fraction of Substance Partitioning to Each Medium (%)			
Substance Released to:	**Air**	**Water**	**Soil**	**Sediment**
- Air (100%)	19.00	6.65	63.00	11.40
- Water (100%)	0.03	36.80	0.10	63.00
- Soil (100%)	0.00	0.03	99.90	0.06
- Air, water, soil (33% each)	0.44	10.50	71.20	17.90

Atmospheric Fate

A vapour pressure of 0.43 Pa and Henry's Law constant of 3.26×10-1 Pa-m3/mol indicates that tetramethyl-m-xylylene diisocyanate is semi/slightly volatile. Therefore, a portion will tend to remain in this compartment; but, the major media into which this substance will partition will be soil (~63%, Table 2).

Terrestrial Fate

If released to soil, tetramethyl-m-xylylene diisocyanate is expected to have extremely high adsorptivity to soil (i.e. expected to be immobile) based upon an estimated Log Koc of ~5. Volatilization from moist soil surfaces is likely a relatively unimportant fate process based upon an estimated Henry's Law constant of 3.22 ×10-6 atm-m3/mol. This chemical may slightly volatilize from dry soil surfaces based upon its vapour pressure. Therefore, if released to soil, tetramethyl-m-xylylene diisocyanate will remain almost

entirely in this environmental compartment, which is illustrated by the results of the Level III fugacity modelling (Table 2).

Aquatic Fate

If released into water, tetramethyl-m-xylylene diisocyanate is expected to strongly adsorb to suspended solids and sediment based upon predicted high values of estimated Koc. Volatilization from water surfaces is expected to be a relatively unimportant fate process based upon this compound's estimated Henry's Law constant. Thus, if water is a receiving medium tetramethyl-m-xylylene diisocyanate is expected to mainly partition in sediments and, to a lesser extent, remain in water (Table 2). It should be noted that the isocyanate group is anticipated to be susceptible to rapid hydrolysis. However, the products of hydrolysis are not currently known by Environment Canada and therefore their environmental fate was not considered.

Presence in the Environment

No monitoring data relating to the presence of this substance in environmental media (air, water, soil, sediment) have yet been identified.

Evaluation of P, B and iT Properties

Environmental Persistence

Once released into the environment, tetramethyl-m-xylylene diisocyanate appears to be relatively persistent in the environment, mainly in soil and sediments. Experimental persistence data in air that are available for tetramethyl-m-xylylene diisocyanate indicates that this substance is degraded relatively rapidly in this media (Table 3b) with a half-life of 0.527 days expected (Cytec, 2005). A predicted atmospheric oxidation half-life value of 1.055 day (Table 3a) is in agreement with the experimental value, and provides further evidence that this chemical is likely to be rapidly oxidized in air. This compound is not expected to react, or react appreciably, with other photo oxidative species in the atmosphere, such as O_3 and NO_3. The rate of degradation, if any, via direct photolysis is not known. Therefore, it is expected that reactions with hydroxyl radicals will be the most important fate process in the atmosphere for tetramethyl-m-xylylene diisocyanate. With a half-life of between 0.527-1.055 days via reactions with hydroxyl radicals, tetramethyl-m-xylylene diisocyanate is not persistent in air.

Table 3a. Modeled persistence data for tetramethyl-m-xylylene diisocyanate

Medium	Fate Process	Degradation Value	Endpoint/Units	Reference
Air	Atm. oxidation	1.055	Half-life, days	AOPWIN v1.91
Air	Ozone reaction	Not reactive	Half-life, days	AOPWIN v1.91
Water/Soil	Biodegradation	60	Half-life, days	BIOWIN v4.02, Ultimate survey
Water/Soil	Biodegradation	0.0403	Probability	BIOWIN v4.02, MITI Non-linear Probability
Water/Soil	Biodegradation	0.00	Probability	TOPKAT v6.2
Water	Hydrolysis	< 10 minutes	Half life	HYDROWIN v1.67

Table 3b. Empirical persistence data for tetramethyl-m-xylylene diisocyanate

Medium	Fate Process	Degradation Value	Endpoint/Units	Reference
Air	Atm Oxidation	0.527	Half life, days	Cytec, 2005
Water	Hydrolysis	0.0125-0.0167	Half-life, days (pH 4-9)	Cytec, 2005
Water	Biodegradation	13.7	Biodegradation, % (over 28 days)	Cytec, 2005

The empirical biodegradation data (Cytec, 2005), show 13.7 % biodegradation over 28 days in a ready-biodegradation test for tetramethyl-m-xylene diisocyanate (Table 3b). This indicates that the half-life in water and soil is longer than 182 days (6 months) (Environment Canada 2003).

For estimating degradation in water, soil and sediment, a QSAR weight-of-evidence approach (ESD, 2006a) was applied using the models shown in Table 3a. Based on these results shown in table 3a, the estimated timeframe for biodegradation indicates that tetramethyl-m-xylylene diisocyanate can be considered as persistent in water and soil. The potential for rapid hydrolysis was not taken into account as part of the weight of evidence and therefore the contribution of this fate process to at least the primary degradation of this substance in water, and potentially moist environments such as sediment and moist soils, is not fully considered.

To extrapolate to a half-life in sediments, an approach as been developed using Boethling's extrapolation factors (Boethling et al., 1995), which involves estimating the half life in sediment from that estimated for water (t1/2 water: t1/2 sediment = 1:4). Therefore, in sediments, the half-life is expected to exceed 365 days. Similar to the fate in water and moist soils, the contribution of hydrolysis to the fate of this chemical in sediment is not considered.

The long-range transport potential (LRTP) of tetramethyl-m-xylylene diisocyanate from its point of release to air is estimated to be low according to the model prediction presented in Table 3c. The TaPL3 model was used to estimate Characteristic Travel Distance (CTD), defined as the maximum distance traveled by 63% of the substance; or in other words, the distance that 37% of the substance may travel beyond. Beyer *et al*. (2000) have proposed CTD's of >2000 km as representing high LRTP, 700-2000 km as moderate, and <700 km as low. Based on the result shown in Table 3c, this substance is expected to remain primarily in areas close to its emission sources.

Table 3c. Model Predicted Characteristic Travel Distance (CTD) for tetramethyl-m-xylylene diisocyanate

Characteristic Travel Distance	Model (Reference)
261 km	TaPL3 (CEMC, 2003)

The empirical and modelled data (Tables 3a and 3b) demonstrate that the substance meets the persistence criteria (half-lives in soil and water ≥ 182 days; half-life in sediment ≥365 days*)* as set out in the Persistence and Bioaccumulation Regulations (Government of Canada, 2000).

Potential for Bioaccumulation

Modelled bioaccumulation and log Kow values for tetramethyl-m-xylylene diisocyanate indicate that this chemical has the potential to bioaccumulate in the environment (Table 4). Experimental bioaccumulation values for this chemical were not found.

The Modified GOBAS BAF middle trophic level model produced a bioaccumulation factor BAF of 6870 L/kg, indicating this has the potential to bioconcentrate and biomagnify in the environment. The three other bioconcentration factor (BCF) models, when used within a weight-of-evidence approach, also provide further evidence to support the bioconcentration potential of this substance.

Table 4. Modelled bioaccumulation data for tetramethyl-m-xylylene diisocyanate

Test Organism	Endpoint	Value wet wt	Reference
Fish	BAF	6870 L/kg	GOBAS BAF T2MTL (Arnot & Gobas, 2003)
Fish	BCF	2700 L/Kg	Gobas BCF T2LTL (Arnot & Gobas, 2003)
Fish	BCF	10326 L/kg	OASIS v1.20
Fish	BCF	887 L/kg	BCFWIN v2.15

The weight of evidence indicates that the tetramethyl-m-xylylene diisocyanate meets the bioaccumulation criterion (BCF, BAF > 5000) as set out in the Persistence and Bioaccumulation Regulations (Government of Canada, 2000).

Ecological Effects

A - In the Aquatic Compartment

There is modelled and experimental evidence that the substance causes harm to aquatic organisms at relatively low concentrations (e.g., LC50 < 1 mg/L) [Table 5a and b].

Table 5a. Empirical aquatic toxicity data for tetramethyl-m-xylylene diisocyanate

Test Organism	Type of Test	Endpoint	Value (mg/L)	Reference
Fish	Acute	LC50	0.67	Cytec, 2005
Fish	Chronic	NOEC	0.32	Cytec, 2005
Daphnia	Acute	LC50	5.2	Cytec, 2005
Daphnia	Chronic	NOEC	< 1.0	Cytec, 2005
Algae	Acute	EC50 (biomass)	0.36	Cytec, 2003

Algae	Acute	EC50 (biomass)	2.1	Cytec, 2005

The empirical toxicity data for tetramethyl-m-xylylene diisocyanate indicates that this substance is highly hazardous to aquatic organisms with an LC50 to *Pimephales promelas* of 0.67 mg/L and an EC50 (biomass) of 0.36 mg/L observed (Cytec, 2005, Cytec, 2003). A number of other chronic and acute toxicity assays also provide evidence of the moderate to high hazard of this substance to aquatic organisms (Cytec, 2005).

Table 5b Modelled aquatic toxicity data for tetramethyl-m-xylylene diisocyanate

Test Organism	Type of Test	Endpoint	Value (mg/L)	Reference
Fish	Acute	LC50	49.76	A.I. Expert System v1.25
Fish	Acute	LC50	1.2	TOPKATv6.2
Fish	Acute	LC50	0.42	OASIS v1.20
Fish	Acute	LC50	1.347	ECOSAR v0.99h
Daphnia	Acute	EC50	1.2	TOPKATv6.2

A range of aquatic toxicity predictions were obtained from the various QSAR models considered. Table 6b list those predictions that were considered reliable and were used in the QSAR weight-of-evidence approach for aquatic toxicity (ESD 2006a). These results indicate that the substance is moderately to highly hazardous to aquatic organisms.

B - In Other Media

No ecological effects studies for non-aquatic non-human organisms were found for this compound.

Potential to Cause Ecological Harm

Evidence that a substance is highly persistent and bioaccumulative as defined in the Persistence and Bioaccumulation Regulations of CEPA 1999 (Government of Canada, 2000) together with evidence of commercial activity provides a significant indication of its potential to be entering the environment under conditions that may have harmful long term ecological effects (ESD, 2006b). Substances that are persistent remain in the environment for a long time after being released, increasing the potential magnitude and duration of exposure. Substances that have long half-lives in mobile media (air and water) and partition into these media in significant proportions, have the potential to cause widespread contamination. Releases of small amounts of bioaccumulative substances may lead to high internal concentrations in exposed organisms. Highly bioaccumulative and persistent substances are of special concern, since they may biomagnify in food webs, resulting in very high internal exposures, especially for top predators. Evidence that a substance is both highly persistent and bioaccumulative, when taken together with other information (such as evidence of toxicity at relatively low

concentrations, and evidence of uses and releases) may therefore be sufficient to indicate that the substance has the potential to cause ecological harm.

The information collected to date suggests that tetramethyl-m-xylylene diisocyanate has the potential to cause ecological harm if it were to be released in the Canadian environment. Once released into the environment, because of its resistance to degradation, it could remain in water, sediment, and/or soil for a long time. As it persists in the environment, and because of its lipophyllic character, it could bioaccumulate and possibly be biomagnified in trophic food chains. It has also demonstrated relatively high toxicity to aquatic organisms. However, the lack of importation or manufacture of tetramethyl-m-xylylene diisocyanate in Canada at significant volumes suggests very low releases of this chemical into the Canadian environment.

Uncertainties

Based on information collected, there is some uncertainty about the precise use patterns of tetramethyl-m-xylylene diisocyanate in Canada. In addition, information on concentrations in the Canadian environment are currently lacking.

The role of hydrolysis in the fate and effects of this substance is not fully understood. As a result, the evidence for high persistence and bioaccumulation potential involves uncertainties. It is generally well recognized that the isocyanate group is subject to hydrolysis (often rapid) and the implications of this in the assessment of the persistence and bioaccumulation of this substance, particularly in aqueous media, is not well understood. Conversely, however, the hazardous properties of the degradation products are similarly not well understood. Evidence that tetramethyl-m-xylylene diisocyanate can harm organisms at relatively low exposure concentrations is provided by results from QSAR modelling and toxicity testing for pelagic organisms. While the question of the role of tetramethyl-m-xylylene diisocyanate in directly exerting these toxic effects, or that of a product of its hydrolysis, is uncertain, the evidence in either case suggests that tetramethyl-m-xylylene diisocyanate, its hydrolysis products, or a combination of the two, is highly hazardous to aquatic organisms.

Regarding toxicity, based on the predicted partitioning behaviour of this chemical, the significance of soil and sediments as important media of exposure is not well addressed by the effects data available. Indeed, the only effects data identified apply primarily to pelagic aquatic exposures, although the water column may not be the medium of primary concern based on partitioning estimates.

The experimental or predicted concentrations, associated with inherent toxicity for aquatic organisms, may have an additional source of uncertainty in some situations, e.g. where these concentrations exceed the solubility of the chemical in water (either experimental or predicted). Given that concentrations for both the toxicity and water solubility often vary considerably (up to several orders of magnitude), it is acknowledged that these uncertainties exist.

There is also uncertainty associated with basing the overall conclusion that tetramethyl-m-xylylene diisocyanate may be causing ecological harm, solely on information relating to its persistence, bioaccumulation, relative toxicity and use pattern. Typically quantitative risk estimates (i.e., risk quotients or probabilistic analyses) are important lines of evidence when evaluating a substances potential to cause environmental harm. However when risks for persistent and bioaccumulative substances such as tetramethyl-m-xylylene diisocyanate are estimated using such quantitative methods, they are highly uncertain and are likely to be underestimated (ESD, 2006b). Given that long term risks associated with persistent and bioaccumulative substances cannot at present be reliably predicted, quantitative risk estimates have limited relevance. Furthermore since accumulations of such substances may be widespread and are difficult to reverse, a conservative response to uncertainty (that avoids underestimation of risks) is justified.

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