Screening Assessment for the Challenge

Phenol, 2,6-bis(1,1-dimethylethyl)-4-(1-methylpropyl)-

**Chemical Abstracts Service Registry Number
17540-75-9**

**Environment Canada
Health Canada**

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Synopsis

Pursuant to section 74 of the *Canadian Environmental Protection Act, 1999* (CEPA 1999), the Ministers of the Environment and of Health have conducted a screening assessment on Phenol, 2,6-bis(1,1-dimethylethyl)-4-(1-methylpropyl)- (DTBSBP), Chemical Abstracts Service Registry Number 17540-75-9. This substance was identified as a high priority for screening assessment and included in the Challenge because it was found to meet the ecological categorization criteria for persistence, bioaccumulation potential and inherent toxicity to non-human organisms and is believed to be in commerce in Canada.

The substance DTBSBP was not considered to be a high priority for assessment of potential risks to human health, based upon application of the simple exposure and hazard tools developed by Health Canada for categorization of substances on the *Domestic Substances List*. Therefore, this assessment focuses on information relevant to the evaluation of ecological risks.

DTBSBP is an organic substance that is used in Canada and elsewhere as an antioxidant and liquid stabilizer in plastics such as PVC and polyurethane foam, as well as in brake fluids, ink resins and mineral/vegetable oils used in industrial applications. It is also used as an antioxidant in the petrochemical sector. This substance is not naturally produced in the environment. A quantity of 16 686 kg of DTBSBP was reported to be imported into Canada in 2006, for use mainly in plastics manufacturing. The quantity of DTBSBP imported into Canada, along with the potentially dispersive uses of this substance, indicates that it may be released into the Canadian environment.

Based on reported use patterns and certain assumptions, 54% of DTBSBP is estimated to end up in waste disposal sites. Small proportions are estimated to be released to water (3.7%), paved/unpaved surfaces (0.2%) and air (0.4%). DTBSBP has a low solubility in water, is moderately volatile and has a tendency to partition to particles and lipids (fat) of organisms because of its hydrophobic nature. DTBSBP will be likely found equally in sediments (51%) and water (48%) when released to water. It is not expected to be subject to long-range atmospheric transport.

Based on its physical and chemical properties as well as empirical biodegradation data, DTBSBP is not expected to degrade quickly in the environment. It is persistent in water, soil and sediments. DTBSBP also has the potential to accumulate in organisms and may biomagnify in food chains. The substance has been determined to meet the persistence and bioaccumulation criteria as set out in the *Persistence and Bioaccumulation Regulations*. In addition, modelled and analogue aquatic toxicity data indicate that the substance is potentially highly hazardous to aquatic organisms. It is therefore concluded that DTBSBP is entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity.

There was no empirical data identified regarding measured concentrations of DTBSBP in environmental media in Canada or elsewhere. DTBSBP may be used in plasticized PVC for food packaging applications. A conservative human exposure estimate derived from the potential use of plasticized PVC films in food packaging was considered. Overall, it is expected that exposure to DTBSBP through dietary intake, if any, in Canada would be minimal. Exposure to DTBSBP by the general population in Canada was examined by considering polyol and polyurethane foam products in mattresses, furniture, and automotive trim materials. Due to the lack of experimental data on DTBSBP, exposure estimates were derived based on the structurally similar but more volatile antioxidant, butylated hydroxytoluene. This likely resulted in overestimates which can be considered as conservative upper-bounding estimates.

The health effects database for DTBSBP is limited, however it was not genotoxic in *in vitro* assays and one study suggests low acute toxicity. Information on analogues indicates that liver and haematological effects are common endpoints which are observed across this group of compounds.

Based on the information available, the margins between upper-bounding estimates of exposure through food (i.e. migration from food packaging) and consumer products and levels associated with effects in experimental animals are considered to be adequately protective of human life and health. It is therefore concluded that DTBSBP 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.

Based on the information available, it is concluded that DTBSBP meets one or more of the criteria set out in section 64 of the *Canadian Environmental Protection Act, 1999*. DTBSBP is persistent and bioaccumulative in accordance with the regulations, and its presence in the environment results primarily from human activity.

This substance will be considered for inclusion in the *Domestic Substances List* inventory update initiative. In addition and where relevant, research and monitoring will support verification of assumptions used during the screening assessment and, where appropriate, the performance of potential control measures identified during the risk management phase.

Introduction

The *Canadian Environmental Protection Act, 1999* (CEPA 1999) (Canada 1999) requires the Minister of the Environment and the Minister of Health to conduct screening assessments of substances that have met the categorization criteria set out in the Act to determine whether these substances present or may present a risk to the environment or human health.

Based on the information obtained through the categorization process, the Ministers identified a number of substances as high priorities for action. These include substances that

- met all of the ecological categorization criteria, including persistence (P), bioaccumulation potential (B) and inherent toxicity to aquatic organisms (iT), and were believed to be in commerce in Canada; and/or
- met the categorization criteria for greatest potential for exposure (GPE) or presented an intermediate potential for exposure (IPE), and had been identified as posing a high hazard to human health based on classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity or reproductive toxicity.

The Ministers therefore published a notice of intent in the *Canada Gazette*, Part I, on December 9, 2006 (Canada 2006a), that challenged industry and other interested stakeholders to submit, within specified timelines, specific information that may be used to inform risk assessment, and to develop and benchmark best practices for the risk management and product stewardship of those substances identified as high priorities.

The substance Phenol, 2,6-bis(1,1-dimethylethyl)-4-(1-methylpropyl)- was identified as a high priority for assessment of ecological risk as it was found to meet the ecological categorization criteria for persistence, bioaccumulation potential and inherent toxicity to aquatic organisms and was believed to be in commerce in Canada. The Challenge for this substance was published in the *Canada Gazette* on January 31, 2009 (Canada 2009a, 2009b). A substance profile was released at the same time. The substance profile presented the technical information available prior to December 2005 that formed the basis for categorization of this substance. As a result of the Challenge, submissions of information pertaining to the uses and exposure of the substance were received.

Although Phenol, 2,6-bis(1,1-dimethylethyl)-4-(1-methylpropyl)- was determined to be a high priority for assessment with respect to the environment, it did not meet the criteria for GPE or IPE, and neither did it meet the criteria for high hazard to human health based on classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity or reproductive toxicity. Therefore, this assessment focuses principally on information relevant to the evaluation of ecological risks

Screening assessments focus on information critical to determining whether a substance meets the criteria as set out in section 64 of CEPA 1999. Screening assessments examine scientific information and develop conclusions by incorporating a weight-of-evidence approach and precaution.[1]

This final screening assessment includes consideration of information on chemical properties, hazards, uses and exposure, including the additional information submitted under the Challenge. 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 August 2009 for the ecological sections of the document and November 2009 for human health–related sections. Key studies were critically evaluated; results from *in silico* modelling were used to reach conclusions.

When available and relevant, information presented in hazard assessments from other jurisdictions was considered. The final screening assessment does not represent an exhaustive or critical review of all available data. Rather, it presents the most critical studies and lines of evidence pertinent to the conclusion.

This final screening assessment was prepared by staff in the Existing Substances Programs at Health Canada and Environment Canada and incorporates input from other programs within these departments. The ecological portions of this assessment have undergone external peer review/consultation. Additionally, the draft of this screening assessment was subject to a 60-day public comment period. While external comments were taken into consideration, the content and outcome of the final screening assessment remain the responsibility of Health Canada and Environment Canada. Approaches used in the screening assessments under the Challenge have been reviewed by an independent Challenge Advisory Panel.

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

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[1] A determination of whether one or more of the criteria of section 64 are met is based upon an assessment of potential risks to the environment and/or to human health associated with exposures in the general environment. For humans, this includes, but is not limited to, exposures from ambient and indoor air, drinking water, foodstuffs, and the use of consumer products. A conclusion under CEPA 1999 on the substances in the Chemicals Management Plan (CMP) Challenge Batches 1-12 is not relevant to, nor does it preclude, an assessment against the hazard criteria specified in the *Controlled Products Regulations*, which is part of regulatory framework for the Workplace Hazardous Materials Information System [WHMIS] for products intended for workplace use.

Substance Identity

For the purposes of this document, this substance will be referred to as DTBSBP, an acronym based on the common name 2,6-di-*tert*-butyl-4-*sec*-butylphenol.

Table 1. Substance identity for DTBSBP

Chemical Abstracts Service Registry Number (CAS RN)	**17540-75-9**
DSL name	**Phenol, 2,6-bis(1,1-dimethylethyl)-4-(1-methylpropyl)-**
National Chemical Inventories (NCI) names[1]	*Phenol, 2,6-bis(1,1-dimethylethyl)-4-(1-methylpropyl)-* (TSCA, ENCS, AICS, PICCS, ASIA-PAC) *4-sec-Butyl-2,6-di-tert-butylphenol* (DSL, EINECS, ECL) *PHENOL, 2,6-DI-TERT-BUTYL-4-SEC-BUTYL-* (PICCS)
Other names	*2,6-Di-tert-butyl-4-sec-butylphenol;* *Isonox 132;* *NSC 14460;* *Phenol, 4-sec-butyl-2,6-di-tert-butyl-;* *Vanox 1320*
Chemical group (DSL Stream)	Discrete organics
Major chemical class or use	Phenols
Major chemical sub-class	Alkylphenols, hindered phenols
Chemical formula	$C_{18}H_{30}O$
Chemical structure	
SMILES[2]	Oc1c(cc(cc1C(C)(C)C)C(CC)C)C(C)(C)C
Molecular mass	262.44 g/mol

[1] National Chemical Inventories (NCI). 2007: AICS (Australian Inventory of Chemical Substances); ASIA-PAC (Asia-Pacific Substances Lists); DSL (Canada's Domestic Substances List); ECL (Korean Existing Chemicals List); EINECS (European Inventory of Existing Commercial Chemical Substances); ENCS (Japanese Existing and New Chemical Substances); PICCS (Philippine Inventory of Chemicals and Chemical Substances); and TSCA (Toxic Substances Control Act Chemical Substance Inventory).

[2] Simplified Molecular Input Line Entry System

Physical and Chemical Properties

Table 2a below contains experimental and modelled physical and chemical properties of DTBSBP that are relevant to its environmental fate.

DTBSBP is a liquid under ambient conditions (SI Group 2009a). Since DTBSBP is not expected to ionize at a relevant environmental pH, ionization of this substance was not considered for prediction of its physical and chemical properties.

Table 2a. Physical and chemical properties of DTBSBP

Property	Type	Value	Temperature (°C)	Reference
Melting point (ºC)	Modelled	102		MPBPWIN 2000
	Experimental	18.9		SI Group 2009a
Freeze point (ºC)	Experimental	24.6		SI Group 2010a
Boiling point (ºC)	Modelled	330		MPBPWIN 2000
	Experimental	275		SI Group 2009a
Density (kg/m^3)	Experimental	0.902	25	Sigma-Aldrich 2009
Vapour pressure (Pa)	Modelled	0.35 (0.00262 mm Hg)	25	MPBPWIN 2000
Henry's Law constant (Pa·m^3/mol)	Modelled	3.71 (3.66×10^{-4} atm·m^3/mol)	25	HENRYWIN 2000

Property	Type	Value	Temperature (°C)	Reference
Log K_{ow} (Octanol-water partition coefficient) (dimensionless)	Modelled	6.1[1]		KOWWIN 2000
Log K_{oc} (Organic carbon-water partition coefficient) (dimensionless)	Modelled	4.47[2]		PCKOCWIN 2000
Water solubility (mg/L)	Not specified	Not very soluble (< 1%)		SI Group 2009a
	Modelled	2.47	25	WSKOWWIN 2000
pK_a (Acid dissociation constant) (dimensionless)	Modelled	11.85		ACD/pK$_a$DB 2005

[1] Log K_{ow} determined by experimental value adjustment in KOWWIN (2000), adjusting the modelled value of 6.43 (KOWWIN 2000) using the measured log K_{ow} of 6.06 of analogue substance 2,4,6-tri-*tert*-butylphenol (CAS RN 732-26-3) (NITE 2002a).

[2] Value was calculated using the adjusted log K_{ow} value of 6.1 (see Note 1).

As noted in Table 2a, the modelled log K_{ow} for DTBSBP was obtained by using the experimental value adjustment feature in KOWWIN (2000), using the measured log Kow of 6.06 of analogue substance 2,4,6-tri-*tert*-butylphenol (CAS RN 732-26-3) (NITE 2002a). This was done due to the very close structural similarity of these two substances, which also have the same molecular weights, and also because the log K_{ow}s of these two substances estimated using KOWWIN (2000) were very close (6.43 for DTBSBP; 6.39 for 2,4,6-tri-*tert*-butylphenol). Therefore, it was deemed that adjusting the predicted Kow for DTBSBP with the experimental value for 2,4,6-tri-*tert*-butylphenol would yield a more accurate result than using the KOWWIN (2000) predicted value on its own.

To fill data gaps for biodegradation, bioaccumulation and ecotoxicity endpoints, a literature search was performed and the database ChemIDplus® (NLM 2009) was used to identify appropriate analogue substances of DTBSBP. The substances 2,4,6-tri-*tert*-butylphenol (CAS RN 732-26-3) and 2,6-di-*tert*-butyl-4-ethylphenol (CAS RN 4130-42-1) were found to be appropriate analogues for DTBSBP as they are similar in molecular mass and have similar structure and functional groups to DTBSBP. The

structures and molecular masses of these analogue substances are shown in Appendix IV, along with those of other analogue substances used in the health portion of this assessment (see Potential to Cause Harm to Human Health section). Estimated physical-chemical property data for these substances, as well as for DTBSBP, for comparison purposes, are presented in Table 2b below. To permit a level comparison between the substances, the estimated data was obtained by running EPI Suite (2008) without the input of any available measured physical-chemical properties. Empirical data found for the analogue substances are also given in Table 2b, along with the source of the data.

Table 2b. Predicted and experimental physical-chemical properties of DTBSBP and analogue substances

CAS RN.	Log Kow	Water solubility (mg/L)	Melting Point (°C)	Boiling Point (°C)	Vapour Pressure (Pa)
17540-75-9 (DTBSBP)	6.43	0.25	102	330	0.0028
732-26-3	6.39 6.06 (1)	0.51	104 131 (2)	324 278 (2)	0.027
4130-42-1	5.52	2.1	92 44 (2)	310 272 (2)	0.29

Notes:
The first line of data for each substance consists of estimates obtained from EPI Suite (2008).
(1) - NITE (2002a)
(2) – Lide (2003)

Sources

DTBSBP is not known to be naturally produced in the environment.

Information was collected through surveys conducted for the years 2005 and 2006 under *Canada Gazette* notices issued pursuant to section 71 of CEPA 1999 (Canada 2006b, 2009b). These notices requested data on the Canadian manufacture and import of DTBSBP.

In Canada, no manufacture of DTBSBP was reported in 2005 or 2006. Currently there is just one known global manufacturer of this substance, the SI Group in the United States (SI Group 2009b). Three companies reported total importations of between 1000 kg and

100 000 kg of the substance into Canada in 2005 (Environment Canada 2006). In 2006, a total of 16 686 kg of DTBSBP was reported to be imported into Canada by five companies, including one company that imported quantities below the reporting threshold of 100 kg/year (Environment Canada 2009a). Six companies identified themselves as "stakeholders" in 2006.

DTBSBP is a High Production Volume (HPV) chemical in the United States. In 2006, between 10 million and 50 million pounds (4.5 million to 23 million kg) were produced and/or imported by only one company, SI Group, Inc. (US EPA 2006). No commercial or consumer usage data in the United States were available, as these were considered to be confidential (US EPA 2006). This substance is also on the Organisation for Economic Co-operation and Development's list of HPV chemicals (OECD 2004a). This substance is included on the Oslo-Paris (OSPAR) Commission's list of substances of possible concern and has been identified as a Low Production Volume (LPV) chemical in the European Union (ESIS 2009).

Uses

In response to the CEPA section 71 notices for the 2005 and 2006 calendar years (Canada 2006b, 2009b), the following business activities were identified as not confidential: plastics product manufacturing, and antioxidant/corrosion inhibitor used in brake fluid.

This information is consistent with the DSL nomination data (1984–1986), which identified the use of DTBSBP as antioxidant/corrosion inhibitor/scavenger/antiscaling agent in the manufacture of plastics products. It is also used as an antioxidant in other manufactured products. Information on the other uses of DTBSBP reported to Environment Canada is not provided here as it is considered to be confidential business information. However, this information was considered in this risk assessment of DTBSBP.

The additional information below on potential uses of DTBSBP was found through searches of the available scientific and technical literature, although potential uses in Canada were not specifically identified.

DTBSBP is listed by the U.S. Food and Drug Administration as an effective food contact substance, which is any substance that is intended for use as a component of materials used in manufacturing, packing, packaging, transporting or holding food (US FDA 2008). It is specifically used as an antioxidant in food contact applications in plasticized vinyl chloride homo- and co-polymers (PVC) (SII 2001). For example, it may be used in PVC films for wrapping meat and produce (personal communication with Health Products and Food Branch, Food Directorate, Health Canada, 2009-03-23; unreferenced).

DTBSBP is used as an antioxidant and liquid stabilizer in polyols used in polyurethane, PVC, adhesives and functional fluids (SII 2001). Although OSPAR lists the functional

use category for DTBSBP as a pesticide, it is further stated in their fact sheet that there is no authorized use in the European Union in plant protection products (OSPAR 2006). It is not registered for use as a pesticide active ingredient (PMRA 2009) or formulant in Canada (PMRA 2007).

According to the North American manufacturer of DTBSBP, it is used in the following industries (SI Group 2009b, 2010b):
- PVC, both rigid and flexible grades – polymerization chain terminator and PVC stabilizer
- thermoplastics, such as low-density polyethylene (LDPE)
- polyols/flexible foams – stabilizer/antioxidant
- brake fluids – stabilizer/antioxidant/corrosion inhibitor
- ink resins – stabilizer/antioxidant
- peroxide inhibitor for petrochemical and refinery streams – stabilizer/antioxidant
- mineral/vegetable oils, such as turbine oil, hydraulic oil, chainsaw oil – stabilizer/antioxidant

When used as an antioxidant, the concentration of DTBSBP ranges from 300 to 1000 ppm (0.03–0.10 weight %) (SI Group 2009b). The purity of DTBSBP is typically 98.6%. DTBSBP is used at a concentration of 0.1% wt in brake fluid (SI Group 2009b).

Because DTBSBP has certain advantages as compared to the antioxidant butylated hydroxytoluene (BHT), such as being a liquid at ambient temperatures and therefore easier to handle, DTBSBP is being used as a replacement for BHT in many of the applications listed above (SI Group 2009b).

Releases to the Environment

The following information on releases for the year 2006 was obtained from a *Canada Gazette* notice issued pursuant to section 71 of CEPA 1999 (Canada 2009b). Some companies reported transfers of small quantities of the substance (less than 100 kg in total) in non-hazardous waste to an off-site waste management facility (Environment Canada 2009a). No companies reported releases of this substance to air, water or soil.

Additionally, the losses of DTBSBP via various routes during its life cycle are estimated based on regulatory survey data, industry data and data published by different organizations. The losses are grouped into seven types: (1) discharge to wastewater; (2) emission to air; (3) loss to land; (4) chemical transformation; (5) disposal to landfill; (6) disposal by recycling; and (7) disposal by incineration. Losses may occur at one or more of the substance's life cycle stages that include manufacture, industrial use, consumer/commercial use, and disposal. To assist in estimating these losses, a spreadsheet (Mass Flow Tool) was used that incorporates all data and assumptions required for the estimation (Environment Canada 2009b). Unless specific information on the rate or potential for release of the substance from landfills and incinerators is

available, the Mass Flow Tool does not quantitatively account for releases to the environment from waste disposal sites.

The losses estimated for DTBSBP over its life cycle for worst-case scenario applications (i.e., maximum potential releases) are presented in Table 3. These losses are based on the total amount of 16 686 kg of DTBSBP reported to be in Canadian commerce in 2006 (Environment Canada 2009c). In this scenario, loss to wastewater pertains to the discharge prior to any treatment, either on-site industrial wastewater treatment or off-site municipal sewage treatment. Loss via chemical transformation refers to changes in substance identity that occur within the manufacture, industrial use or consumer/commercial use stages, but excludes those during waste management operations such as incineration and wastewater treatment. Loss to recycling refers to the quantity sent to recycling facilities. The substance can further be released from the recycling facilities to the environment. The quantity exported is included in Table 3 in order to present a complete mass balance for the substance.

Of the total quantity of DTBSBP used in Canadian commerce, 3.9% (644 kg) is expected to be released to wastewater (see Table 3). In general, wastewater is a common source for releases to water and soil (via biosludge application) through wastewater treatment facilities. Industrial formulation and container handling accounts for the largest proportion (81%) of the releases to wastewater, while consumer uses account for 19 % of the releases to wastewater, mainly from use of brake fluid (Environment Canada 2009c). The plastics products industry sector is estimated to account for the largest total losses, as this is the sector that uses the greatest mass of DTBSBP in Canada (Environment Canada 2009a). The consumer releases from brake fluid would be widely dispersive (e.g., a large number of very small sources), while the industrial releases would be point sources.

DTBSBP is also expected to be released to the environment via routes other than wastewater. Emissions to air can lead to atmospheric exposure if the substance remains in air, or to exposures in soil and water if the substance is subject to atmospheric deposition. Losses to land accounts for 0.2% of the total mass of DTBSBP. Mechanisms for losses to land include consumer use of brake fluid and leaks and spills during industrial use. The substance lost to land can be washed onto soil or into a nearby sewer, resulting in soil or aquatic exposure. DTBSBP is not expected to leach from waste into landfill leachate. Due to its high sorptivity ($Koc = 4.47$), it is expected to sorb strongly to soil and sediments. As well, based on laboratory testing, DTBSBP is not extractable from rigid PVC into the solvent heptane (SI Group 2009b).

This substance is expected to be used in some manufactured items and consumer products. Although no information is available on the quantity of manufactured items or consumer products containing DTBSBP that are imported into Canada, it is anticipated that the loss proportions from these goods would be similar to those estimated here (see Table 3). However, the quantities sent for waste management and losses to wastewater from use of brake fluid and other consumer/commercial products could be significantly higher if importation of these items were taken into consideration.

Table 3. Estimated losses of DTBSBP during its life cycle

Type of loss	Proportion (%)	Mass (kg)	Pertinent life cycle stages
Wastewater	3.9	644	Industrial use, and consumer/commercial use
Air emission	0.5	88	Industrial use
Land	0.2	32	Consumer/commercial use, and disposal
Chemical transformation	0.0	0.0	
Landfill	54.0	9010	Industrial use, consumer/commercial use, and disposal
Recycling	38.0	6338	Consumer/commercial use, and disposal
Incineration	1.6	276	Consumer/commercial use, and disposal
Export out of Canada	1.7	290	By industry

Environmental Fate

Based on its physical and chemical properties (Table 2a), the results of Level III fugacity modelling (Table 4) suggest that DTBSBP is expected to predominantly reside in sediment and air if released to air, in sediment if released to water, and in soil if released to soil.

The relatively high acid dissociation constant (pK_a) of 11.85 for the hydroxyl group of DTBSBP indicates that, in water bodies at environmentally relevant pH (6–9), nearly 100% of the substance will be undissociated. This indicates that biotic exposure in water will be from the neutral form of the substance. The relatively low proportion of dissociated chemical also indicates that partitioning behaviour predicted using the log K_{ow} and log K_{oc} is appropriate.

Based on the Mass Flow Tool results discussed in the Releases to the Environment section above, significant releases from industry and consumer uses to water are expected, with the air and soil compartments receiving small proportionate releases.

Table 4. Results of the Level III fugacity modelling (EQC 2003)

Substance released to:	Percentage of substance partitioning into each compartment (%)			
	Air	**Water**	**Soil**	**Sediment**
Air (100%)	36.4	2.04	7.70	53.9
Water (100%)	0.046	3.65	0.010	96.3
Soil (100%)	0.00	0.00	99.9	0.09
Equal releases to all three compartments	0.134	2.01	44.8	53.1

If released solely to air, 36.4% of the substance will remain in air, and the greatest proportion of the substance is predicted to partition to sediment from atmospheric deposition to water bodies (~54%; Table 4), with small amounts partitioning to soil and water. The moderate estimated vapour pressure of 0.35 Pa and Henry's Law constant (3.70 Pa·m^3/mol) indicate that DTBSBP is slightly volatile.

Based on its high estimated log K_{oc} value of 4.47, if released into water, DTBSBP is expected to adsorb strongly to suspended solids and sediment. 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, DTBSBP is expected to partition mainly into sediment (~96%).

Based on its high estimated log K_{oc}, if released to soil, DTBSBP will have high adsorptivity to soil (i.e., is expected to be immobile). Volatilization from moist soil surfaces will be a relatively unimportant fate process, based upon the substance's estimated Henry's Law constant. This chemical will slightly volatilize from dry soil surfaces, based upon its vapour pressure. Therefore, if released to soil, DTBSBP will remain there (~99.9%; Table 4).

If DTBSBP is released equally to air, water and soil, it will reside primarily in sediment and soil (Table 4).

Persistence and Bioaccumulation Potential

Environmental Persistence

Table 5a presents the empirical biodegradation data for DTBSBP. Since only one experimental study on the biodegradation of DTBSBP was available, a quantitative structure-activity relationship (QSAR) and analogue-based weight-of-evidence approach (Environment Canada 2007) was applied using the data shown in Tables 5b, 5c and 5d below.

Table 5a. Empirical data for degradation of DTBSBP

Test method	Fate process	Degradation value	Time (d)	Conclusion	Reference
MITI–I (OECD TG 301 C)	Aerobic	0 % BOD[1]	28	Not readily biodegradable	NITE 2002b

[1]BOD = biological oxygen demand

Modelled data for degradation of DTBSBP are presented in Table 5b. In air, a predicted atmospheric oxidation half-life value of 0.52 days demonstrates that DTBSBP is likely to be rapidly oxidized. The substance is not expected to react with other photo-oxidative species in the atmosphere, such as O_3. Therefore, it is expected that reactions with hydroxyl radicals will be the most important fate process in the atmosphere for DTBSBP. With a half-life of 0.52 days via reactions with hydroxyl radicals, DTBSBP is considered not persistent in air.

Empirical biodegradation data were identified for the analogue substances 2,4,6-tri-*tert*-butylphenol (CAS RN 732-26-3) and 2,6-di-*tert*-butyl-4-ethylphenol (CAS RN 4130-42-1) and are presented in Tables 5c and 5d below, respectively.

All models predicting ultimate biodegradation agree that DTBSBP will not biodegrade rapidly and is expected to have a half-life > 182 days (Table 5b) in water. These ultimate degradation results are consistent with the properties associated with the functional groups in the chemical structure of DTBSBP (*tert*-butyl). These results, predicting an ultimate degradation half-life of ≥ 182 days, are supported by the empirical data for the substance itself (Table 5a) and the analogue data (Tables 5c, d), which indicate that the analogue substances 2,4,6-tri-*tert*-butylphenol and 2,6-di-*tert*-butyl-4-ethylphenol do not readily biodegrade. Also, DTBSBP does not contain functional groups expected to undergo hydrolysis in water, and this substance contains structural features associated with chemicals that are persistent (i.e., – *tert*-butyl branches, benzene ring with more than two substituents and K_{ow} >3). Therefore, the substance's degradation half-life in water is expected to be ≥ 182 days. Thus, DTBSBP is considered to be persistent in water.

Using an extrapolation ratio of 1:1:4 for a water:soil:sediment biodegradation half-life (Boethling et al. 1995), the ultimate degradation half-life in soil is also > 182 days and the half-life in sediments is > 365 days. Therefore, DTBSBP is expected to be persistent in soil and sediment.

Table 5b. Estimated data for degradation of DTBSBP

Fate process	Model and model basis	Estimation from the model and prediction	Extrapolated half-life (days)
AIR			
Atmospheric oxidation	AOPWIN 2000[1]	$t_{1/2} = 0.52$ days (based on 12 h day; 1.56×10^{-6} OH/cm³)	< 2
Ozone reaction	AOPWIN 2000[1]	Not reactive	n/a
WATER			
Hydrolysis	HYDROWIN 2000[1]	n/a[2]	n/a
Biodegradation (aerobic)	BIOWIN 2000[1] Sub-model 3: Expert Survey (ultimate biodegradation)	2.2[3] (biodegrades slowly)	≥ 182
Biodegradation (aerobic)	BIOWIN 2000[1] Sub-model 4: Expert Survey (primary biodegradation)	3.1[3] (biodegrades fast)	< 182
Biodegradation (aerobic)	BIOWIN 2000[1] Sub-model 5: MITI linear probability	0.19[4] (biodegrades slowly)	≥ 182
Biodegradation (aerobic)	BIOWIN 2000[1] Sub-model 6: MITI non-linear probability	0.064[4] (biodegrades very slowly)	≥ 182
Biodegradation (aerobic)	TOPKAT 2004 Probability	0[4] (biodegrades very slowly)	≥ 182
Biodegradation (aerobic)	Canadian POPs Model (CPOPs 2008) % BOD (biological oxygen demand)	% BOD = 1.8 (biodegrades very slowly)	≥ 182

[1] EPI Suite (2008).
[2] Model does not provide an estimate for this type of structure.
[3] Output is a numerical score from 0 to 5.
[4] Output is a probability score.

Table 5c. Empirical data for biodegradation of 2,4,6-tri-*tert*-butylphenol

Test method	Fate process	Biodegradation value	Time (d)	Conclusion	Reference
MITI–I (OECD TG 301 C)	Aerobic	0% BOD[1]	28	Not readily biodegradable	NITE 2002a

[1]BOD = biological oxygen demand

Table 5d. Empirical data for biodegradation of 2,6-di-*tert*-butyl-4-ethylphenol

Medium/ Method	Fate process	Biodegradation value	Time (d)	Conclusion	Reference
MITI–I (OECD TG 301 C)	Aerobic	0% BOD[1]	28	Not readily biodegradable	NITE 2002c

[1]BOD = biological oxygen demand

Long-range Transport Potential

The Transport and Persistence Level III Model (TaPL3) (TaPL3 2000) was used to estimate the characteristic travel distance (CTD), defined as the maximum distance traveled in air by 63% of the substance. Beyer et al. (2000) have proposed CTDs of > 2000 km as representing high long-range atmospheric transport potential (LRATP), 700–2000 km as moderate LRATP, and < 700 km as low LRATP. Based on the CTD estimate of 259 km, the long-range atmospheric transport potential of DTBSBP is considered to be low. This means that DTBSBP is not expected to be transported through the atmosphere a significant distance from its emission sources.

The OECD Persistent Organic Pollutants (POPs) Screening Model can also be used to help identify chemicals with high persistence and long-range transport potential (Scheringer et al. 2006). The OECD model is a global model that compartmentalizes the earth into air, water and soil phases. This model is "transport-oriented" rather than "target-oriented," as it simply identifies the CTD without indicating specifically where a substance may be transported to (Fenner et al. 2005). Klasmeier et al. (2006) have suggested that a threshold of 5098 km, based on the model's CTD estimate for PCB-180, can be used to identify substances with high long-range transport potential. PCB-180 is empirically known to be found in remote regions. The CTD calculated for DTBSBP using the OECD model is 280 km, indicating that DTBSBP has low long-range-transport potential. The OECD POPs Screening Model also calculates the transfer efficiency (TE), which is the percentage of emission flux to air that is deposited to the surface (water and soil) in a remote region (TE % = D/E x 100, where E is the emission flux to air and D = the deposition flux to surface media in a target region). The TE for DTBSBP was calculated to be 3.9E-06%, which is well below the boundary of 4.65E-04% (PCB-28) established based on the model's reference substances empirically known to be deposited from air to soil or water. The low TE means that DTBSBP is unlikely to be deposited to Earth's surface in any remote region.

It is therefore concluded that DTBSBP does not have the potential to be transported over long distances in the atmosphere. It is expected that airborne DTBSBP that is not transferred to water or soil will be degraded by hydroxyl radicals in air.

Thus, the empirical, analogue and modelled data (Tables 5a, 5b, 5c and 5d) demonstrate that DTBSBP meets the persistence criteria in water, soil and sediment (half-lives in soil and water ≥ 182 days and half-life in sediment ≥ 365 days), but does not meet the criteria for persistence in air (half-life criteria of ≥ 2 days) as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Potential for Bioaccumulation

When considered alone, the log K_{ow} value of 6.1 (Table 2a) suggests that DTBSBP could have the potential to be highly bioaccumulated in the environment. However, log Kow on its own does not take into account factors that mitigate bioaccumulation (e.g., metabolism). These factors are considered further in the evaluation of bioaccumulation potential below.

Since no experimental bioaccumulation data for DTBSBP were available, a QSAR and analogue weight-of-evidence approach (Environment Canada 2007) was applied using available analogue data and bioaccumulation factor (BAF) and bioconcentration factor (BCF) models as shown in Tables 6a, 6b, 6c and 6d below. Table 6a presents the empirical bioconcentration factor (BCF) for the analogue substances. No other empirical BCF data were found for these substances.

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Table 6a. Empirical data for bioconcentration of analogue substances

Substance	Test organism	Test duration	BCF value wet weight (L/kg)	Reference
2,4,6-tri-*tert*-butylphenol	Carp (*Cyprinus carpio*)	8 weeks	4830–16 000 (exposed to 10 µg/L)[1] 4320–23 200 (exposed to 1 µg/L)[1]	CERI 2009a
2,6-di-*tert*-butyl-4-ethylphenol	Rice fish (*Oryzias latipes)*	8 weeks	1420–5060 (exposed to 10 µg/L) 930–4870 (exposed to 1 µg/L)	CERI 2009b

[1] The surfactant HCO-40 was used in the test water to increase the solubility of the test substance. Therefore, the BCF values may indicate greater bioavailability than under environmental conditions. The upper BCFs reported are thus regarded as a "worst-case" estimate of bioconcentration.

The empirical data in Table 6a indicate that the analogue substances 2,4,6-tri-*tert*-butylphenol and 2,6-di-*tert*-butyl-4-ethylphenol bioconcentrate in fish tissues to a high degree, with 2,4,6-tri-*tert*-butylphenol appearing to be more bioaccumulative than 2,6-di-*tert*-butyl-4-ethylphenol. This is expected, given that 2,4,6-tri-*tert*-butylphenol has a higher measured log K_{ow} value of 6.06 (NITE 2002a) than the predicted logK_{ow} value of 5.52 for 2,6-di-*tert*-butyl-4-ethylphenol (no measured K_{ow} value was found for this substance) and both are expected to have similar rates of biotransformation and elimination.

Mass balance BCF and BAF estimates for the analogue substances, corrected for potential biotransformation, were generated using the BCFBAF model (EPI Suite 2008), and are shown in Table 6b. The mean BCF values from Table 6a were used to derive the *in vivo*-based metabolic rate constants (k_M) according to the method of Arnot et al. (2008a). Since metabolic potential can be related to body weight and temperature (Hu and Layton 2001, Nichols et al. 2007), the BCFBAF (2008) model further normalizes the k_M for a 10g fish at 15°C to the body weight of the middle trophic level fish in the Arnot-

Gobas model (184 g) (Arnot et al. 2008b). The middle trophic level fish was used to represent overall model output as suggested by the model developer and is most representative of fish weight likely to be consumed by an avian or terrestrial piscivore.

Table 6b. Mass-Balance BAF and BCF predictions for analogue substances using the BCFBAF (2008) model

Substance	Endpoint	Value wet weight (L/kg)
2,4,6-tri-*tert*-butylphenol	BCF	14 050
	BAF	324 700
2,6-di-*tert*-butyl-4-ethylphenol	BCF	3119
	BAF	7534

The Arnot-Gobas (2003) modelled BCF values for the analogue substances shown in Table 6b, which are corrected for metabolism, are in good agreement with the empirical data (Table 6a). Therefore, this model seems to produce good results for this type of substance (hindered phenol).

It should be noted that the structure and molecular weight of 2,4,6-tri-*tert*-butylphenol are more similar to DTBSBP than those of 2,6-di-*tert*-butyl-4-ethylphenol. As well, the measured log K_{ow} value of 2,4,6-tri-*tert*-butylphenol is more similar to the KOWWIN predicted log K_{ow} value of 6.43 (non-adjusted) for DTBSBP (see Table 2a) than that of 2,6-di-*tert*-butyl-4-ethylphenol. Therefore, 2,4,6-tri-*tert*-butylphenol seems to be the better analogue of the two substances discussed here, and therefore, DTBSBP would be expected to bioconcentrate in fish tissues to a similar extent as 2,4,6-tri-*tert*-butylphenol.

According to the *Persistence and Bioaccumulation Regulations* (Canada 2000) a substance is bioaccumulative if its BCF or BAF is $\geq$ 5000; however measures of BAF are the preferred metric for assessing bioaccumulation potential of substances. This is because BCF may not adequately account for the bioaccumulation potential of substances via the diet, which predominates for substances with log K_{ow} > ~4.0 (Arnot and Gobas 2003). Kinetic mass-balance modelling is in principle considered to provide the most reliable prediction method for determining the bioaccumulation potential because it allows for correction for metabolic transformation as long as the log K_{ow} of the substance is within the log K_{ow} domain of the model, which is the case for DTBSBP and the analogue substances.

The geometric mean of the highest BCF range (4320–23 200 L/kg) for analogue substance 2,4,6-tri-*tert*-butylphenol from Table 6a, which is equal to 10 011 L/kg, was used to derive the median *in vivo*-based metabolic rate constant (k_M) according to the method of Arnot et al. (2008a). This metabolic rate constant, as well as the predicted

adjusted log K_{ow} value for DTBSBP of 6.1 (Table 2a), was used to estimate metabolism-corrected BCF and BAF values for DTBSBP, as shown in Table 6c.

Because metabolic potential can be related to body weight and temperature (e.g., Hu and Layton 2001; Nichols et al. 2007), the k_M was further normalized to 15°C and then corrected for the body weight of the middle trophic level fish in the Arnot-Gobas model (184 g) as explained previously (Arnot et al. 2008b). After normalization routines, the median k_M was calculated to be 0.001 (Table 6c).

Table 6c. Middle Trophic Level Fish Mass-Balance BAF and BCF predictions for DTBSBP using the 2003 Arnot-Gobas kinetic model corrected for metabolic rate

Metabolic rate constant k_M (1/days)	LogK_{ow} used	BCF (L/kg)	BAF (L/kg)	Reference
0.0044 (median)	6.1	15 135	407 380	Arnot and Gobas 2003
k_M = 0 (default)	6.1	26 303	1 202 264	

The median metabolism-corrected BCF value for DTBSBP is 15 135 L/kg (Table 6c). The geometric mean of the steady-state BCF range reported in Japan's National Institute of Technology and Evaluation (NITE) database for 2,4,6-tri-*tert*-butylphenol is 10 011 L/kg, which is consistent with the above value for DTBSBP. The BAF for DTBSBP calculated using this metabolism value is 407 380 L/kg (Table 6c). This value is also in good agreement with the predicted BAF of 2,4,6-tri-*tert*-butylphenol of 324 700 L/kg (Table 6b).

Additional modelled BCF data for DTBSBP are given in Table 6d. The models employed in Table 6d use linear regression methods based on log K_{OW} to derive the BCFs. All of the modelled data are considered valid, as the model output indicates that DTBSBP is within the domains of the models. In the Dimitrov model, DTBSBP is modelled as part of the "phenols and anilines" class, and in BCFBAF model, it is modelled as a "*tert*-butyl ortho-phenol type." The OECD (2008) prediction was obtained using the OECD QSAR Application Toolbox (v. 1.1.02). Chemicals from the phenols class with ≥90% similarity to DTBSBP, and that had BCF studies of 28 days in length or greater were used to generate the QSAR. Eleven substances from the phenols class met the above criteria. The resulting BCF prediction equation is: BCF[log(L/kg wet)] = -0.979 + 0.768*log K_{OW} (EPI Suite). There was no BAF data for similar substances within the OECD (2008) Toolbox, so a prediction for BAF was not possible.

Table 6d. Additional predicted BCF data for DTBSBP

Test organism	BCF value wet weight (L/kg)	Reference
Fish	2766	Dimitrov et al. 2005
Fish	2950	BCFBAF 2008, linear regression sub-program
Fish	9050[1]	OECD QSAR (2008)

1 – 95% fiduciary limits: 722-1.13 x10^5 L/kg

A weight-of-evidence approach was used to determine whether DTBSBP meets the bioaccumulation criteria (BCF, BAF ≥ 5000) as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000). The high K_{ow} value of DTBSBP (log K_{ow} = 6.1) indicates that bioaccumulation in fish is expected to be primarily through the diet rather than through uptake through the gills. Therefore, more weight was given to the bioaccumulation (BAF) data than the bioconcentration (BCF) data. The modelled BAF data indicate that DTBSBP is likely to be highly bioaccumulative (see Table 6b). The BCF values obtained with the Arnot-Gobas model (Tables 6b and 6c), as well as the empirical analogue BCF data (Table 6a) also indicate that DTBSBP is highly bioaccumulative. The Arnot-Gobas (2003) model (Table 6b) was shown to be a good predictor of the empirical BCF data for the analogue substances (Table 6a). Therefore, more weight is given to the results of the Arnot-Gobas model than to the results of the other BCF models in Table 6d), which produced lower BCF values (< 5000). The OECD (2008) QSAR Application Toolbox also produced a BCF result for DTBSBP of greater than 5000. This prediction takes into account the inherent biotransformation potential of this class of substances under experimental tests conditions.

Considering the above data, it is concluded that DTBSBP meets the bioaccumulation criteria (BCF, BAF ≥ 5000) as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Potential to Cause Ecological Harm

Ecological Effects Assessment

A – In the Aquatic Compartment

There are no experimental data available for the aquatic toxicity of DTBSBP; therefore, modelled and analogue data were used to estimate the potential for aquatic toxicity using a weight-of evidence-approach (Environment Canada 2007). Table 7a contains predicted ecotoxicity values, and Table 7b contains empirical data for the analogue 2,4,6-tri-*tert*-butylphenol that were considered reliable. No empirical aquatic toxicity data were found for the analogue 2,6-di-*tert*-butyl-4-ethylphenol. The reliability of the empirical toxicity data is based on the quality of the studies as determined by robust study summaries, which are included in Appendix I.

Table 7a contains toxicity predictions for DTBSBP modelled as a phenol rather than as a neutral organic. However, the predictions for DTBSBP modelled as a neutral organic in ECOSAR are very similar to the ECOSAR values modelled as a phenol found in Table 7a. All of the modelled toxicity predictions are within the applicability domains of the models, as none of the maximum K_{ow} and molecular weight cut-off values specified in ECOSAR (2004) were exceeded. In addition, the predictions are all below the estimated water solubility of the substance, with the exception of the earthworm prediction. Therefore, no effects at saturation are predicted for the earthworm (ECOSAR 2004).

The OECD (2008) fish toxicity prediction in Table 7a was obtained using the OECD QSAR Application Toolbox (v. 1.1.02). To generate this prediction, fathead minnow 96 hour toxicity data for substances from the Phenols and Anilines class were considered, which was further refined to just include phenols. This class was again refined to only consider substances not predicted to be protein or estrogen receptor (ER) binders, since DTBSBP was also predicted not to be a protein or ER binder, based on its structure (OECD 2008). Twenty-eight substances met the above criteria. The resulting LC_{50} prediction equation is: LC50 [log(1/mol/L)] = 2.44 + 0.666*Log K_{OW} (EPI Suite).

Table 7a. Modelled data for aquatic toxicity of DTBSBP

Test organism	Type of test	Endpoint	Value (mg/L)	Reference
Fish	Acute (96 hours)	LC_{50}[1]	0.039	ECOSAR 2004
			0.15	CPOPs 2008
			0.10	AIEPS 2003–2007
			0.05[4]	OECD (2008)
	Chronic (60 days)	EC_{50}[2]	0.007	ECOSAR 2004
Water flea *(Daphnia)*	Acute (96 hours)	EC_{50}[2]	0.065	ECOSAR 2004
			0.015	TOPKAT 2008
			0.93	CPOPs 2008
	Chronic (21 days)	EC_{50}[2]	0.012	ECOSAR 2004
Algae	Acute (96 hours)	EC_{50}[2]	0.20	ECOSAR 2004
	Chronic[3]	EC_{50}[2]	0.09	ECOSAR 2004
Earthworm	Chronic (14 days)	LC_{50}[1]	5.1[5]	ECOSAR 2004

[1] LC_{50} – The concentration of a substance that is estimated to be lethal to 50% of the test organisms.
[2] EC_{50} – The concentration of a substance that is estimated to cause some effect in 50% of the test organisms.
[3] No exact time period specified for this value.
[4] 95% fiduciary limits: 1.65×10^{-3} to 1.50 mg/L
[4] Prediction exceeds the water solubility of the substance. Therefore, no effects are predicted at saturation.

Table 7b. Empirical data for aquatic toxicity of 2,4,6-tri-*tert*-butylphenol

Test organism	Type of test	Endpoint	Value (mg/L)	Reference
Algae *(Selenastrum capriconutum)*	Chronic (72 hours)	IC_{50}[1] (growth rate) NOEC[4]	> 0.32 0.32	NITE 2002a
Water flea *(Daphnia magna)*	Acute (48 hours)	LC_{50}[2]	0.11	NITE 2002a
	Chronic (21 days)	EC_{50}[3] NOEC[4] (reproduction)	2.2 0.36	NITE 2002a
Fish *(Oryzias latipes)*	Acute (48 hours)	LC_{50}[2]	> 10	NITE 2002a; CITI 1992
Fish *(Pimephales promelas)*	Acute (96 hours)	LC_{50}[2]	0.06	Geiger et al. 1990

[1] IC_{50} – The inhibiting concentration for a specified percent effect. A point estimate of the concentration of a test substance that causes a 50% reduction in a quantitative biological measurement such as growth rate.
[2] LC_{50} – The concentration of a substance that is estimated to be lethal to 50% of the test organisms.
[3] EC_{50} – The concentration of a substance that is estimated to cause some effect on 50% of the test organisms.

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[4] NOEC – The No-observed-effect concentration is the highest concentration in a toxicity test not causing a statistically significant effect in comparison to the controls.

The measured analogue toxicity values (Table 7b) seem to generally support the modelled toxicity values for DTBSBP (Table 7a).

Based on the above modelled and analogue data, there is evidence that DTBSBP has the potential to cause harm to aquatic organisms following short-term (acute) and longer-term (chronic) exposure at relatively low concentrations (i.e., acute $LC/EC_{50} \le 1.0$ mg/L and/or chronic LC/EC_{50} or NOEC ≤ 0.1 mg/L).

B - In Other Environmental Compartments

No ecological effects studies were found for DTBSBP in any media. Mammalian data were found and considered in the Potential to Cause Harm to Human Health section of this report. One model prediction for earthworm was available, and is included in Table 7a, which indicates no effects at saturation. As such, effect levels for this substance have not been estimated for soil and sediment. However, DTBSBP could end up in these media as a result of releases to the aquatic environment, landfill disposal of sludge from wastewater treatment plants, disposal of products containing these substances, or sludge application to soils.

Ecological Exposure Assessment

No environmental monitoring data from Canada or elsewhere were found for DTBSBP.

Characterization of Ecological Risk

The approach taken in this ecological screening assessment was to examine all of the available information and develop conclusions based on a weight-of-evidence approach and using precaution as required under CEPA 1999. Lines of evidence considered included information on persistence, bioaccumulation, toxicity, sources and fate of this substance.

Based on empirical, modelled and analogue data, DTBSBP is expected to be persistent in water, soil and sediment. It is also expected to have a high bioaccumulation potential and high potential for toxicity to aquatic organisms based on analogue and modelled data.

The importation volume of DTBSBP into Canada (16 686 kg in 2006), along with information on its industrial and consumer uses, indicates the potential for widespread and point-source releases into the Canadian environment, including an estimated 623 kg to wastewater (see Releases to the Environment section). DTBSBP is expected to be

released mainly to water (Table 3), though it is expected to reside in sediment as well (Table 4).

Evidence that a substance is highly persistent and bioaccumulative as defined in the *Persistence and Bioaccumulation Regulations* of CEPA 1999 (Canada 2000), when taken together with potential for environmental release or formation and potential for toxicity to organisms, provides a significant indication that it may be entering the environment under conditions that may have harmful long-term ecological effects. 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.

Given the information on the amount of DTBSBP that is imported into Canada and on the nature of its reported industrial and consumer uses, there is potential for release of this substance into the Canadian environment. Once released in the environment, because of its resistance to degradation, it will remain in water, sediment and soil for long times. As it persists in the environment, and because of its lipophilic character, it will likely bioaccumulate and may be biomagnified in trophic food chains. It has also demonstrated potential for relatively high toxicity. This information indicates that DTBSBP has the potential to cause ecological harm in Canada.

Uncertainties in Evaluation of Ecological Risk

In general, DTBSBP is a data-poor substance. There are very few measured physical and chemical property data, and no measured data on its bioaccumulation or toxicity were found. However, a close analogue substance with measured data was found (2,4,6-tri-*tert*-butylphenol), and these data were found to agree well with the predicted data for DTBSBP. DTBSBP as a neutral organic phenol is also well covered in the training sets of models (neutral organics), and thus predictions of persistence, bioaccumulation and ecotoxicity are considered reliable.

There is uncertainty regarding the risk that DTBSBP may pose now or in the future. Typically quantitative risk estimates (i.e., risk quotients or probabilistic analyses) are important lines of evidence when evaluating a substance's potential to cause environmental harm. However, when risks for persistent and bioaccumulative substances such as DTBSBP are estimated using such quantitative methods, they are highly uncertain and are likely to be underestimated. 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 is justified.

Also, regarding ecotoxicity, based on the predicted partitioning behaviour of this chemical, the significance of soil and sediment as important media of exposure is not well addressed by the effects data available. Indeed, the only effects data identified apply to pelagic aquatic exposures, although the water column is not the only medium of concern based on partitioning estimates.

Given the use of DTBSBP in other countries such as the U.S., it is possible that this substance is entering the Canadian market as a component of manufactured items and consumer products. Therefore, quantities of DTBSBP released to the various environmental media are likely higher than those estimated here. It is also recognized that releases from recycling and waste disposal sites may be possible and may contribute to the overall environmental concentration. However, available information is currently not sufficient to derive a quantitative estimate for these releases.

Potential to Cause Harm to Human Health

Exposure Assessment

In the published literature, there were no empirical data identified regarding measured concentrations of DTBSBP in environmental media in Canada (air, water, soil and sediment) or elsewhere. In responses to a notice issued under section 71 of CEPA 1999, there were no reported releases of DTBSBP to air, water or soil (Environment Canada 2009a).

No studies were identified reporting the presence of DTBSBP in food. DTBSBP has been approved by the U.S. Food and Drug Administration for use as an antioxidant in plasticized PVC for food packaging (US FDA 2008). Plasticized PVC may be used in films for wrapping fresh and frozen meat and produce. A conservative DTBSBP probable daily intake (PDI) of 0.0581 µg/kg-bw was estimated assuming that some plasticized PVC films may be used for wrapping meat (March 2009 email from Food Directorate, Health Canada, to Risk Management Bureau, Health Canada; unreferenced). In the case of using PVC films for wrapping produce, a PDI was not considered because its value is expected to be much lower in comparison (about 10 000 times lower) to that for the use of PVC films for wrapping meat.

DTBSBP is also used as an antioxidant in plastic hoses used in the Canadian food industry (March 2009 email from Food Directorate, Health Canada, to Risk Management Bureau, Health Canada; unreferenced). These plastic hoses are employed to transfer food during processing and packaging and are intended to be used in contact with all kinds of foods. A PDI for DTBSBP of 0.36×10^{-6} ng/kg-bw was derived, taking into

consideration that the hose was a repeated-use article (March 2009 email from Food Directorate, Health Canada, to Risk Management Bureau, Health Canada; unreferenced). The contribution of this source to the total intake is considered to be negligible.

Overall confidence in the exposure characterization for environmental media and dietary intake is considered to be low. There is uncertainty in the exposure to DTBSBP from environmental media in Canada, as no information is available; however, based on the conservative assumptions modelled for exposure from the potential use of plasticized PVC films in food packaging, it is expected that exposure to DTBSBP through dietary intake, if any, in Canada is very low.

In Canada, DTBSBP is used in the manufacture of plastics foam products (not including polystyrene), such as flexible polyurethane foams (Canada 2006b; Canada 2009b). It is also used in the manufacture of PVC (SI Group 2009b). According to laboratory testing, DTBSBP is not extractable from rigid PVC (SI Group 2009b); therefore exposure to this substance in rigid PVC-associated applications is expected to be negligible. Flexible PVC containing DTBSBP may be used in plastic hoses in the food industry, and exposure to this substance in this application was also shown to be negligible (see previous section). Thus, exposure to DTBSBP via usage of consumer items was examined by considering its presence in foam products.

Canadian consumer use of flexible foams lies in three major markets: bedding, furniture and transportation (Chinn et al. 2006). Flexible foam is used for cushioning in these applications, and in interior trim materials in transportation vehicles (Meyer-Ahrens 2005). DTBSBP is a substitute in the foam industry for BHT, a solid-form antioxidant that is structurally similar (see Figure 1), because DTBSBP is a liquid and less volatile, making it easier to handle in industrial applications (SI Group 2009b).
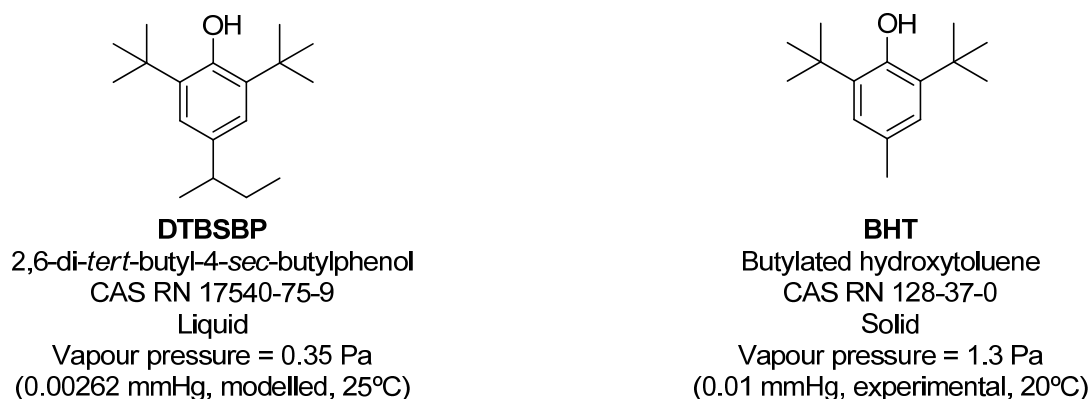

DTBSBP
2,6-di-*tert*-butyl-4-*sec*-butylphenol
CAS RN 17540-75-9
Liquid
Vapour pressure = 0.35 Pa
(0.00262 mmHg, modelled, 25ºC)

BHT
Butylated hydroxytoluene
CAS RN 128-37-0
Solid
Vapour pressure = 1.3 Pa
(0.01 mmHg, experimental, 20ºC)

Figure 1. Comparison of structurally similar antioxidants, DTBSBP and BHT

No data were identified with regard to the loss of DTBSBP from mattresses, furniture foam and automotive interiors. Since the volatility of DTBSBP is lower than that of BHT, studies that investigated the volatilization loss of BHT from foam mattresses and auto interior trim were considered in this assessment to screen the upper level of potential

inhalation exposure to DTBSBP. Direct skin contact with the actual foam material inside mattresses, furniture and automotive interior foam is rare for the general population; therefore dermal exposure, if any, was considered to be negligible.

An investigation into volatile emissions from foam mattresses found BHT emissions from one of five fresh foam mattress samples (Hillier et al. 2003). The authors did not state if DTBSBP was screened in this study. Since DTBSBP is a less volatile substitute than BHT, as a conservative approach, the extrapolated concentration of BHT is taken as the upper limit of DTBSBP atmospheric concentration from foam mattress emissions. Considering an upper-bound-scenario whereby the maximum potential atmospheric concentration of DTBSBP ($2.02 \ \mu g/m^3$) persists continually, the maximum potential inhalation chronic dose was calculated to be 0.178 μg/kg-bw per day for the 0.5–4 years age group (refer to Appendix III).

Potential volatile emissions from foam-filled furniture were also estimated and resulted in a mean event concentration of 2.69 μg DTBSBP/m^3 and a maximum potential inhalation chronic dose of 0.872 μg DTBSBP/kg-bw per day (0.5–4 years age group) as an upper-bounding scenario (refer to Appendix III). While the representativeness of a "standardised mattress" for the quantity of foam in household furniture is unknown, the extrapolated BHT exposure values can still be expected to overestimate the maximum potential exposure to DTBSBP from household furniture because DTBSBP is less volatile than BHT.

Flexible polyurethane foam is used for headlining and auto seat cushioning in transportation vehicles (ISOPA 2005). A study of volatile emissions from polymeric materials used as automotive interior trim (Loock et al. 1993) detected BHT, and the emission rate was derived at 90ºC to be 12.8 μg per gram of polyurethane foam per hour. The authors did not state if they screened for DTBSBP. Considering this emission rate of BHT, the fact that emission rates would be lower at temperatures below the experimental temperature, a quantity of 15 kg of polyurethane in a typical medium-sized car (ISOPA 2005) and the lower volatility of DTBSBP compared to that of BHT, potential inhalation exposure to DTBSBP emissions from automotive interior trim is reasoned to be minimal (refer to Appendix III).

Although direct skin contact with the actual foam materials (e.g., inside mattresses) is rare for the general population, a conservative approach was used when considering exposure for infants and toddlers. In fact, oral exposure may result from mouthing activities on foam objects, such as toys, packaging and children's furniture (Norris and Smith 2002). While it is uncertain whether DTBSBP is contained in common foam objects mouthed by toddlers and infants, a conservative approach to consider possible oral exposure is necessary in order to ensure consideration of this younger demographic, since foam is a common material for toys and packaging. Since the mouthing behaviour of infants on soft furnishings and other foam objects is well documented (Norris and Smith 2002), an exposure scenario of infants and toddlers mouthing foam objects was considered. Following the method used in VCCEP (Voluntary Children's Chemical Evaluation Program) assessments to estimate oral exposure via mouthing of foam

(Environ 2003a, 2003b), the maximum potential intake was estimated to be 6.52×10^{-4} mg/kg-bw per day for infants and 3.16×10^{-4} mg/kg-bw per day for toddlers (refer to Appendix III). Another method was considered to approximate oral exposure from mouthing foam objects and yielded similar estimated exposure values: 2.17×10^{-4} mg/kg-bw per day for infants and 1.05×10^{-4} mg/kg-bw per day for toddlers (refer to Appendix III).

Confidence in the numerical results of the exposure estimations is low in the absence of experimental data for DTBSBP. The estimations presented are likely to be overestimates, as they are based on conservative assumptions and derived from experimental data on the structurally similar and more volatile antioxidant, BHT, to screen the upper level of exposure. As a result, there is confidence that the exposure estimates are conservative upper-bounding estimates.

Health Effects Assessment

DTBSBP was negative in *in vitro* mutagenicity assays in *E. coli* strain WP2 uvrA or *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538, with or without metabolic activation, and was negative for chromosomal aberrations in Chinese hamster ovary cells with or without metabolic activation (SII 2002).The available toxicity data indicate low acute toxicity for DTBSBP, with an oral LD_{50} of 4800 mg/kg bw in rats (Springborn Laboratories, Inc. 1980). The outputs of predictive models, as summarized in Appendix V, were also considered using four different QSAR models—DEREK, TOPKAT, CASETOX and Leadscope Model Applier—for which the predictions for carcinogenicity, genotoxicity, and developmental and reproductive toxicity were predominately negative (DEREK 2008; TOPKAT 2008; CASETOX 2008; Leadscope 2009).

For this assessment, data on several analogue substances (Appendix IV) were examined to inform the understanding of the potential health effects associated with exposures to DTBSBP.

Data were available from several analogues for toxicological endpoints including carcinogenicity; genotoxicity; reproductive and developmental toxicity; and chronic, sub-chronic and acute toxicity as shown in Appendix IV. Genotoxicity data for CAS 4130-42-1, phenol, 2,6-bis(1,1-dimethylethyl)-4-ethyl-, was negative in *E. coli* strain WP2 pkm101 and *S. typhimurium* strains TA97, TA98, TA100 and TA102, with or without metabolic activation (Hachiya and Takizawa 1994). Similarly, CAS 2416-94-6 and CAS 128-39-2 were also negative for gene mutations in *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 with or without metabolic activation. Additionally, CAS 128-39-2 was also negative in *E. coli* with and without metabolic activation and did not induce chromosomal aberrations in Chinese hamster V79 cells with and without activation (US EPA 2009a).

Chronic toxicity data for analogue CAS 732-26-3, TTBP, showed no statistically significant increased incidence of tumours compared to controls in a 24-month feeding study in male and female rats exposed to 0, 30, 100, 300 or 1000 ppm of TTBP. In the same study, no non-neoplastic effects were observed at 30 ppm (equivalent to 1.5 mg/kg-bw/day; based on Health Canada 1994) (Matsumoto et al. 1991). Effects included increased liver weights and increased platelet count, phospholipids and total cholesterol at 100 ppm and higher.

In a 28-day study administering the analogue CAS 128-39-2, 2,6-di-*tert*-butylphenol, to Wistar rats via gavage at 0, 15, 100 or 600 mg/kg-bw/day, no effects were observed at 100 mg/kg bw/day; however at 600 mg/kg-bw/day, increased liver weight in males and females was observed with a slight increase in the incidence of hepatocellular hypertrophy in the centrilobular area in both sexes and eosinophilic inclusions in the renal cortex of males (US EPA 2009a).

In a combined reproductive and developmental toxicity screening test conducted with analogue CAS 128-39-2, 2,6-di-*tert*-butylphenol, Wistar rats were administered 0, 30, 150 or 750 mg/kg-bw/day of the substance by gavage. At 150 mg/kg-bw/day no adult systemic and developmental toxicity were observed. At 750 mg/kg-bw/day, there were marginal effects on body weight in adults and reduced viability and weight gain in the pups. No reproductive effects were observed at the exposure levels tested (US EPA 2009a).

In a short-term study, male beagle dogs were fed 0, 49.2, 173 or 454 mg/kg-bw/day of TTBP (CAS 732-26-3) for 11 days. At the highest dose tested (454 mg/kg-bw/day), the dogs showed signs of behavioural abnormalities and increased glutamic-oxalacetic transaminase (GOT), glutamic-pyruvic transaminase (GPT) and alkaline phosphatase (ALP). The lowest-observed-effect level (LOEL) of 173 mg/kg-bw/day was established based on diarrhea, and blood in the feces was observed at both the mid and low doses of 173 and 454 mg/kg-bw/day respectively (Anonymous 1987). In addition, a dermal LD$_{50}$ of greater than 1000 mg/kg-bw/day in rats was reported for analogue, 2,6-di-*tert*-butylphenol,CAS 128-39-2.

Another analogue identified, CAS 128-37-0 BHT, has been considered by the Organisation for Economic Co-operation and Development's HPV Chemicals Programme (2002) and was determined not to be a genotoxic carcinogen, and a threshold level of 100 mg/kg-bw/day was established for the possible carcinogenic and tumour-promoting effects of BHT (OECD 2004c).

Characterization of Risk to Human Health

Inhalation of DTBSBP from consumer products is the main estimated route of exposure for the general population. However, health effects data available for DTBSBP and its analogue substances were conducted via the oral route. Therefore daily intake was estimated from predicted air concentrations for the characterization of risk. Comparison

of the chronic no-observed-effects level (NOEL) of 30 ppm (1.5 mg/kg-bw per day) for the TTBP analogue (CAS RN 732-26-3) via oral exposure with the upper-bounding estimate of daily intake of DTBSBP by toddlers through inhalation exposure of volatile emissions from foam-filled furniture (8.72×10^{-4} mg/kg-bw per day) results in a margin of exposure of approximately 1720. No health effects studies via a similar comparison using the chronic NOEL of 30 ppm for the TTBP analogue (CAS RN 732-26-3) with the estimated probable daily intake (PDI = 0.0581 μg/kg-bw) due to potential migration of DTBSBP from meat and produce plastic packaging yields a margin of exposure of approximately 25 800. Based on the information available, it is considered that the estimated margins of exposure are considered adequate to protect human health.

Uncertainties in Evaluation of Risk to Human Health

Due to the limited data available for DTBSBP, the confidence in the toxicological dataset is considered to be low; however, data from analogue substances were available to address data gaps. There is uncertainty surrounding the extrapolation of data on analogous substances to predict the health effects of DTBSBP, as it is possible that other characteristics specific to each substance may influence their toxic potential. In addition, no studies conducted via the inhalation route of exposure were available.

There is uncertainty in the exposure estimation of DTBSBP from environmental media, dietary intake (i.e. migration from food packaging) and consumer products due to the limited information available. However, estimations are based on conservative assumptions and thus considered to be conservative upper-bounding estimates.

Conclusion

Based on the information presented in this final screening assessment, it is concluded that DTBSBP is entering or may be entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity.

Based on the information presented in this final screening assessment, it is concluded that DTBSBP 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 DTBSBP meets one or more criteria under section 64 of CEPA 1999. Additionally, DTBSBP meets the criteria for persistence and bioaccumulation as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

This substance will be considered for inclusion in the Domestic Substances List inventory update initiative. In addition and where relevant, research and monitoring will support

verification of assumptions used during the screening assessment and, where appropriate, the performance of potential control measures identified during the risk management phase.

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Appendix I - Robust Study Summaries for Aquatic Toxicity of 2,4,6-tri-*tert*-butylphenol

Item	Yes	No
Reference: Biodegradation and bioaccumulation data of existing chemicals based on the CSCL Japan, 1992. Chemicals Inspection and Testing Institute (Ed.). Published by: Japan Chemical Industry Ecology-Toxicology & Information Center. **Note**: Evaluation is based on both the MITI book (1992) and additional information on ecotoxicological tests, which is available on the website of the Institute.		
Test Substance: CAS RN and name: Generic for all CAS RNs assessed using MITI (1992) methodology		
* Substance purity reported? (Y/N **and** specify)		**X**
Persistence/stability of test substance in aquatic solution reported? (Y/N)		**X**
Method		
References (Y/N)	**X**	
*OECD, EU, national, or other standard method? (Y/N) Japanese Industrial Standard (JIS K 0102-1986-71) entitled "Testing methods for industrial waste water"	**X**	
If not a standard method, justification of the method/protocol provided? (Y/N)	**N/A**	
*GLP (Good Laboratory Practice) (Y/N) (note: if study prior to 1997, N/A). Study performed before 1997.	**N/A**	
Test organisms (specify common and/or Latin names)		
Latin or both Latin and common names reported? (Y/N) Orange-red killifish (*Oryzias latipes*)	**X**	
Life cycle age / stage of test organism (Y/N)		**X**
Sex (Y/N) Not applicable since the age / size of fish is quite small, which does not significantly affect the results of the test	**N/A**	
Length and/or weight of test organisms (Y/N) 2.3 ± 1.2 cm	**X**	
Number of test organisms per replicate (Y/N) at least 7 fish for each of test concentration and control	**X**	
Food type / feeding periods (acclimation / during test) (Y/N) Fish were not fed during the test, and acclimatized to test water for at least 7 days.	**X**	
Test design/conditions		
Test type – acute or chronic: acute		
Experiment type (laboratory or field) specified? (Y/N) Laboratory	**X**	
System type (static, semi-static, flow-through) (Y/N) Static or semi-static	**X**	
Negative or positive controls? (Y/N **and** specify) Negative control	**X**	
Number of replicates (including controls) and concentrations (Y/N) At least 5 concentrations that are set up in a geometric progression, preferably at a geometric ratio of within 2.2. Number of replicates not mentioned.	**½**	
Exposure pathways (food, water, both) (Y/N) Water	**X**	
Exposure duration (Y/N **and** specify) 48 hours	**X**	
*Measured concentrations reported? (Y/N) At the beginning and end of the exposure, measure the test substance concentrations at least in the lowest and highest test concentration groups.	**X**	
Exposure media conditions (temperature, pH, electrical conductivity, hardness, TOC,	**X**	

DOC, DO, major cations and anions; other) (Y/N) pH, dissolved oxygen concentration and water temperature at least once daily		
Was pH within 6–9 range? Natural water (surface water or groundwater), de-chlorinated tap water or artificially prepared water. The recommended total hardness was 10–250 mg/L in terms of calcium carbonate concentration, and the recommended pH was 6.0–8.5.	X	
Was temperature within 5–28°C range? Recommended 21 to 25°C	X	
Photoperiod and light intensity (Y/N) The photoperiod is set to 12–16 hr light per day	X	
Stock and test solution preparation (Y/N) Directly dissolve the required amount of the test substance in the material water, or prepare a stock solution of the test substance at an appropriate concentration and dilute it with the material water.	X	
Information on emulsifiers used for poorly soluble / unstable substances (Y/N) Not used	N/A	
Analytical monitoring intervals (Y/N)	X	
Statistical methods used (Y/N) Doudoroff or PROBIT method	X	
Results		
Toxicity endpoints/values/units: 48-h LC_{50}		
Other endpoints reported (e.g., BCF/BAF, LOEC/NOEC, etc.): BCF (evaluated separately)		
*Was toxicity value below the chemical's water solubility? (Y/N) See note below for sparingly soluble substances.		X
Other adverse effects (carcinogenicity, mutagenicity, etc.)		X
Score: major items – **2/4**; overall score: 17.5/22 = **80%**		
*Environment Canada Reliability code***:** 1 to 2 (For sparingly-soluble: 2 to 3 – see note below)		
Reliability category (high, satisfactory, low): Satisfactory to high (for sparingly soluble: satisfactory to low)		

Comments: **Important for sparingly-soluble substances:**

There is an important lack of information on how the water sample for chemical analysis was processed. For example, was centrifugation or filtration used? What was the analytical approach used to measure the chemical? Because of this important omission, the Environment Canada reliability code (for sparingly soluble substances) should be lowered to <satisfactory to low>.

The Japanese Industrial Standard (JIS K 0102-1986-71) entitled "Testing methods for industrial waste water" has established the following for insoluble substances:

"Handling of water-insoluble substances: Even if the test substance is insoluble in water, basically avoid using any dispersant. Set the test concentrations so that they do not exceed the solubility limit of the test substance. However, if the test substance has an extremely low solubility in the medium, etc. and its solubility limit cannot be determined by usual methods, and if test concentrations above the solubility limit are inevitable for determining the toxicity values such as LC_{50}, perform the test using a dispersed system. If such test substances are intended to be used with dispersants or emulsifiers, perform the test using a dispersant. Before concluding that the toxicity values such as LC_{50} cannot be determined at concentrations within the soluble or dispersible limit of the test substance in the medium, etc., take every possible measure for dissolving or dispersing the test substance in the medium, etc. and determine the upper limit of the concentration at which the test substance can be dissolved or dispersed in the medium, etc."

This method is (in a way) consistent with the OECD 202 test method for evaluation of acute toxicity in that the test concentrations must approach the saturation of the substance in water. High substance loadings, as prescribed with the present test method, favour the condition of solubility limit.

No	Item	Weight	Yes/No	Specify
**Robust Study Summary Form: Aquatic iT**			
1	Acute Toxicities of Organic Chemicals to Fathead Minnows (*Pimephales promelas*). Volume 5. Center for Lake Superior Environmental Studies. University of Wisconsin-Superior. D.L. Geiger, L.T. Brooke and D.J. Call Editors. 1990. Test Date = 09/21/1987			
2	Substance identity: CAS RN	n/a	Y	732-26-3
3	Substance identity: chemical name(s)	n/a	Y	2,4,6-Tri-*tert*-butylphenol
4	Chemical composition of the substance	2	Y	C18H3O
5	Chemical purity	1	Y	97%
6	Persistence/stability of test substance in aquatic solution reported?	1	Y	94.6% recovery n = 5
*Method*			
7	Reference	1	Y	
8	OECD, EU, national, or other standard method?	3	Y	Consistent with US EPA methods
9	Justification of the method/protocol if a non-standard method was used	2	n/a	n/a
10	GLP (good laboratory practice)	3	Y	Y
*Test organism*			
11	Organism identity: name	n/a	Y	*Pimephales promelas* (Fathead minnow)
12	Latin or both Latin and common names reported?	1	Y	
13	Life cycle age / stage of test organism	1	Y	30–31 days
14	Length and/or weight	1	Y	Mean length: 18.4 mm, mean weight: 0.086 g
15	Sex	1	N	
16	Number of organisms per replicate	1	Y	5
17	Organism loading rate	1	Y	0.0860 g/L/d
18	Food type and feeding periods during the acclimation period	1	Y	Larvae fed 40-48 h old brine shrimp (*Artemia* sp.) nauplii in excess twice daily.
*Test design/conditions*			
19	Test type (acute or chronic)	n/a	Y	Acute
20	Experiment type (laboratory or field)	n/a	Y	Laboratory, flow-through
21	Exposure pathways (food, water, both)	n/a	Y	Water
22	Exposure duration	n/a	Y	96 hr
23	Negative or positive controls (specify)	1	Y	Negative control
24	Number of replicates (including controls)	1	Y	4
25	Nominal concentrations reported?	1	Y	Nominal also reported

26	Measured concentrations reported?	3	Y	Measured also reported
27	Food type and feeding periods during the long-term tests	1	n/a	n/a
28	Were concentrations measured periodically (especially in the chronic test)?	1	Y	5 times
29	Were the exposure media conditions relevant to the particular chemical reported? (e.g., for the metal toxicity - pH, DOC/TOC, water hardness, temperature)	3	Y	Temperature, dissolved oxygen, hardness, alkalinity, pH
30	Photoperiod and light intensity	1	N	
31	Stock and test solution preparation	1	Y	
32	Was solubilizer/emulsifier used if the chemical was poorly soluble or unstable?	1	Y	Test substance was dissolved in acetone and applied onto a glass wool column due to limited solubility. Acetone was then evaporated.
33	If solubilizer/emulsifier was used, was its concentration reported?	1	n/a	Acetone not present in the test solution (see above comment).
34	If solubilizer/emulsifier was used, was its ecotoxicity reported?	1	n/a	n/a
35	Analytical monitoring intervals	1	Y	Daily
36	Statistical methods used	1	Y	
37	Was the endpoint directly caused by the chemical's toxicity, not by the organism's health (e.g., when mortality in the control > 10%) or physical effects (e.g., shading effect)?	n/a	Y	No mortalities in control
38	Was the test organism relevant to the Canadian environment?	3	Y	Fathead minnow found in Canada
39	Were the test conditions (pH, temperature, DO, etc.) typical for the test organism?	1	Y	Temp = 25.3°C, pH = 7.5, alkalinity = 39.6 mg/L, hardness = 45.1 mg/L, DO = 6.5
40	Do system type and design (static, semi-static, flow-through; sealed or open; etc.) correspond to the substance's properties and the organism's nature/habits?	2	Y	Flow-through design
41	Was pH of the test water within the range typical for the Canadian environment (6 to 9)?	1	Y	7.5
42	Was temperature of the test water within the range typical for the Canadian environment (5 to 27°C)?	1	Y	25.3
43	Was toxicity value below the chemical's water solubility?	3	Y	Experimenter noted this
Results				

44	Toxicity values (specify endpoint and value)	n/a	n/a	0.061 mg/L
45	Other endpoints reported - e.g., BCF/BAF, LOEC/NOEC (specify)?	n/a	N	
46	Other adverse effects (e.g., carcinogenicity, mutagenicity) reported?	n/a	N	
47	*Score: ... %*	*43/45 = 96%*		
48	*Environment Canada reliability code:*	*1*		
49	*Reliability category (high, satisfactory, low):*	*High confidence*		
50	*Comments*			

Appendix II – PBT Model Inputs Summary Table for DTBSBP

	Phys-Chem/Fate	Fate	Fate	Fate	Fate	PBT Profiling	Ecotoxicity
Model input parameters	EPI Suite (all models, including: AOPWIN, KOCWIN, BCFBAF BIOWIN and ECOSAR)	EQC (required inputs are different if Type I vs. Type II chemical)	TaPL3	OECD POPs Screening Model	Arnot-Gobas BCF/BAF Model	CPOPs Canadian POPs Model (2008) (including: Dimitrov Model (2005), OASIS Toxicity Model (2005))	Artificial Intelligence Expert System (AIEPS)/ TOPKAT
SMILES code	Oc(c(cc(c1)C(CC)C)C(C)(C)C)c1C(C)(C)C					Same as EPI Suite	Same as EPI Suite
Molecular weight (g/mol)		262.44	262.44	262.44			
Melting point (ºC)	18.9	18.9	18.9				
Boiling point (ºC)	275						
Data temperature (ºC)		20	20				
Density (kg/m^3)							
Vapour pressure (Pa)		0.35	0.35				
Henry's Law constant (Pa·m^3/mol)							

Log K$_{aw}$ (Air-water partition coefficient) (dimensionless)				-3.4			
Log K$_{ow}$ (Octanol-water partition coefficient) (dimensionless)	6.1	6.1	6.1	6.1	6.1	6.1	
Log K$_{oc}$ (Organic carbon-water partition coefficient – L/kg)							
Water solubility (mg/L)		2.47	2.47	2.47			
Log K$_{oa}$ (Octanol-air partition coefficient) (dimensionless)				9.5			
Soil-water partition coefficient (L/kg)[1]							
Sediment-water partition coefficient (L/kg)[1]							

Suspended particles-water partition coefficient (L/kg)[1]						
Fish-water partition coefficient (L/kg)[2]						
Aerosol-water partition coefficient (dimensionless)[3]						
Vegetation-water partition coefficient (dimensionless)[1]						
Enthalpy (K_{ow})			-20 [3]			
Enthalpy (K_{aw})			55 [3]			
Half-life in air (days)		0.52	0.52	0.52		
Half-life in water (days)		182	182	182		
Half-life in sediment (days)		728	728			
Half-life in soil (days)		182	182	182		
Half-life in vegetation						

(days)[4]							
Metabolic rate constant (1/days)					0.001		

[1] derived from log K_{oc}
[2] derived from BCF data
[3] default value
[4] derived from half-life in water

Appendix III – Exposure Estimations

In the following exposure estimations, it was assumed that Canadians spend, on average, 8 hours sleeping (Hillier et al. 2003), and through professional judgement, 3 hours driving. Canadians are assumed to spend 21 hours indoors each day (Health Canada 1998), taking into account the assumption of 8 hours sleeping, it was assumed that the remaining 13 hours were spent indoors, out of the bedroom.

Inhalation chronic doses due to DTBSBP emissions from foam mattresses and foam-filled furniture were estimated for all age groups, and are shown in the Table 1 below. The calculations for these estimations are illustrated in Table 2 using adult exposure as an example. Oral exposures of infants and toddlers from mouthing foam were also estimated (refer to Table 1); details are shown in Table 2.

Table 1. Upper-bounding estimates of intake of DTBSBP from consumer products by the general population of Canada

Consumer product	Estimated intake (µg/kg-bw per day) of DTBSBP by various age groups					
	0–6 months[1]	0.5–4 years[2]	5–11 years[3]	12–19 years[4]	20–59 years[5]	60+ years[6]
Foam mattress[7] (inhalation)	0.068	0.178	0.135	0.104	0.097	0.096
Foam-filled furniture (inhalation)	0.406	0.872	0.679	0.386	0.332	0.288
Mouthing foam (oral)	0.652	0.316	NA	NA	NA	NA

NA = Not applicable.

[1] Assumed to weigh 7.5 kg and to breathe at a rate of 2.1 m³/d (Health Canada 1998). No distinction was made between sleeping and non-sleeping inhalation rates.

[2] Assumed to weigh 15.5 kg (Health Canada 1998), to breathe at a rate of 4.14 m³/d during sleep (ConsExpo 2006) and 9.3 m³/d otherwise (Health Canada 1998).

[3] Assumed to weigh 31.0 kg (Health Canada 1998), to breathe at a rate of 6.28 m³/d during sleep (ConsExpo 2006) and 14.5 m³/d otherwise (Health Canada 1998).

[4] Assumed to weigh 59.4 kg (Health Canada 1998), to breathe at a rate of 9.28 m³/d during sleep (ConsExpo 2006) and 15.8 m³/d otherwise (Health Canada 1998).

[5] Assumed to weigh 70.9 kg (Health Canada 1998), to breathe at a rate of 10.3 m³/d during sleep (ConsExpo 2006) and 16.2 m³/d otherwise (Health Canada 1998).

[6] Assumed to weigh 72.0 kg (Health Canada 1998), to breathe at a rate of 10.4 m³/d during sleep (ConsExpo 2006) and 14.3 m³/d otherwise (Health Canada 1998).

[7] Assumed to be the standard size of a crib mattress (1.31 m × 0.69 m × 0.15 m) (October 2009 email from Product Safety, Health Canada, to Risk Assessment Bureau, Health Canada; unreferenced) for infants of age 0–6 months. Assumed to be 2 m long by 1.4 m wide by 0.15 m thick for other age groups (Hillier et al. 2003).

Table 2. Exposure estimates from the use of consumer products

Consumer product scenario	Assumptions	Estimated exposure
Sleeping on foam mattress in a bedroom	Since DTBSBP is a less volatile substitute for BHT, exposure to BHT due to emissions from foam mattresses was used to screen the upper limit of DTBSBP exposures in this consumer product scenario. An investigation into volatile emissions from foam mattresses found BHT emissions (highest concentration = 8.3 μg/m^3) from one of five fresh foam mattress samples in a test chamber (Hillier et al. 2003). To estimate exposure, the foam mattress sample and the test chamber were scaled up to a "standardized mattress" in a conservative-sized room. It was assumed that the volatile emissions could be released from all 6 surfaces of the mattress. C_e = extrapolated concentration of BHT in bedroom C_m = measured concentration of BHT in test chamber = 8.3 μg/m^3 S_e = surface area of "standardized" mattress = 6.62 m^2 (Hillier et al. 2003) S_m = surface area of foam sample in test chamber = 2.72 m^2 V_e = volume of bedroom = 16 m^3 (RIVM 2006) V_m = volume of test chamber = 3.2 m^3 A_e = air exchange in bedroom = 1 h^{-1} (RIVM 2006) A_m = air exchange in test chamber = 0.5 h^{-1} $$C_e = C_m \times \frac{S_e}{S_m} \times \frac{V_m}{V_e} \times \frac{A_m}{A_e}$$ $$C_e = 8.3\,\mu g/m^3 \times \frac{6.62\,m^2}{2.72\,m^2} \times \frac{3.2\,m^3}{16\,m^3} \times \frac{0.5\,h^{-1}}{1\,h^{-1}}$$ $$C_e = 2.02\,\mu g/m^3$$ 2.02 μg/m^3 was taken as the upper limit of the concentration of DTBSBP due to emissions from foam mattresses. To calculate the inhalation chronic dose, assuming a continuous DTBSBP atmospheric concentration of 2.02 μg/m^3, the following parameters were employed: f_{upt} = uptake fraction = 1 Q_{inh} = inhalation rate = 10.3 m^3/d (ConsExpo 2006) t = exposure time per event = 8 h = 0.33 d (Hillier et al. 2003) F = frequency = 365/year BW = 70.9 kg (Health Canada 1998) Inhalation chronic dose	DTBSBP air concentration = 2.02 μg/m^3 Inhalation chronic dose = 0.097 μg/kg-bw per day

	$$= C_e \times \frac{f_{upt} \times Q_{inh} \times t}{BW} \times \frac{F}{365\,\text{d/year}}$$ $$= 2.02\,\mu\text{g/m}^3 \times \frac{1 \times 10.3\ \text{m}^3/\text{d} \times 0.33\ \text{d}}{70.9\ \text{kg}} \times \frac{365/\text{year}}{365\ \text{d/year}}$$ $$= 0.097\ \mu\text{g/kg-bw per day}$$	
Household foam-filled furniture	The investigation into volatile emissions from foam mattresses (Hillier et al. 2003) was not extended to foam-filled furniture, but the findings are thought to be equally applicable to these consumer items. Since the total quantity of foam in household furniture items varies and a standard value has not been defined, exposure was estimated by extrapolating the laboratory data of the sample foam in a test chamber to a "standardized mattress" in an unspecified room. It was assumed that the volatile emissions could be released from all 6 surfaces of the mattress. Since DTBSBP is a less volatile substitute for BHT, exposure to BHT was used to screen the upper limit of DTBSBP exposures in this consumer product scenario. C_e = extrapolated concentration of BHT in unspecified room C_m = measured concentration of BHT in test chamber = 8.3 µg/m^3 S_e = surface area of "standardized" mattress = 6.62 m^2 (Hillier et al. 2003) S_m = surface area of foam sample in test chamber = 2.72 m^2 V_e = volume of unspecified room = 20 m^3 (RIVM 2006) V_m = volume of test chamber = 3.2 m^3 A_e = air exchange in unspecified room = 0.6 h^{-1} (RIVM 2006) A_m = air exchange in test chamber = 0.5 h^{-1} $$C_e = C_m \times \frac{S_e}{S_m} \times \frac{V_m}{V_e} \times \frac{A_m}{A_e}$$ $$C_e = 8.3\,\mu\text{g/m}^3 \times \frac{6.62\ \text{m}^2}{2.72\ \text{m}^2} \times \frac{3.2\ \text{m}^3}{20\ \text{m}^3} \times \frac{0.5\,\text{h}^{-1}}{0.6\,\text{h}^{-1}}$$ $$C_e = 2.69\,\mu\text{g/m}^3$$ 2.69 µg/m^3 was taken as the upper limit of the concentration of DTBSBP due to emissions from foam-filled furniture. To calculate the inhalation chronic dose, assuming a continuous DTBSBP atmospheric concentration of 2.69 µg/m^3, the following parameters were employed: f_{upt} = uptake fraction = 1 Q_{inh} = inhalation rate = 16.2 m^3/d (Health Canada 1998) t = exposure time per event = 13 h = 0.54 d F = frequency = 365/year BW = 70.9 kg (Health Canada 1998)	DTBSBP air concentration = 2.69 µg/m^3 Inhalation chronic dose = 0.332 µg/kg-bw per day

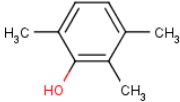|		
	Inhalation chronic dose $$= C_e \times \frac{f_{upt} \times Q_{inh} \times t}{BW} \times \frac{F}{365\,\text{d/year}}$$ $$= 2.69\ \mu\text{g/m}^3 \times \frac{1 \times 16.2\ \text{m}^3/\text{d} \times 0.54\ \text{d}}{70.9\ \text{kg}} \times \frac{365/\text{year}}{365\,\text{d/year}}$$ $= 0.332$ µg/kg-bw per day	
Driving in a typical medium-sized car	Since DTBSBP is a less volatile substitute for BHT, exposure to BHT due to emissions from automotive interior trim materials was used to screen the upper limit of DTBSBP exposures in this consumer product scenario. At 90ºC, the rate of formation of fogging condensate from polyurethane auto seat foam was measured to be 340.4 µg from a gram of polyurethane foam material per hour (Loock et al. 1993). Analysis of the fogging condensate showed 3.76% BHT content. Therefore, the rate of BHT emission (in µg per gram of polyurethane foam over one hour), *E*, can be calculated as = 340.4 µg/g × 3.76% = 12.8 µg/g Accordingly, 12.8 µg of BHT is emitted per gram of polyurethane foam in one hour. The atmospheric concentration of BHT in a car, C_{air}, while driving can be calculated using the following parameters: M_{PU} = mass of polyurethane in a medium-sized car = 15 000 g (ISOPA 2005) V = auto interior volume = 2.4 m^3 (Versar 1986) A = air exchange rate = 25 h^{-1} (Versar 1986) d = exposure duration (corresponding to the emission rate) = 1 h $$C_{air} = \frac{E \times M_{PU}}{V} \times e^{-Ad}$$ $$C_{air} = \frac{12.8\ \mu\text{g/g} \times 15000\ \text{g}}{2.4\ \text{m}^3} \times e^{-25\,\text{h}^{-1} \bullet 1\,\text{h}}$$ $$C_{air} = 1.11 \times 10^{-6}\ \mu\text{g/m}^3$$ 1.11×10^{-6} µg/m^3 was taken as the upper limit of the atmospheric concentration of DTBSBP due to emissions from automotive interior trim materials. To calculate the inhalation chronic dose, assuming a continuous DTBSBP atmospheric concentration of 1.11×10^{-6} µg/m^3, the following parameters were employed:	DTBSBP air concentration = 1.11×10^{-6} µg/m^3 Inhalation chronic dose = 3.17×10^{-8} µg/kg-bw per day

	f_{upt} = uptake fraction = 1 Q_{inh} = inhalation rate = 16.2 m³/d (Health Canada 1998) t = exposure time per event = 3 h = 0.125 d F = frequency = 365/year BW = 70.9 kg (Health Canada 1998) Inhalation chronic dose $$= C_e \times \frac{f_{upt} \times Q_{inh} \times t}{BW} \times \frac{F}{365\,\text{d/year}}$$ $$= 1.11 \times 10^{-6}\ \mu\text{g/m}^3 \times \frac{1 \times 16.2\ \text{m}^3/\text{d} \times 0.125\ \text{d}}{70.9\ \text{kg}} \times \frac{365/\text{year}}{365\ \text{d/year}}$$ $= 3.17 \times 10^{-8}$ µg/kg-bw per day	
Mouthing foam objects[1]	Exposure is estimated below for infants of age 0–6 months (body weight 7.5 kg). This exposure scenario is equally applicable to toddlers of age 0.5–4 years (body weight 15.5 kg). Default values for ingestion from mouthing: WS = water solubility of DTBSBP = 2.47 mg/L (modelled) V_s = salivary flow rate = 0.22 mL/min (Environ 2003a, 2003b) CF = Convert L to mL = 0.001 L/mL FR = Fractional rate of extraction by saliva = 1 AF_o = Absorption factor by oral =1 EF= Exposure frequency of mouthing behaviour = 9 min/d (Environ 2003a, 2003b) BW = body weight = 7.5 kg (infants, age 0–6 months) (Health Canada 1998) The estimated daily intake: $$= \frac{WS \times V_s \times CF \times FR \times AF_o \times EF}{BW}$$ $$= \frac{2.47\ \text{mg/L} \times 0.22\ \text{mL/min} \times 0.001\ \text{L/mL} \times 1 \times 1 \times 9\ \text{min/d}}{7.5\,\text{kg}}$$ $= 6.52 \times 10^{-4}$ mg/kg-bw per day	Oral exposure = 6.52×10^{-4} mg/kg-bw per day (infants, 0–6 months); 3.16×10^{-4} mg/kg-bw per day (toddlers, 0.5–4 years)
Mouthing foam objects	It is assumed that the size of the object being mouthed, s, is limited by the interior volume of the mouth. The average-sized oral cavity in adults was measured to be 159.78 cm³ (mean amongst 20 male adults) (Iida-kondo et al. 2006). Since a toddler's head is on average 68% of the size of an adult's head (RIVM 2006), the oral cavity of a toddler was assumed to be 68% that of an adult. Therefore $s = 68\% \times 159.78$ cm³ = 108.65 cm³. The loss factor of antioxidants from plastics over the service lifetime of the plastic product was determined to be 0.05% (OECD 2004b). Exposure is estimated below for infants of age 0–6 months (body weight 7.5 kg). This exposure scenario is equally applicable to toddlers	Oral exposure = 2.17×10^{-4} mg/kg-bw per day (infants, 0–6 months); 1.05×10^{-4} mg/kg-bw per day (toddlers, 0.5–4 years)

of age 0.5–4 years (body weight 15.5 kg).

s = size of the object involved in mouthing (in cm^3) = 108.65 cm^3
p = density of foam = 30 kg/m^3 (Klempner and Sendijarevic 2004) = 0.03 g/cm^3
C = concentration of DTBSBP in foam = 0.001 g DTBSBP/g of foam (Environment Canada 2009a)
F = loss factor by leaching under aqueous conditions = 0.05 % (OECD 2004b)
BW = body weight of toddler = 15.5 kg (Health Canada 1998)

Estimated Daily Intake

$$= \frac{s \times p \times C \times F}{BW}$$

$$= \frac{108.65\,\text{cm}^3 \times 0.03\,\text{g of foam/cm}^3 \times 0.001\,\text{g DTBSBP/g of foam} \times 0.0005}{7.5\,\text{kg}}$$

= 2.17 × 10^{-7} g DTBSBP/kg-bw
= 2.17 × 10^{-4} mg DTBSBP/kg-bw

[1] The method used to calculate oral exposure via mouthing of foam containing DTBSBP was derived from a Voluntary Children's Chemical Evaluation Program Pilot (VCCEPP) assessment (Environ 2003a, 2003b).

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Appendix IV: Structures and data for DTBSBP analogues considered in this assessment

Name / CAS RN	Structure	Molecular weight (g/mol)	Analogue identification method (% similar)	Health effects toxicity data available
Phenol, 2,6-bis(1,1-dimethylethyl)-4-ethyl-4130-42-1		234.4	Tanimoto coeff. (79) Chemid (88.16)	Genetox: Negative in TA97, TA98, TA100, TA102, WP2 p with/without activation (Hachiya and Takizawa 1994)
Phenol, 2,4,6-tris(1,1-dimethylethyl)-(TTBP) 732-26-3		262.4	Chemid (93.36)	Chronic: Negative for carcinogenicity; Non-neoplastic effects NOEL=30ppm (Matsumoto et al. 1991) Short-term: LOEL= 173 mg/kg bw/day based on diarrhea, and blood in the feces (Anonymous 1987)
Butylated hydroxytoluene (BHT) 128-37-0		220.4	Tanimoto coeff. (75) Chemid (83.3)	Considered by the OECD SIDS programme and determined not to be a genotoxic carcinogen and a threshold of 100 mg/kg-bw/day was established for the possible carcinogenic and tumour-promoting effects of BHT (OECD 2004c)
2,6-Di-*tert*-butylphenol 128-39-2		206.3	US EPA Hazard Characterization Category Di and Tri-Substituted Mixed Alkylphenols	Genetox: Negative in *S. typhimurium* (TA98, TA100, TA 1535, TA1537 and TA1538) with and without activation (US EPA 2009a) Negative for chromosomal aberrations in Chinese hamster V79 cells with and without activation (US EPA 2009a). Repeated-dose (28 day) (US EPA 2009a): LOAEL=600 mg/kg-bw/day based on increase liver weight and a slight increase in the incidence of hepatocellular hypertrophy in the centrilobular area in both sexes and eosinophilic inclusions in the renal cortex of males NOAEL=100 mg/kg-bw/day Combined repro/devo study:

				(US EPA 2009a) Reproductive toxicity: LOAEL= None established NOAEL= 750 mg/kg-bw/day Adult systemic and Developmental toxicity: LOAEL= 750 mg/kg-bw/day NOAEL=150 mg/kg-bw/day Acute: LD_{50} (dermal)> 1000 mg/kg-bw/day in rats
2,3,6-Trimethylphenol 2416-94-6		136.2	U.S. EPA Hazard Characterization Category Di and Tri-Substituted Mixed Alkylphenols	Genetox: *In vitro*: Negative in *S. typhimurium* (TA98, TA100, TA 1535, TA1537 and TA1538) with and without activation (US EPA 2009a).

Note: Other CAS numbers were included in the U.S. EPA Hazard Characterization Document (2772-45-4; 120-95-6; 96-76-4); however, they were not included, as the data did not further contribute to the overall health effects assessment.

Appendix V: Summary of (Q)SAR Predictions

(Q)SAR PREDICTIONS ON CARCINOGENICITY

Model/ Species	Mice		Rat		Rat	Mice	Rodent	Mammal
	Male	Female	Male	Female				
Model Applier	N	N	N	N	N	N	N	-
Multicase Casetox	NR	N	NR	N	NR	NR	NR	-
Topkat	N	NR	NR	NR	NR	NR	NR	-
Derek	-	-	-	-	-	-	-	NR

MA – model applier
CT – Multicase Casetox
TK – Topkat
TT – Toxtree
BB – Benigni-Bossa rule
ND – not in domain
'-' no model available in QSAR suite
NR – no result
N – negative
P - positive

(Q)SAR PREDICTIONS ON GENOTOXICITY

Model/endpoints	chrom. ab.	chrom. ab. other rodent	chrom. ab. rat	micronucleus mice	micronucleus rodent	drosophila	drosophila HT	drosophila SLRL	mam. mutation	mam. mutation DL	UDS	UDS human lymphocytes	UDS rat hepatocytes	mouse lymphoma mut	S. cerevisiae	yeast	hgprt	E. coli	E. coli w	microbial	salmonella	BB cancer alert
MA	N	N	N	N	N	N	N	N	N	N	N	N	N	-	N	N	N	N	N	N	N	-
CT	N	-	-	N	-	N	-	-	-	-	N	-	-	P	-	-	-	-	-	-	N	-
TK	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	N	-
TT	-	-	-	-	N	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	N

MA – model applier
CT – Multicase Casetox
TK – Topkat
TT – Toxtree
BB – Benigni-Bossa rule
ND – not in domain
'-' no model available in QSAR suite
NR – no result
N – negative
P - positive

(Q)SAR PREDICTIONS ON DEVELOPMENTAL TOXICITY

Model Applier

Endpoint/ Species	Mice	Rabbit	Rat	Rodent
Retardation	N	N	N	N
Weight decrease	N	N	ND	N
Fetal death	N	N	N	N
Post impl. loss	N	N	N	N
Pre impl. loss	N	N	N	N
Structural	N	ND	N	N
Visceral	N	N	N	N

Multicase Casetox

Endpoint/Species	Hamster	Mammal	Miscellaneous
Teratogenicity	-	P	N
Developmental	N	-	-

MA – model applier
CT – Multicase Casetox
TK – Topkat
TT – Toxtree
BB – Benigni-Bossa rule
ND – not in domain
'-' no model available in QSAR suite
NR – no result
N – negative
P - positive

(Q)SAR PREDICTIONS ON REPRODUCTIVE TOXICITY

Model Applier

Model/ endpoint	Female			Male		
Species	Mice	Rat	Rodent	Mice	Rat	Rodent
Repro	N	ND	ND	N	P	N
Sperm	-	-	-	N	ND	N

Multicase Casetox

Mice	Rat	Rabbit	Human
N	N	N	NR

MA – model applier
CT – Multicase Casetox
TK – Topkat
TT – Toxtree
BB – Benigni-Bossa rule
ND – not in domain
'-' no model available in QSAR suite
NR – no result
N – negative
P - positive