Screening Assessment for the Challenge

Decanedioic acid, bis(1,2,2,6,6-pentamethyl-4-piperidinyl)-ester

Chemical Abstracts Service Registry Number
41556-26-7

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 decanedioic acid, bis(1,2,2,6,6-pentamethyl-4-piperidinyl)-ester (PEDA), Chemical Abstracts Service Registry Number 41556-26-7. 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, PEDA, 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 principally on information relevant to the evaluation of ecological risks.

PEDA is an organic substance that is used in Canada and elsewhere in paint and coatings for automobiles, as a component of polymers and as a photosensitive agent. Although the products are not intended to be used by the general population, the following consumer products that contain PEDA were identified in the Canadian consumer market: automobile interior protectants, waterborne semi-transparent stain products, aerosol solvent borne paints, paint coating additives and window sealants.

The substance is not naturally occurring in the environment. A total of 54 358 kg of PEDA was imported into Canada and 9 541 kg were used in 2006. The quantity of PEDA imported into Canada, along with the potentially dispersive uses of this substance, indicate that it could be released into the Canadian environment.

Based on reported use patterns and certain assumptions, the majority of the substance ends up in waste disposal sites (71.7%) with a lesser amount going to recycling (15.1%). Smaller proportions are estimated to be lost to water (6.2% - wastewater), paved/unpaved land surfaces (3.8%), incineration (2.2%) and export (1.0%).

The primary dissociation constant of the substance (pK_{a1} = 10.02; base form) indicates that there is complete protonation of the substance at ambient pHs (6-9) such that only the positively charged form is present. However, the protonation of the substance was not accounted for during Categorization.

Based on experimental and modelled physical and chemical properties, the charged form of the substance is moderately soluble in water, is non-volatile and is unlikely to partition in significant amounts to particles and lipids (fat) of organisms because of its charged nature and large molecular size. For these reasons, PEDA will be found mostly in water and in soil, depending upon the medium to which it is released. It is not expected to be significantly present in other media.

Based on an atmospheric oxidation half-life of 0.067 days, PEDA is expected to rapidly oxidize in air. Model results indicate that PEDA may undergo relatively rapid primary biodegradation in

water but biodegradation modeling results indicate that in both water, and soil, as well as in sediments the ultimate biodegradation half-life of PEDAis likely to be greater than 182 days in both water, and soil, and greater than 365 days in sediments. It is, therefore, persistent in water, soil and sediments. PEDA was initially categorized as bioaccumulative based on model predictions for the neutral molecule, however, modeling results that take into consideration the presence of the charged form of the compound indicate that this substance does not have the potential to accumulate to a significant extent in aquatic organisms or biomagnify in trophic food chains. The substance has therefore been determined to meet the persistence criteria but not the bioaccumulation criteria as set out in the *Persistence and Bioaccumulation Regulations*.

Empirical acute toxicity data indicate that PEDA has the potential to cause adverse effects to aquatic organisms at relatively low concentrations. However, no empirical chronic effects data were available for PEDA. Modelled chronic data based on results that take into account the charged character of the substance, suggest that PEDA has the potential to be moderately to highly toxic to aquatic organisms.

With regard to human health, no measured concentrations of PEDA in environmental media were identified in Canada or elsewhere. No information with regards to the presence of PEDA in foods was identified. Exposure of the Canadian population to this substance from environmental media is expected to be negligible according to estimates based on the quantity of PEDA in Canadian commerce in 2006. Exposures to PEDA resulting from its use in food packaging applications are expected to be negligible. Estimates of exposure to PEDA from its use in consumer products were derived.

Limited empirical data related to health effects were available for PEDA. The outputs of PEDA quantitative structure activity relationship (QSAR) model predictions for carcinogenicity, genotoxicity, reproductive and developmental toxicity were mixed. Information on analogues of PEDA indicate potential effects on the liver and nervous system in experimental animals.

Based on the information available, the margins of exposure between upper-bounding estimates of exposure to PEDA from use of consumer products and levels associated with effects in experimental animals observed in studies with analogues of PEDA are considered to be adequately protective.

For this screening assessment, two very conservative exposure scenarios were selected to predict the environmental concentrations of PEDA in Canada; one to predict the potential industrial emissions of the substance to the aquatic environment and the other to quantify the level of aquatic exposure to a substance released from consumer products. Risk quotient analysis comparing the predicted environmental concentration (PEC) associated with industrial releases with a predicted no-effect concentration (PNEC) resulted in a risk quotient value of 0.02 to 0.46. The PEC for the consumer release was below the PNEC calculated for sensitive aquatic life. These results suggest that releases of PEDA are not likely to be harming the aquatic environment.

Therefore, it is concluded that PEDA not 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 or that constitute or may constitute a danger to the environment on which life depends.

Based on the information available, PEDA meets the criteria for persistence but does not meet the criteria for bioaccumulation as set out in the *Persistence and Bioaccumulation Regulations*.

Given the information presented in this final screening assessment, it is concluded that PEDA is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

This 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.

Based on the information available, PEDA does not meet any of the criteria set out in section 64 of the *Canadian Environmental Protection Act, 1999*.

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 to 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 2006), 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 PEDA had been identified as a high priority for assessment of ecological risk as it had been found to be persistent, bioaccumulative and inherently toxic to aquatic organisms and is believed to be in commerce in Canada. The Challenge for this substance was published in the *Canada Gazette* on March 14, 2009 (Canada 2009). 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 physical and chemical properties, persistence, toxicity and uses of the substance were received.

Although PEDA 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 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 September 2009 for ecological sections of the document and December 2009 for human health-related sections. Key studies were critically evaluated; modelling results may have been 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 portion of this assessment has undergone external written 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 final content and outcome of the 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 final assessment is based are summarized below.

[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.

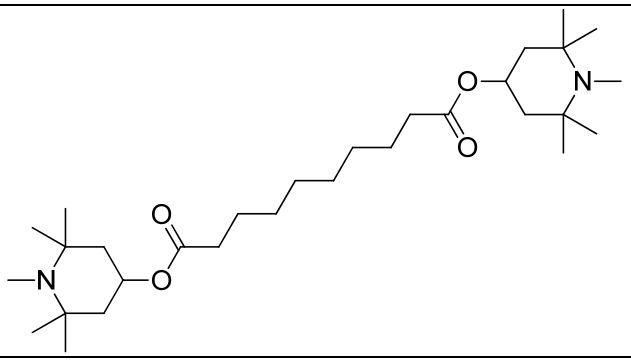
Substance Identity

Substance name

For the purposes of this document, decanedioic acid, bis(1,2,2,6,6-pentamethyl-4-piperidinyl)-ester will be referred to as PEDA derived from the chemical name listed on the Canadian Domestic Substances List (DSL).

Table 1. Substance identity for PEDA

Chemical Abstracts Service Registry Number (CAS RN)	**41556-26-7**
DSL name	**Decanedioic acid, bis(1,2,2,6,6-pentamethyl-4-piperidinyl)-ester**
National Chemical Inventories (NCI) names[1]	*Decanedioic acid, 1,10-bis(1,2,2,6,6-pentamethyl-4-piperidinyl) ester* (TSCA) *Decanedioic acid, bis(1,2,2,6,6-pentamethyl-4-piperidinyl) ester* (AICS, SWISS, PICCS, ASIA-PAC, NZIoC) *bis(1,2,2,6,6-pentamethyl-4-piperidyl) sebacate* (EINECS) *Bis(1,2,2,6,6-pentamethyl-4-piperidyl) decanedioate* (ENCS) *Decanedioic acid bis(1,2,2,6,6-pentamethyl-4-piperidinyl)* ester (ECL) *Decanedioate, Bis(1,2,2,6,6-Pentamethyl-4- Piperidinyl* (PICCS) *Bis(1,2,2,6,6-Pentamethyl-4-Piperidinyl)sebacate* (PICCS)
Other names	*Bis(1,2,2,6,6-pentamethyl-4-piperidinyl) sebacate* *Bis(1,2,2,6,6-pentamethyl-4-piperidyl) 1,8-octanedicarboxylate* *Bis(N-methyl-2,2,6,6-tetramethyl-4-piperidinyl) sebacate* *HALS 4; Lowilite 76; LS 508; LS 765; Sanol 292; Sanol LS 292 ; Sanol LS 508; Sanol LS 765; TIN 292; Tinuvin 292; Tinuvin 765; TN 765; UV 55-07051 ; TK 12576*
Chemical group (DSL Stream)	Discrete organics
Major chemical class or use	Piperidine compounds
Major chemical sub-class	Hindered Amine Light Stabilizer (HALS)
Chemical formula	$C_{30}H_{56}N_2O_4$

Chemical structure	
SMILES [2]	O=C(CCCCCCCCC(=O)OC1CC(N(C(C1)(C)C)C)(C)C)OC2CC(N(C)C(C2)(C)C)(C)C
Molecular mass	508.79 g/mol

[1] National Chemical Inventories (NCI). 2007 AICS (Australian Inventory of Chemical Substances); ASIA-PAC (Asia-Pacific Substances Lists); ECL (Korean Existing Chemicals List); EINECS (European Inventory of Existing Commercial Chemical Substances); ELINCS (European List of Notified 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 2 contains experimental and modelled physical and chemical properties of PEDA that are relevant to its environmental fate. PEDA exists entirely as a charged molecule over the range of environmentally-relevant pHs (6-9), therefore, partitioning properties presented are based on the empirical log of the distribution coefficient between n-octanol and water (logD) and solubility information that reflect behaviour of the charged molecule.

PEDA has two functional groups that will become positively charged at slightly different pHs, such that there are two pKa values describing the pH at which these functional groups become protonated. Thus, there are two charged forms for PEDA that will co-occur in varying proportions with the neutral form depending on the pH of the environmental medium.

The water solubility of PEDA is expected to vary with pH, by one to two orders of magnitude or more (see Table 2).

Table 2. Physical and chemical properties of PEDA[1].

Property	Type	Value[2]	Temperature (°C)	Reference
Melting point (ºC)	Modelled	205.29		MPBPWIN 2000
Boiling point (ºC)	Modelled	485.55		MPBPWIN 2000
Density (kg/m^3)	Experimental	990	20	Ciba Additive GmbH 2000
Vapour pressure (Pa)	Experimental	$1.0x10^{-4}$	20	Ciba Additive GmbH 2000
	Modelled	$1.05x10^{-7}$ ($7.85x10^{-10}$ mm Hg)		MPBPWIN 2000
Henry's Law constant ($Pa·m^3/mol$)	Modelled	$7.76x10^{-7}$ ($7.76x10^{-12}$ $atm·m^3/mol$)	25	HENRYWIN 2000
Log D_{ow}[3] (Distribution	Modelled	3.35 at pH 7	25	ACD/pK_aDB 1994-2009

Property	Type	Value[2]	Temperature (°C)	Reference
coefficient) (dimensionless)				
Log D_{oc} (Organic carbon-water partition coefficient) (dimensionless)	Modelled	1.34 at pH 7 2.56 at pH 8 3.81 at pH 9	25	ACD/pK_aDB 1994-2009
Water Solubility (mg/L)	Modelled	8.8	25	WSKOWWIN 2000
	Modelled	980 630 at pH 6 837 330 at pH 7 1370 at pH 9		ADME Toxweb 2008
pK_{a1} (Acid dissociation constant) (dimensionless)	Modeled	10.02	25	ACD/pK_aDB 1994-2009
pK_{a2}		9.42		

[1] The EPIWIN 4.0 modeling results are based on the modeled input data: predicted log D (3.35)

[2] Values and units in brackets represent those originally reported by the authors or estimated by the models.
[3] Distribution coefficient taking into account the presence of the ionic species; represents the net amount of the neutral and ionic forms expected to partition into the lipid phase at a given pH.

Sources

PEDA is an anthropogenic substance that has not been identified to occur naturally.

In response to a notice issued under section 71 of CEPA 1999, PEDA was not identified to be manufactured in Canada in 2006 (Environment Canada 2009a). Importation activities (whether alone, in a mixture, in a product or in manufactured items above the reporting threshold of 100

kg) were reported at a quantity of 100 000 kg in 2006 (Environment Canada 2006). The substance was included in certain imports as additives in paint and coatings for automobiles and other uses, as a component of polymers and as a photosensitive agent. The use quantity reported in 2006 in the response to the notice issued under section 71 was 9 541 kg for the activities identified above.

PEDA is a high production volume (HPV) chemical in the United States (1 – 10 million lbs; 0.453-453,592 kg) (US EPA 2005) and is on the 2007 Organisation for Economic Co-operation and Development (OECD) list of high production volume chemicals (> 1 000 tonnes per year in at least one member country/region) (OECD 2009). PEDA was used in Sweden, Denmark, Norway, and Finland from 1999 to 2007 (SPIN 2009). Norway, Sweden, Finland and Denmark used 12.1, 25.0, 51.9 and 55.1 tonnes, respectively in 2007.

Uses

PEDA is a hindered amine light stabilizer (HALS), used for stabilising polymer products against light which has application for automotive coatings in order to provide extended life to coatings by minimizing paint defects such as cracking and dullness. It is often used together with benzotriazol-based substances which can also absorb the free radicals that are formed in organic substances exposed to UV light, causing the polymer to disintegrate. The radicals become "trapped" within substituted piperidinyl rings.The stabilising behaviour arises from the *ortho*-methyl-substituted piperidinyl moieties; the long carbon chain serves to make the molecule dispersible (KEMI 2009).

According to data submitted under section 71 of CEPA 1999 and other publicly available sources, PEDA is primarily used in industrial and automotive paints and coatings in Canada (Mayzo 2005; Akzo Nobel 2006a, b, c; Environment Canada 2009a). These industrial and automotive products are generally not intended to be used by the general population. However, some consumer products have been identified in the Canadian consumer market that contain PEDA. These include: auto interior protectants, waterborne semi-transparent stain products, aerosol solvent-borne paints and window sealants (TopSeal 2008; Environment Canada 2009a; 2009 email from Risk Management Bureau, Health Canada, to Risk Assessment Bureau, Health Canada, unreferenced).

PEDA is not approved for any food additive use in Canada, but is used in coatings for large containers for transporting and holding dry foods (2009 email from Food Directorate, Health Canada, to Risk Management Bureau, Health Canada; unreferenced).

Given the use of this substance in Canada and other countries, it is known that the substance is entering the Canadian market as a component of manufactured items and consumer products. The main North American Industry Classification System (NAICS) code used by importers was 325510 which corresponds to paint and coating manufacturing. Other designated uses include plastics material and resin manufacturing, and those requested to be confidential business

information by the respondent. However, the confidential business uses were considered in the estimation of release of the substance to the Canadian environment.

Releases to the Environment

The use of PEDA as an additive in paints and coatings, as a polymer in formulation and as a photosensitive agent, could result in the release of the substance to the environment through processing activities, transportation and storage, including during the consumer life and disposal of the finished product. Most of the substance is expected to be disposed of in landfills, although there are some releases to paved and unpaved land surfaces and wastewater.

The losses of PEDA via various routes during its lifecycle are estimated based on regulatory survey and industry data, and information published by different organizations. The losses are grouped into six types: (1) discharge to wastewater; (2) emission to air; (3) loss to paved/unpaved surfaces; (4) chemical transformation; (5) disposal to landfill; and (6) disposal by incineration. Losses may occur at one or more of the substance's lifecycle 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.

In the context of the loss estimates made by the Mass Flow tool, the discharge to wastewater refers to raw wastewater prior to any treatment, either on-site industrial wastewater treatment or off-site municipal sewage treatment. In a similar manner, the 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.

The losses estimated for PEDA over its lifecycle are presented in Table 3 (Environment Canada 2009b). A total of 6.2% of the total quantity of the substance used in Canadian commerce is expected to be released to wastewater. In general, wastewater is a common source for releases to water and soil (when biosolids from wastewater treatment facilities are disposed of on agricultural land).

Table 3. Estimated Losses of PEDA during its Lifecycle

Type of Loss	Proportion (%)	Pertinent Lifecycle Stages
Wastewater	6.2	Industrial use, and consumer/commercial use
Air emission	0	
Paved/unpaved surfaces	3.8	Industrial use, consumer/commercial use, and disposal
Chemical transformation	0	
Landfill	71.7	Industrial use, consumer/commercial use, and disposal
Incineration	2.2	Industrial use, consumer/commercial use, and disposal
Recycling	15.1	Industrial use
Export	1.0	Industrial use

PEDA is also expected to be released to the environment via routes other than wastewater. There are various mechanisms for the loss to paved/unpaved land surfaces such as leaks and spills, wear and tear, and weathering. The substance lost to paved/unpaved surfaces can be blown to nearby soil or washed into sewers or local surface waters, resulting in soil or aquatic exposure. A small proportion of the substance disposed of in landfill has a potential to leach out into groundwater, however the larger landfills have liners to collect the leachate. Incineration can lead to atmospheric releases and eventual transfer to soil and surface water by atmospheric deposition.

This substance is used in some consumer products. Information on the quantity of consumer products containing PEDA imported into Canada is known, but has been identified as confidential business information.

Environmental Fate

This substance ionizes in water at environmentally relevant pHs (6-9). The primary dissociation constant of the substance is relatively high (pK_{a1} = 10.02; base form) which indicates that there is a complete protonation of the substance at pH 7, and that the neutral form will only exist in low amounts at alkaline pHs (e.g., ~9% at pH 9) (ACD/pK_aDB 1994-2009). Given its dissociation constants, most chemical species of PEDA released to water bodies at pH ranging from 6 to 9 would be present in cationic forms. In addition, the cationic species may undergo significant ion bonding from electrostatic interactions with negatively charged substrates (e.g., organic and inorganic particles), resulting in reversible to irreversible binding and this is pH dependent (pH 7-9). The Equilibrium Criterion model (EQC 2003) is unable to account for ionic interactions and estimates of partitioning from the water column to sediment are therefore uncertain. Also,

the ionic interactions may be sterically hindered. For these reasons, the Level III fugacity modelling is not presented.

If released to air, very low amounts of the substance are expected to remain in air. This is because the substance is likely to have no vapour pressure since it exists essentially in the charged form at environmentally-relevant pHs. Therefore, if released solely to air, it will tend to partition out of this compartment - the major compartments into which the substance will partition being soil and water.

If released into water, some PEDA is expected to remain in that compartment (log D_{oc} of 1.34), but some will also likely adsorb electrostatically to suspended particulate material and bottom sediments. Volatilization from water surfaces is expected to be an unimportant fate process based upon this compound's estimated Henry's Law constant (see Table 2).

With a log D_{oc} of 1.34 the substance is expected to be somewhat mobile in soil, but some PEDA will also likely adsorb electrostatically to soil particles. Volatilization from moist soil surfaces is expected to be an unimportant fate process based upon its estimated Henry's Law constant. This chemical is also unlikely to volatilize from dry soil surfaces based upon its negligible vapour pressure.

Persistence and Bioaccumulation Potential

Table 5a presents empirical biodegradation data (Ciba Additive GmbH 2000) that show 38% biodegradation over 28 days in a ready biodegradability test for PEDA. This test indicates that the substance is not “ready biodegradable” but that the biodegradation half-life in water may not be long – approximately 40 days assuming first order degradation kinetics.

Table 5a. **Empirical data for degradation of PEDA**

Medium	Fate process	Degradation value	Degradation endpoint, units	Reference
Water	Biodegradation	38	Biodegradation, %	Ciba Additive GmbH 2000

Modeling results indicate that the half-life of PEDA at pH 7 will be longer, 19.9 years, compared to a half-life of 1.9 years at pH 8 (HYDROWIN 2008). However, there is some uncertainty about the half-life results from HYDROWIN. Examination of the molecule’s structure indicates that PEDA contains functional groups (esters) expected to undergo hydrolysis. HYDROWIN (2008) model results indicate that pH-related hydrolysis may occur, it appears to overestimate the half lives of PEDA since one would expect a shorter half-life for such a substance given that it has functional groups amenable to hydrolysis (Table 5b).

Since few experimental data on the biodegradation of PEDA are available, a quantitative structure activity relationship (QSAR) based weight-of-evidence approach (EPIsuite 2000-2008) was also applied using the degradation models shown in Table 5b below. Given the ecological importance of the water compartment, the fact that most of the available models apply to water and the fact that PEDA is expected to be released to this compartment, biodegradation in water was primarily examined using predictive QSAR models for biodegradation. Table 5b summarizes the results of available QSAR models for degradation in water and air .

Table 5b. Modelled data for degradation of PEDA

Fate Process	Model and model basis	Model Result and Prediction	Extrapolated Half-life (days)
AIR			
Atmospheric oxidation	AOPWIN 2000[1]	$t_{1/2}$ = 0.067 days	< 2
Ozone reaction	AOPWIN 2000[1]	n/a[1]	n/a
WATER			
Hydrolysis	HYDROWIN 2000[1]	$t_{1/2}$ = 1.99 years (pH7) $t_{1/2}$ = 19.91 years (pH8)	n/a
Biodegradation (aerobic)	BIOWIN 2000[1] Sub-model 3: Expert Survey (ultimate biodegradation)	0.99[2] "biodegrades slowly"	> 182[4]
Biodegradation (aerobic)	BIOWIN 2000[1] Sub-model 4: Expert Survey (primary biodegradation)	2.38[2] "may biodegrade fast"	< 182[4]
Biodegradation (aerobic)	BIOWIN 2000[1] Sub-model 5: MITI linear probability	0.49[3] "may biodegrade fast"	< 182[4]
Biodegradation (aerobic)	BIOWIN 2000[1] Sub-model 6: MITI non-linear probability	0.046[3] "biodegrades very slowly"	> 182[4]
Biodegradation (aerobic)	TOPKAT 2004 Probability	0.0[3] "biodegrades very slowly	> 182[4]
Biodegradation (aerobic)	CATABOL 2004-2008 % BOD (biological oxygen demand)	% BOD = 27.4 "biodegrades slowly"	> 182[4]

[1] EPIsuite (2000-2008)
[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

In air, a predicted atmospheric oxidation half-life value of 0.067 days (see Table 5b above) demonstrates that this substance 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 nor is it likely to degrade via direct photolysis. Therefore, it is expected that reactions with hydroxyl radicals will be the most important fate process in the atmosphere for PEDA. With a half-life of 0.067 days via reactions with hydroxyl radicals, PEDA is considered not persistent in air.

Model results generally suggest that PEDA will undergo ultimate biodegradation (i.e., complete mineralization) slowly and the half-life in water would be >182 days. Although the primary biodegradation model (BIOWIN 4) suggests relatively rapid primary biodegradation, the

identities of degradation products are not known. Only one ultimate degradation model (BIOWIN 5) indicates that PEDA may biodegrade relatively quickly. It should be noted that the predictions for CATABOL and TOPKAT which are in all the domains of both models are considered to be the most reliable and suggest a very slow rate of biodegradation. The substance also contains structural features associated with chemicals that are not easily biodegraded (e.g., branched, tertiary amine).

Since both model results and structural features suggest that the ultimate degradation half-life in water is > 182 days, and given that the results of the empirical biodegradation study do not unequivocally indicate that biodegradation is fast, experimental data indicate that hydrolysis occurs relatively quickly. Haacke et al. 1999 reported that the hydrolysis products of PEDA in coatings is carboxylate salts and alcohols. It is concluded that PEDA is persistent in water.

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

Based on the empirical and modelled data (see Tables 5a and 5b) PEDA 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 air (half-life in air ≥ 2 days) as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Potential for Bioaccumulation

The modelled log D value (3.35) that takes into account the presence of the charged form of PEDA suggests that this chemical has low potential to bioaccumulate in biota (see Table 2) (ACD/pK_aDB 1994-2009).

Since no acceptable experimental BCF studies for PEDA were available, a predictive approach was applied using available bioaccumulation factor (BAF) and BCF models as shown in Tables 6a and Table 6b. BCF and BAF model estimates were generated using EPI suite (2000-2008) and the modelled log D_{ow} of 3.35 to account for the occurrence of the charged form of the substance in the environment.

According to the *Persistence and Bioaccumulation Regulations* (Canada 2000) a substance is bioaccumulative if its BCF or BAF is ≥ 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 metabolism correction as long as the log K_{ow} of the substance is within the log K_{ow} domain of the model.

Metabolism information for this substance was not available, nor was it necessary to consider in the BAF model as the log D_{ow} of the substances is less than 4 which suggests that uptake via the

gills will predominate rather than the diet. The BAF is therefore predicted to not be significantly different from BCF. The middle trophic level estimate was used as this is intended by the developer to represent overall model output and is most representative of fish weight likely to be consumed by an avian or terrestrial piscivore. The modelled BCF for the charged form of PEDA is low (75.4; Table 6a).

The estimate for the Baseline BCF model is 6, indicating again that PEDA has a low bioconcentration potential.

Table 6a. Fish BAF and BCF predictions for PEDA using the Arnot-Gobas kinetic model (Arnot and Gobas 2003) with default of no metabolism.

Test organism	Endpoint	Value wet weight (L/kg)	Log D_{ow}	Reference
Fish	BAF	75.39	3.35	Gobas BAF Middle Trophic Level (Arnot and Gobas 2003)
Fish	BCF	75.39	3.35	Gobas BCF Middle Trophic Level (Arnot and Gobas 2003)

Table 6b: Additional Modelled data for bioaccumulation for PEDA

Test organism	Endpoint	Value wet weight (L/kg)	Log D_{ow}	Reference
Fish	BCF	6.06	3.35	BBM with Mitigating Factors 2008

Recent investigations relating fish BCF data and molecular size parameters (BBM 2008; Dimitrov et al. 2002, 2005) suggest that the probability of a molecule crossing cell membranes as a result of passive diffusion declines significantly with increasing maximum cross-sectional diameter (D_{max}). The probability of passive diffusion lowers appreciably when maximum diameter is > ~1.5 nm and more significantly for molecules having a maximum diameter of > 1.7 nm. Sakuratani et al. (2008) have also investigated the effect of cross-sectional diameter on passive diffusion in a BCF test set of about 1200 new and existing chemicals. They observed that substances having a relatively low bioconcentration potential (BCF < 5000) often have a D_{max} > 2.0 nm and an effective diameter (D_{eff}) > 1.1 nm.

However, as Arnot et al. (2010) have noted there are uncertainties associated with the thresholds proposed by Dimitrov et al. (2002, 2005) and Sakuratani et al. (2008) since the BCF studies used to derive them were not critically evaluated. As Arnot et al. (2010) point out, molecular size influences solubility and diffusivity in water and organic phases (membranes), and larger molecules may have slower uptake rates. However, these same kinetic constraints apply to diffusive routes of chemical elimination (i.e., slow in = slow out). Thus, significant bioaccumulation potential may remain for substances that are subject to slow absorption processes, if they are slowly biotransformed or slowly eliminated by other processes. Consequently, when evaluating bioaccumulation potential molecular size information should be

considered with care, and used together with other relevant lines of evidence in a weight of evidence approach

PEDA is a relatively large molecule with a high molecular weight (508.79 g/mol). The maximum cross-sectional diameters (D_{max}) for this structure are estimated by CATABOL (c2004-2008) to be large. The values for different conformers range from 1.6 to 2.7 nm which is comparable to some of the values cited above and suggests that the uptake rate of this substance may be slower compared to that of smaller more compact substances, thus mitigating the overall bioconcentration potential.

The available evidence indicates that PEDA has a low bioaccumulation potential. This is indicated by its physical and chemical properties (i.e., low log D_{ow}, ionic character, as well as high molecular weight and large cross-sectional diameter), and results of BCF and BAF model estimates. It is therefore concluded that PEDA does not meet the bioaccumulation criterion (BAF or BCF ≥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 is experimental and modeled evidence that PEDA causes harm to aquatic organisms following short-term (acute) and longer-term (chronic) exposure at relatively low to moderate concentrations.

Experimental acute toxicity values for *Daphnia* (48-hr EC_{50}) and fish (96-hr LC_{50}) range from 0.97 to 20 mg/L (Table 7a). These empirical tests were conducted at exposure concentrations below the measured water solubility. Results of another toxicity study - carried out at concentrations above the measured water solubility - indicate that PEDA has a low potential to harm microorganisms.

Table 7a. Empirical data for aquatic toxicity.

Test organism	Type of test	Endpoint	Value (mg/L)	Reference
Daphnia magna	Acute (24 hours)	EC_{50}[1]	20	Ciba Additive GmbH 2000
Rainbow trout (*Oncorhynchus mykiss*)	Acute (96 hours)	LC_{50}[2]	7.9	Ciba Additive GmbH 2000
Bluegill (*Lepomis macrochirus*)	Acute (96 hours)	LC_{50}[2]	0.97-1.0	Ciba Additive GmbH 2000
Microorganisms (Bacteria)	Acute (3 hours)	IC_{50}	>100	Ciba Additive GmbH 2000

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

Table 7b. Modelled data for aquatic toxicity

Test organism	Type of test	Endpoint	Value (mg/L)	Reference
Fish	Acute (96 hours)	LC_{50}[1]	0.76[2]	OASIS Forecast 2005
Fish	Acute (96 hours)	LC_{50}	13.77	ECOSAR 2004 (Amines)
Fish	Acute (96 hours)	LC_{50}	11.70	ECOSAR 2004 (Esters)
Fish	Chronic		0.266[2]	ECOSAR 2004 (Amines)
Fish	Chronic (32-33day)		0.76[2]	ECOSAR 2004 (Esters)
Daphnia	Acute (48 hours)	EC_{50}	<0.40[2]	OASIS Forecast 2005
Daphnia	Acute (48 hours)	LC_{50}	1.83	ECOSAR 2004 (Amines)
Daphnia	Acute (48 hours)	LC_{50}	20.20	ECOSAR 2004 (Esters)
Algae	Acute (96 hours)	EC_{50}	1.22	ECOSAR 2004 (Amines)
Algae	Acute (48 hours)	EC_{50}	7.44	ECOSAR 2004 (Esters)
Algae	Chronic		0.33[2]	ECOSAR 2004 (Amines)
Algae	Chronic		2.91[2]	ECOSAR 2004 (Esters)

[1] LC_{50} – The concentration of a substance that is estimated to be lethal to 50% of the test organisms.
[1] EC_{50} – The concentration of a substance that is estimated to cause some effect on 50% of the test organisms.
[2] Model predictions used log D_{ow} of 3.35.
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Aquatic toxicity predictions were also obtained from the various QSAR models (Table 7b). ECOSAR results indicate that PEDA may have an aliphatic amine or ester mode of toxic action and that the substance is potentially moderately to highly hazardous to aquatic organisms (acute $LC/EC_{50} \leq 1.0$ mg/L). The toxicity potential from amines may be mitigated by the stearic hindrance of the tertiary amine moiety. The QSAR results in Table 7b take into account both the possibility of the amine and ester modes of action.

Based on the available toxicity information, it is considered that PEDA has the potential to cause adverse effects in sensitive aquatic organisms at relatively low concentrations.

B - In Other Environmental Compartments

No ecological effects studies were found for this compound in media other than water.

Ecological Exposure Assessment

No data concerning concentrations of this substance in water in Canada have been identified; therefore environmental concentrations are estimated from available information, including estimated substance quantities, release rates, and size of receiving water bodies.

Consumer Release

As PEDA is found in consumer products and can be released to water, Mega Flush, Environment Canada's spreadsheet model for estimating down-the-drain releases from consumer uses was employed to estimate the potential substance concentration in multiple water bodies receiving sewage treatment plant effluents to which consumer products containing the substance may have been released (Environment Canada 2009c). The spreadsheet model is designed to provide these estimates based on conservative assumptions regarding the amount of the substance used and released by consumers.

We assume primary and secondary sewage treatment plant (STP) removal rates to be 0%, consumer use of the substance to be over 365 days/year, and the flow rate at all sites to be relatively low (tenth percentile values). These estimates are made for approximately 1000 release sites across Canada, which account for most of the major STPs in the country.

The equation and inputs used to calculate the predicted environmental concentration (PEC) of PEDA in the receiving water bodies are described in Environment Canada (2009d). A scenario was run assuming a total consumer use quantity of 100 000 kg/year and that approximately 9% of this is lost annually during consumer use.

Using this scenario, the model estimates that the maximum PEC in the receiving water is 0.0064 mg/L.

Industrial Release

The aquatic exposure of PEDA is expected if the substance is released from industrial use to a wastewater treatment plant and the treatment plant discharges its effluent to a receiving water body. The concentration of the substance in the receiving water near the discharge point of the wastewater treatment plant is used as the PEC in evaluating the aquatic risk of the substance.

A site-specific exposure analysis was conducted for the aquatic water compartment at six industrial sites where PEDA was used in high quantities (Environment Canada 2009e). These sites considered were those of the industrial users identified from the companies who responded to the CEPA Section 71 Survey (Environment Canada 2009a). Each user reported an annual quantity of PEDA in the range of 100 to 10 000 kg. These sites are expected to represent realistic worst case release scenarios across Canada based on a general assumption that the quantity released is proportional to the quantity consumed or imported.

In this site-specific exposure analysis, each site includes one facility, one wastewater treatment plant and one receiving water body (Environment Canada 2009f). The PEC in the receiving water was estimated based on the concentration in the wastewater treatment effluent and dilution factors ranging from 2.5 up to 10, depending upon conditions in the receiving water. The concentration in the wastewater treatment effluent was calculated based on an estimate of the fraction of the substance lost from the facility to a local municipal wastewater treatment plant, and of the wastewater treatment plant's removal rate and its effluent flow. The loss fraction was conservatively estimated to be 5%. This loss fraction is expected to represent the upper bound of the losses to wastewater. The effluent flows of the local wastewater treatment plants are proportional to the population served and were in the range of 30 000 to 400 000 m^3 per day.

Based on the above assumptions, the PECs are estimated to be in the range of 0.0002 to 0.0045 mg/L for the industrial sites considered. An assumption for the frequency of release was also used in the estimation which is 250 days/year. As these sites were considered using certain upper bound assumptions, the PEC values obtained in this site-specific analysis are considered to represent the level of exposure under a realistic worst case release scenario in the receiving water near the point of the discharge from the wastewater treatment plant at industrial sites in Canada.

Characterization of Ecological Risk

The approach taken in this ecological screening assessment was to examine scientific and technical information and develop conclusions based on a weight-of-evidence approach and using precaution as required under CEPA 1999. Lines of evidence considered include results from conservative risk quotient calculations, as well as information on persistence, bioaccumulation, toxicity, sources and fate of the substance.

PEDA is expected to be persistent in water, soil and sediment, but it is also expected to have a low bioaccumulation potential. PEDA is not expected to be persistent in air. The relatively high importation volumes of PEDA into Canada, along with information on its uses, indicate potential for widespread release into the Canadian environment. Depending upon the compartment to

which it is released, it will be found mainly in water and soil. It has also been demonstrated to have moderate to high potential for toxicity to aquatic organisms.

A risk quotient analysis, integrating conservative estimates of exposure with toxicity information, was performed for the aquatic medium to determine whether there is potential for ecological harm in Canada. The site-specific industrial scenario (considering the actual receiving water bodies) presented above yielded PECs of ranging from 0.0002 to 0.0045 mg/L (Environment Canada 2009f). A predicted no-effect concentration (PNEC) was derived from the acute toxicity value of 0.97 mg/L for Bluegill (*Lepomis macrochirus*) by dividing this value by an assessment factor of 100 (10 to account for interspecies and intraspecies variability in sensitivity and 10 to estimate a long-term no-effects concentration from a short-term LC_{50}) to give a value of 0.0097 mg/L. The resulting risk quotients (PEC/PNEC) ranged from 0.02 to 0.46. Therefore harm to aquatic organisms is unlikely at industrial sites across Canada. Using a similar PEC/PNEC approach, outputs from the consumer release scenario model indicated that PECs for PEDA are not expected to exceed the PNEC in any of the water bodies receiving wastewater across Canada under low (10th percentile) flow conditions (Environment Canada, 2009b).

This information suggests that PEDA is unlikely to cause ecological harm in Canada.

Uncertainties in Evaluation of Ecological Risk

Gaps in available experimental data were filled through the use of QSARs. There were limited experimental data available for physical and chemical properties, biodegradation and ecotoxicity and QSARs were used to supplement them. Generally there was reasonable agreement between the results from QSAR models and available empirical tests.

There is however uncertainty about persistence in water, and by extension soils and sediment. Only one ready biodegradation study was available, which indicated that the substance is partly degradable. Since the empirical result was not definitive, it was concluded that the half-life of the substance is likely to be > 182 days, based mainly on QSAR predictions.

Although experimental acute toxicity data for fish, *Daphnia* and microorganisms were available, no chronic studies were identified. Empirical chronic data would be especially useful in evaluating the toxicity of this substance since it is expected to be persistent in the environment. An assessment factor was used in determining the chronic no-effect concentration, in part to address this data gap.

The lack of measured environmental concentrations in Canada was addressed by evaluating the risk based on predicted concentrations in water near industrial point sources. Conservative assumptions were made using models to estimate concentrations in such receiving water bodies. Conservative assumptions were also made in modelling down-the-drain releases resulting from consumer use of products containing this substance.

Potential to Cause Harm to Human Health

Exposure Assessment

Environmental Media and Food

In the published literature, there were no empirical data identified regarding measured concentrations of PEDA 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 PEDA to air, water, or soil (Environment Canada 2009a). In the absence of monitoring and release data, ChemCAN, a Canadian-specific environmental exposure model (ChemCAN 2003), was used to predict concentrations in environmental media. The estimated concentrations were based on the Canadian import quantity of PEDA in 2006 (100 000 kg) and the loss percentages by the Mass Flow tool by Environment Canada (see Table 3) (Environment Canada 2009b). Conservative upper-bounding daily intakes of PEDA for the general population in Canada were derived based on the estimated environmental concentrations resulting in the order of nanograms per kg-bw (kilogram of body weight) per day.

PEDA is not approved for any food additive use in Canada and no studies were identified reporting the presence of PEDA in food. However, PEDA is used in coatings for large containers for transporting and holding dry foods; this application leads to negligible exposures (2009 email from Food Directorate, Health Canada, to Risk Management Bureau, Health Canada; unreferenced). Confidence in the exposure estimates from environmental media is low in the absence of empirical data, but confidence is high that these exposure estimates are conservative.

Consumer Products

PEDA functions as an antioxidant and an ultraviolet light stabilizer in products and provides protection against photodegradation. As mentioned in the Uses section of this document, some consumer products in the Canadian consumer market were identified that contain PEDA: auto interior protectants, waterborne semi-transparent stain products, aerosol solventborne paints and window sealants (TopSeal 2008; Environment Canada 2009a; 2009 email from Risk Management Bureau, Health Canada, to Risk Assessment Bureau, Health Canada; unreferenced). These products are expected to contribute to the exposure to PEDA in the general population of Canada; the estimated exposure levels are summarized in Table 8 and the details of the consumer product exposure assessment is presented thereafter.

Table 8. Estimated exposures[1] to PEDA from consumer products

Product	PEDA maximum concentration (% by weight)	Mean event concentrations (mg/m^3)	Acute dermal exposure (mg/kg-bw)
Auto interior protectant	1	0.004[2]	0.117
Waterborne semi-transparent stain	0.23	NA	0.117
Aerosol paint	0.3	NA	0.0635
Sealant	1	Neg	0.211

Abbreviation: NA, not applicable; Neg, negligible.
[1] Body weight assumed to be 70.9 kg (Health Canada 1998)
[2] Equivalent acute inhalation dose = 3.91×10^{-5} mg/kg-bw

The maximum concentration of PEDA is 1% by weight in auto interior protectants (based on available information). Inhalation exposure was assumed to occur during application of the product (e.g. from spraying). Using ConsExpo 4.1 (ConsExpo 2006), the mean atmospheric concentration of PEDA inside a medium-sized car during application was estimated to be 0.004 mg/m^3, which translates to an associated acute dose of 3.91×10^{-5} mg/kg-bw (refer to Appendix 2). Post-application exposure (i.e. due to volatilization of the product from treated surfaces) is expected to be minimal because the vapour pressure of PEDA is very low. Dermal exposure is expected to occur during normal use of the product (e.g.wiping the product from surfaces with a cloth during the application process) and was estimated to be 0.117 mg/kg-bw (refer to Appendix 3). Estimated exposures to PEDA from the use of auto interior protectants are considered to be overestimates as these values were based on conservative assumptions and on the maximum concentration of PEDA in these products (i.e. 1% by weight).

PEDA is also an ingredient in some waterborne semi-transparent stain products and aerosol solvent borne paints intended for outdoor use. Inhalation exposure from outdoor uses is considered minimal. Estimates of dermal exposures from these uses were derived using ConsExpo 4.1 (ConsExpo 2006). Dermal exposures were estimated to be 0.117 mg/kg-bw for the usage of a waterborne stain and 0.0635 mg/kg-bw for the usage of an aerosol paint (refer to Appendix 2).

PEDA is also found in sealants (TopSeal 2008; Environment Canada 2009a). Exposures were estimated using ConsExpo 4.1. The dermal exposure was estimated to be 0.211 mg/kg-bw (refer to Appendix 2), while inhalation exposure was estimated to be negligible.

Confidence in the numerical results of the exposure estimations from consumer products is low to moderate in the absence of exposure data of PEDA. The estimates presented are considered to be overestimates as they are based on conservative assumptions. Furthermore, the degradation via hydrolysis of PEDA in coatings into carboxylate salts and alcohols, thereby reducing PEDA content, was not considered (Haacke et al. 1999). Therefore, there is confidence that the exposure estimates are conservative and upper-bounding.

Health Effects Assessment

Structures and identities of relevant analogues of PEDA are presented in Appendix 3. The available health effects information for PEDA and its analogues is summarized in Appendix 4.

Very limited toxicological data was identified for PEDA. An *in vitro* mutagenicity assay was negative in *Salmonella typhimurium* at various dose levels either with or without metabolic activation (European Commission 2000). The acute toxicity of PEDA was reported to have an oral LD_{50} between 2369 to 3920 mg/kg-bw in rats (European Commission 2000) and a dermal LD_{50} greater than 2000 mg/kg-bw in rabbits (Eastman Kodak 1992). A test article containing an

unknown amount of PEDA and other chemicals was reported to be a dermal irritant when applied to rabbits, causing sever irritation, ulcers and blanching 24-72hrs following topical application of 0.5 ml (Eastman Kodak 1992). A mixture containing 70-80% PEDA and 15-25% of a close structural analogue (Tinuvin 765, see Appendix 3) was reported as a strong skin sensitizer in guinea pigs (Ciba-Geigy 1992a, 1992b). In a study investigating dermal sensitization in humans, a test mixture containing PEDA and eleven other substances at unknown levels produced intense responses typical of allergic contact dermatitis in all test subjects (TSCAT 1992). While the contribution of skin sensitization from other components in the mixture can not be excluded in the human study, the positive results in guinea pigs suggest that high concentrations of PEDA can have skin sensitizing properties. Predictions for the toxicity of PEDA using five different (Q)SAR packages (DEREK (2008), TOPKAT (2004), CASETOX (2008), Toxtree (2009) and Leadscope Model Applier (2009)) gave results that were either negative, inconclusive, or were out of the domain of applicability for the models.

Since limited health effects information were available for PEDA, relevant information on analogue substances was also considered. Two suitable analogues were identified based on chemical similarity and availability of empirical hazard data: CAS RN 52829-07-9 (bis-TMPS), CAS RN 82919-37-7 (Tinuvin 765) and CAS RN 122586-52-1 (Tinuvin 123) (see Appendix 3 for structures and similarity). The toxicity data for bis-TMPS and Tinuvin 123 are largely summarized from previous evaluations by the OECD (2008) and the Australian National Industrial Chemicals Notification and Assessment Scheme (NICNAS 1992), while additional studies not cited in these sources have also been considered where relevant. The only empirical data identified for Tinuvin 765 was a guinea pig skin sensitization study tested as a mixture with PEDA (Ciba-Geigy 1992a, 1992b) and is already described in the preceding section. A summary of the available hazard data for bis-TMPS and Tinuvin 123 is presented below.

With respect to genotoxicity, studies reported bis-TMPS to be negative both for mutagenicity in multiple strains of *Salmonella thyphimurium* and for chromosomal aberrations in cultured human lymphocytes either with or without metabolic activation (OECD 2008). Similarly, Tinuvin 123 was negative for mutagenicity in both *Salmonella typhimurium* and *Eschericia coli* with or without metabolic activation and did not induce micronuclei in bone marrow of mice (Ciba-Geigy 1990a, b).

Acute toxicity of the two analogues showed good correlation with those for PEDA with rat oral LD_{50}s of > 2000 mg/kg-bw (Tinuvin 123) and 3700 mg/kg-bw (bis-TMPS) and rat dermal LD_{50}s of > 2000 mg/kg-bw (Tinuvin 123) and > 3170 mg/kg-bw (bis-TMPS). The rat inhalation LC_{50} (4hr) was 500 mg/m^3 while various clinical effects were also observed at 232 mg/m^3 (the lowest concentration tested) (Ciba-Geigy 1989a, b; OECD 2008). No skin sensitization response was observed in guinea pigs for either bis-TMPS (OECD 2008) or Tinuvin 123 (NICNAS 1992).

In a short-term oral gavage study in rats, doses of bis-TMPS at 600 mg/kg-bw per day and above resulted in clinical observations suggestive of neurological effects (eyelid ptosis, muscular hypotonia, sedation) including neurohistochemical changes at 1000 mg/kg-bw per day (decreased levels of noradrenaline content of the superior cerical ganglia) (Ciba-Geigy 1993). Studies of bis-TMPS in Xenopus oocytes showed dose-dependent inhibition of nicotinic acetylcholine receptors while repeated intraperitoneal injections in rats indicated histological

changes in mycardial cells as well as altered urinary noradrenaline levels compared to controls (OECD 2008). These effects are consistent with similar effects (eyelid ptosis, pupil dilation) observed in rats following repeated oral exposures to TMP (CASRN 2403-88-5, OECD 2002), a known hydrolysis product of the ester bond in bis-TMPS (OECD 2008). It has been shown that the degradation of PEDA in coatings can yield similar hydrolysis products as those of bis-TMPS (Haacke et al. 1999). For the other analogue Tinuvin 123, an acute subcutaneous study in mice did not indicate any dopaminergic neurological effects (Xiao et al. 2000).

Effects on the liver were also observed in short-term and subchronic studies for analogues. In short-term studies, when bis-TMPS was administered to rats via gavage at 0, 50, 200 or 600 mg/kg-bw per day, decreased body weight gain and gross pathology (distensions of small intestine in some male and female animals) were observed in mid- and high-dose groups (OECD 2008). When Tinuvin 123 was orally administered to rats at 0, 10, 100 or 1000 mg/kg-bw per day for the same dose term, significant dose related increase in prothrombin time and total bilirubin levels in males in mid-dose group (and hepatic extramedullary haematopoiesis in high-dose group were observed (Ciba–Geigy 1991). Based on the available information, NICNAS suggested that the liver is the potential target organ for Tinuvin 123 (NICNAS 1992). In oral subchronic studies for bis-TMPS, the lowest-observed-effect levels (LOELs) for decreased bodyweight gain were identified as 29 mg/kg-bw per day in female rats, 261 mg/kg-bw per day in male rats and about 150 mg/kg-bw per day in both sexes of dogs. Liver hypertrophy was also reported in test dogs at this dose level (OECD 2008).

In a one-generation reproductive toxicity study for bis-TMPS, both sexes of rats were dosed at 0, 3, 30 or 300 mg/kg-bw per day by gavage. Decreased body weight gain, increased spleen (males only) and uterus weights were observed in parental animals at 300 mg/kg-bw per day, thus the no-observed-effect level (NOEL) for parental (systemic) toxicity was established to be 30 mg/kg bw per day. The NOEL for reproductive toxicity (fertility) was derived to be ≥ 300 mg/kg-bw per day due to the absence of effects at the highest tested dose while the LOEL for developmental toxicity was established at 300 mg/kg-bw per day based on slightly reduced pup weight during lactation (OECD 2008).

The range of LOELs is summarized below for the above repeated-dose studies on the two analogues of PEDA (all oral studies; no repeated-dose inhalation or dermal studies were indentified for Tinuvin 123 or bis-TMPS). The lowest oral short-term LOELs identified ranged from 100 mg/kg-bw per day (NOEL = 10 mg/kg-bw per day) for Tinuvin 123 in rats (increased prothrombin time and total bilirubin, extramedulary hematopoiesis, Ciba-Geigy 1991) to 200 mg/kg-bw per day (NOEL = 50 mg/kg-bw per day) for bis-TMPS in rats (decreased body weight gain and distension of small intestine; OECD 2008). The lowest oral sub-chronic LOELs identified ranged from ≤ 29 mg/kg-bw per day (lowest tested dose) for bis-TMPS in rats (decreased body weight gain, OECD 2008) to150 mg/kg-bw per day (NOEL = 80 mg/kg-bw per day) for bis-TMPS in dogs (decreased body weight gain, liver hypertrophy, OECD 2008). A developmental oral LOEL of 300 mg/kg-bw per day (NOEL of 30 mg/kg-bw per day) was also reported in rat pups (decreased pup weight), however, a decrease in maternal weight at this dose level indicated maternal toxicity may have contributed to the lower pup weights (OECD 2008).

No chronic/carcinogenicity studies were available for PEDA and the two analogues Tinuvin 123, and bis-TMPS. The confidence in the toxicological dataset for PEDA is low.

Characterization of Risk to Human Health

Although there were no chronic/carcinogenic studies available for PEDA or the two analogues (Tinuvin 123 and bis-TMPS), the lack of mutagenicity observed in studies for PEDA is supported by similar negative genotoxicity profile for both Tinuvin 123 and bis-TMPS as well as results from (Q)SAR predictions on mutagenicity and carcinogenicity for PEDA. Therefore, the focus of the characterization of risk to human health in this assessment is based on non-cancer effects.

Acute inhalation and dermal exposure during use of consumer products were determined to be the most likely exposure scenarios for the general population. Exposure to PEDA from environmental media is considered to be negligible. Single event dermal exposure from use of consumer products was estimated to be the highest (0.211 mg/kg-bw) for use of sealants. Dermal exposure is several orders of magnitude below the dermal LD_{50} values for PEDA and its analogues. Furthermore, assuming 100% dermal absorption, comparison of exposure via the dermal route with the lowest LOEL among the short-term oral studies conducted with an analogue (Tinuvin 123, LOEL of 100 mg/kg-bw/day, Ciba-Geigy 1991) results in a margin of exposure of approximately 500. This margin of exposure is considered adequate to account for uncertainty in the hazard and exposure database for the dermal route. Although high concentrations of PEDA (70 – 80%) have demonstrated skin sensitization in guinea pigs, the relevance of this effect is uncertain at the much lower concentrations in consumer products (< 1%) where there is a potential exposure for the general population.

Characterization of exposure indicated that application of auto interior protectant is likely to result in the highest level of inhalation exposure to PEDA, with an estimated mean air concentration of 0.004 mg/m^3. This exposure is several orders of magnitude below the acute inhalation effect level of 232 mg/m^3 for the analogue bis-TMPS based on respiratory effects in rats following 4 hours exposure (OECD 2008). The mean air concentration of 0.004 mg/m^3 corresponds to a systemic exposure of 3.91×10^{-5} mg/kg-bw. Comparison of this value to the above-noted LOEL of 100 mg/kg-bw per day results in a margin of exposure of several orders of magnitude. These margins are considered adequate to address uncertainties in the health effects and exposure databases, including suggestive neurologic effects observed for the analogue bis-TMPS at levels of 600 mg/kg-bw per day.

Uncertainties in Evaluation of Risk to Human Health

Due to the limited health effects data available for PEDA, the confidence in the toxicological dataset is considered to be low; however data from analogues were available to characterize human health effects for PEDA. There is uncertainty associated with the use of analogues to characterize human health effects. However, the use of the lowest effect level from a short-term oral toxicity study to characterize risk from an acute exposure is considered conservative. There are also uncertainties with using an effect level from an oral study to characterize risk from

dermal and inhalation exposures; however the assumption of complete absorption is considered conservative. Although there are uncertainties in exposure characterization, estimates are considered to be overestimates as these values were based on conservative assumptions and on the maximum concentration of PEDA in these products (i.e. 1% by weight), and degradation by hydrolysis of PEDA was not considered, which increases confidence in the overall risk characterization.

Conclusion

Based on the information presented in this final screening assessment, it is concluded that PEDA is not 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 or that constitute or may constitute a danger to the environment on which life depends. Additionally, PEDA meets the criteria for persistence but does not meet the criteria for bioaccumulation as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Based on the information presented in this final screening assessment, it is concluded that PEDA 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 PEDA does not meet any of the criteria under section 64 of CEPA 1999.

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.

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Appendix I – Model Inputs Summary Table

	Phys-Chem/Fate	**Fate**	**Fate**	**PBT Profiling**	**Ecotoxicity**
Model Input Parameters	EPIWIN Suite (all models, including: AOPWIN, KOCWIN, BCFWIN BIOWIN and ECOSAR)	EQC (required inputs are different if Type I vs. Type II chemical)	Arnot-Gobas BCF/BAF Model	Canadian-POPs (including: Catabol, BCF Mitigating Factors Model, OASIS Toxicity Model)	Artificial Intelligence Expert System (AIES)/ TOPKAT/ ASTER
SMILES Code	O=C(CCCCCCCCC(=O)OC1CC(N(C(C1)(C)C)C)(C)C)OC2CC(N(C)C(C2)(C)C)(C)C			O=C(CCCCCCCCC(=O)OC1CC(N(C(C1)(C)C)C)(C)C)OC2CC(N(C)C(C2)(C)C)(C)C	O=C(CCCCCCCCC(=O)OC1CC(N(C(C1)(C)C)C)(C)C)OC2CC(N(C)C(C2)(C)C)(C)C
Molecular weight (g/mol)		II 508.79			
Data temperature (ºC)		II 20-25			
Log K_{aw} (Air-water partition coefficient; dimensionless)		II $3.13x10^{-10}$)			
Log K_{ow} (Octanol-water partition coefficient; dimensionless)	6.92	II	3.35	3.35	
Log D (distribution coefficient ; dimensionless)	3.35	II	3.35		
Log K_{oc} (Organic carbon-water partition coefficient – L/kg)		II 1.94			
Water solubility (mg/L)	29.8; 0.06	II			
Soil-water partition coefficient (L/kg)[1]		II 1.88			
Sediment-water		II			

partition coefficient (L/kg)[1]		3.768			
Suspended particles-water partition coefficient (L/kg)[1]		II 18.84			
Fish-water partition coefficient (L/kg)[2]		II 17			
Aerosol-water partition coefficient; dimensionless[3]		II 100			
Half-life in air (days) [4]	1.603				
Half-life in water (days)		II 4320			
Half-life in sediment (days)		II 38880			
Half-life in soil (days)		II 8640			
Metabolic rate constant (1/days)					

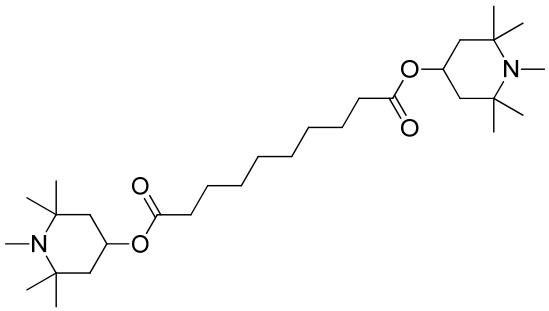
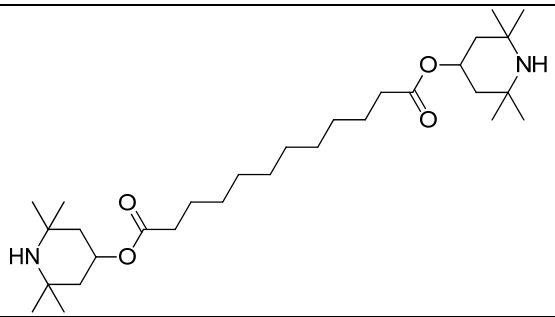
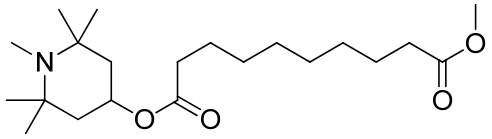
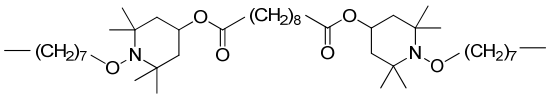
[1] derived from K_{oc} value of 66.5 at pH 7 (ACD/pK_aDB 1994-2009)
[2] derived from BCF at pH 7 (ACD/pK_aDB 1994-2009)
[3] default value
[4] based on 12-h day (i.e., 1.298 h)

Appendix II – Exposure Estimations

Consumer product	Assumptions	Estimated exposure
Auto interior protectant	Concentration: <1% (based on available information). Inhalation exposure is expected during application of the product (e.g. from spraying). Dermal exposure is expected to occur as the consumer, using a cloth, wipes the product from surfaces during application. **Inhalation route** (estimated using ConsExpo 4.1) - Exposure type: exposure to spray (RIVM 2006) - Auto interior volume: 2.4 m^3 (VERSAR 1986) - Ventilation rate: 12.5 h^{-1} (VERSAR 1986) - Mass generation rate: 1.5 g/sec (RIVM 2006) - Spray duration: 1.38 min (VERSAR 1986) - Airborne fraction: 1 (RIVM 2006) - Weight fraction of non-volatile: 0.36 (product-specific) - Density of non-volatile: 1.5 g/cm^3 (RIVM 2006) - Auto interior height: 1 m (estimated) - Inhalation cut-off diameter: 15 μm (RIVM 2006) - Inhalation rate = 16.2 m^3/d (Health Canada 1998) **Dermal route** The mass of product on skin per event, M_{skin}, was estimated as shown below: $M_{skin} = SA_{skin} \times FT \times \rho$ $M_{skin} = (400\ cm^2) \times (2.03 \times 10^{-3}\ cm) \times (1.018\ g/cm^3)$ $M_{skin} = 0.827\ g = 827\ mg$ where: SA_{skin} = skin area exposed = 400 cm^2 (both palms) (VERSAR 1986) FT = film thickness on skin = 2.03×10^{-3} cm (VERSAR 1986) ρ = density of product = 1.018 g/cm^3 (product-specific) Dermal exposure during application was estimated using the following assumptions: WF = weight fraction of PEDA in product = 0.01 EV = number of events per day = 1 (VERSAR 1986) (but used on average twice a year) AF = absorption factor = 1 BW = 70.9 kg (Health Canada 1998) Acute dermal exposure $= \frac{M_{skin} \times WF \times EV \times AF}{BW}$ $= \frac{827\,mg \times 0.01 \times 1 \times 1}{70.9\,kg}$ $= 0.117\,mg/kg\text{–}bw$	**Inhalation** Mean concentration of PEDA inside the car during application of product = 0.004 mg/m^3 Acute dose = 3.91×10^{-5} mg/kg-bw **Dermal** Acute dose = 0.117 mg/kg-bw

Water-borne semi-transparent stain	Concentration: <0.23% (2009 email from Risk Management Bureau, Health Canada, to Risk Assessment Bureau, Health Canada; unreferenced) **General assumptions** - Exposure frequency: 1 time/year (RIVM 2007a) - Body weight: 70.9 kg (Health Canada 1998) **Dermal route** (estimated using ConsExpo 4.1) - Exposure type: direct dermal contact with product: constant rate (RIVM 2007a) - Contact rate: 30 mg/min (RIVM 2007a) - Release duration: 7200 sec (RIVM 2007a)	**Dermal** Acute applied dose = 0.117 mg/kg-bw
Aerosol solvent-borne paint	Concentration: 0.01 – 0.30% (2009 email from Risk Management Bureau, Health Canada, to Risk Assessment Bureau, Health Canada; unreferenced) **General assumptions** - Exposure frequency: 2 times/year (RIVM 2007a) - Body weight: 70.9 kg (Health Canada 1998) **Dermal route** (estimated using ConsExpo 4.1) - Exposure type: direct dermal contact with product: constant rate (RIVM 2007a) - Contact rate: 100 mg/min (RIVM 2007a) - Release duration: 900 sec (RIVM 2007a)	**Dermal** Acute applied dose = 0.0635 mg/kg-bw
Sealant	Concentration: 1%% (TopSeal 2008) **General assumptions** - Exposure frequency: 3 times/year (RIVM 2007b) - Body weight: 70.9 kg (Health Canada 1998) **Dermal route** (estimated using ConsExpo 4.1) - Exposure type: direct dermal contact with product: constant rate (RIVM 2007) - Exposed area: 2 cm^2 (RIVM 2007b) - Contact rate: 50 mg/min (RIVM 2007b) - Release duration: 1800 sec (RIVM 2007b)	**Dermal** Acute applied dose = 0.211 mg/kg-bw

Appendix III: PEDA and Its analogues Identified

Name / CAS RN / Short Name	Structure	Molecular Formula / Molecular weight (g/mol) / Mass Solubility	Analogue Identification Method (% similar)
Decanedioic acid, 1,10-bis(1,2,2,6,6-pentamethyl-4-piperidinyl) ester 41556-26-7 **PEDA**		**$C_{30}H_{56}N_2O_4$** MW: 508.7824 Slightly Soluble (0.013 mol/L) at pH 7 Temp: 25 °C	
Decanedioic acid, 1,10-bis(2,2,6,6-tetramethyl-4-piperidinyl) ester 52829-07-9 **bis-TMPS**		**$C_{28}H_{52}N_2O_4$** MW: 480.729 Slightly Soluble (5.3 g/L) at pH 7 Temp: 25°C	SciFinder: 89%
Decanedioic acid, 1-methyl 10-(1,2,2,6,6-pentamethyl-4-piperidinyl) ester 82919-37-7 **Tinuvin 765**		**$C_{21}H_{39}NO_4$** MW: 369.542 Slightly soluble (4.1 g/L) at pH 7 Temp: 25°C	ChemID: 89%
Decanedioic acid, 1,10-bis[2,2,6,6-tetramethyl-1-(octyloxy)-4-piperidinyl] ester 122586-52-1 **Tinuvin 123**		**$C_{44}H_{84}N_2O_6$** MW: 737.15 Sparingly Soluble (5.9E-7 g/L) at pH 7 Temp: 25 °C	SciFinder : 83%

Appendix IV – Summary of health effects information for PEDA and its analogues

Endpoint	Lowest effect levels[1]/Results
Laboratory animals and *in vitro*	
Acute toxicity	**PEDA (CAS RN 41556-26-7)** **Lowest oral LD_{50}** (rat) = 2369 – 3920 mg/kg-bw (European Commission 2000). **Dermal LD_{50}** (rabbit) > 2000 mg/kg-bw (Eastman Kodak 1992). **Tinuvin 123 (analogue, CAS RN 122586-52-1)** **Oral LD_{50}** (rat) > 2000 mg/kg-bw (Ciba–Geigy 1989a). **Dermal LD_{50}** (rat) > 2000 mg/kg-bw (Ciba–Geigy 1989b). **bis-TMPS (analogue, CASRN 52829-07-9)** **Oral LD_{50}** (rat) = 3700 mg/kg bw (OECD 2008). **Dermal LD_{50}** (rat) > 3170 mg/kg bw (OECD 2008). **Inhalation LC_{50}** (rat, 4h) = 500 mg/m^3 Various effects were observed in all tested groups (dyspnea, salivation, trismus, tremor and sedation) with severity increasing in dose-dependent manner. The lowest tested concentration from this study was 232 mg/m^3 (OECD 2008).

Endpoint	Lowest effect levels[1]/Results
Short-term repeated-dose toxicity	**PEDA (CAS RN 41556-26-7)** No short-term studies were identified. **Tinuvin 123 (analogue, CAS RN 122586-52-1)** **Oral LOEL** = 100 mg/kg-bw per day (NOEL = 10 mg/kg-bw per day) based on statistically significant dose-related increase in prothrombin time and total bilirubin level in mid- and high-dose males and in high-dose females when both sexes of rats [Tif: RAIf (SPF), 8 per group] were exposed to Tinuvin 123 by gavage at 0, 10, 100 or 1000 mg/kg-bw per day for 4 weeks. Hepatic extramedullary haematopoiesis was observed in animals in all dose groups with a significant incidence and severity observed in high dose males. NICNAS suggested the liver to be a potential target organ of toxicity based on the hepatic effects (Ciba–Geigy 1991, cited in NICNAS 1992). **Subcutaneous route:** Male C57Bl/6 mouse (12 per group) was administered subcutaneously (twice, 16 h apart) with Tinuvin 123 at doses of 0, 2, 20 or 200 mg/kg-bw. Low dose group exhibited no changes in striatal dopamine or metabolite concentrations compared with control. A moderate loss of striatal dopamine (31 and 38%) but unchanged concentrations of dopamine metabolites and neurotransmitters were observed in mid- and high-dose groups. The total numbers of tyrosine hydroxylase-immunoreactive neurons in the entire substantia nigra were equivalent to control in all dose groups (Xiao et al. 2000). **bis-TMPS (analogue, CAS RN 52829-07-9)** **Oral LOEL** = 200 mg/kg-bw per day (NOEL = 50 mg/kg-bw per day) based on decreased body weight gain and gross pathology (distensions of small intestine in some male and female animals) in both sexes of rats (strain not specified, 10 per group) when exposed by gavage to 0, 50, 200 or 600 mg/kg-bw per day of bis-TMPS for 28-days (OECD 2008). **Oral LOEL** = 600 mg/kg-bw per day (lowest tested dose, a NOEL was not established). Both sexes of Tif: RAIf (SPF) rats (5 per group) were exposed to BIS-TMPS by single daily oral gavage at 0, 600, 1000 and 2000 mg/kg-bw per day for 4 weeks. All rats from the high dose group died during the study while mortality in the mid-dose group was 2/10. No treatment-related macrosopic observations were noted while nearly all treated rats from the mid- and low-dose groups displayed histologically increases in eosinophilic and neutrophilic leucocytes in the spleen, blood vessels, and perivascular tissues of the lungs. Neurohistochemical examination neurons and ganglia from a sample of the 1000 mg/kg-bw/day group showed that the average noradrenaline content of the principal perikarya of the superior cervical ganglion of treated rats was distinctly lower than in the controls (Ciba–Geigy 1993).

Endpoint	Lowest effect levels[1]/Results
Sub-chronic repeated-dose toxicity	**PEDA (CAS RN 41556-26-7)** No sub-chronic studies were identified. **Tinuvin 123 (analogue, CAS RN 122586-52-1)** No sub-chronic studies were identified. **bis-TMPS (analogue, CAS RN 52829-07-9)** **Oral LOEL** = 29 mg/kg-bw per day in females (lowest tested dose) and or 261 mg/kg-bw per day in males based on decreased body weight gain. Sprague-Dawely rats (20 per sex per dose + 5 per sex controls and high dose recovery for 4 weeks) were exposed to bis-TMPS in the diet for 90 days at concentrations of 0, 400, 1300, or 4000 ppm (reported as equivalent to 0, 26, 80 or 261mg/kg-bw per day in males and 0, 29, 90 or 277 mg/kg-bw per day in females). Decreased body weight gain was observed in males (high dose, 17% decrease from control) and females at all tested doses (13%, 23%, 24% lower than controls at low-, mid- and high-doses, respectively). Changes in organ weights were also reported in mid-dose females and both sexes at the high-dose; however the actual incidences were not indicated in the secondary source. No effects were observed in the recovery groups. No other treatment effects were observed for any other endpoints measured (OECD 2008). **Oral LOEL** = 150-155 mg/kg-bw per day (NOEL = 69-78 mg/kg-bw per day) for males and females respectively based on decreased body weight gain and liver hypertrophy when both sexes of dogs (strain not specified, 4 per sex per group) were exposed to 0, 800, 2600, or 5000/8000[2] ppm bis-TMPS in the diet for 90 days (reported to be equivalent to 0, 27, 69 or 150 mg/kg-bw per day in males and at 0, 27, 78 or 155mg/kg-bw per day in females). After 13 weeks, decreased body weight changes were observed in the high dose group (11 and 16% of controls for males and females, respectively). However, it should be noted that poor palatability of feed in the high-dose of 8000 ppm (which was reduced ultimately to 5000 ppm) limited feed intake and likely contributed to the decreased weight gain in the high-dose groups. Minimal hepatic periportal hypertrophy was also reported in the high dose group, however no changes were observed following a 4 week recovery. The OECD considered 2600 ppm (69-78 mg/kg-bw per day) to be the NOEL for this study based on decreased body weight and liver hypertrophy (OECD 2008). **Oral LOEL** = 300 mg/kg-bw per day (NOEL = 30 mg/kg-bw per day) based on decreased body weight gain and increased spleen (in males only) were observed in parental animals in a one-generation reproduction toxicity study. For details see reproductive and developmental toxicity section below (OECD 2008).

Endpoint	Lowest effect levels[1]/Results
Reproductive and developmental toxicity	**PEDA (CAS RN 41556-26-7)** No reproductive or developmental toxicity studies were identified. **Tinuvin 123 (analogue, CAS RN 122586-52-1)** No reproductive or developmental toxicity studies were identified. **bis-TMPS (analogue, CAS RN 52829-07-9)** **Developmental Oral LOEL**= 300 mg/kg-bw per day (NOEL= 30 mg/kg-bw per day) based on decreased pup weight. **Reproductive Oral NOEL** > 300 mg/kg-bw per day (no effects observed at the highest tested dose). In a one-generation reproduction-developmental toxicity study, parents of both sexes of rats (strain not specified, 24 per group) exposed to bis-TMPS at 0, 3, 30 or 300 mg/kg-bw per day by gavage: males were exposed 10 weeks before mating, during mating and up to termination (after delivery of litters), while females were exposed two weeks before mating, during post-coitum and during 20 to 22 days of lactation. Effects observed in the parents are reported for this in subchronic section. There was no treatment related effect on fertility reported for this study. Pups of both sexes exhibited a statistically significant decreased body weight on post-gestational days 14 (90% of controls) and 21 (89% of controls). No other treatment related effects in pups were observed for the measured endpoints (viability, clinical and macroscopic examination) (OECD 2008). Effects on the parental animals were reported in the section of Sub-chronic Studies.
Genotoxicity and related endpoints: *in vivo*	**Tinuvin 123 (analogue, CAS RN 122586-52-1)** **Negative:** Micronuclei formation in bone marrow cells after single intraperitoneal administration of 5000 mg/kg of the test substance in both sexes of Tif: MAGf (SPF) mice (Ciba–Geigy 1990b). No *in vivo* genotoxicity studies were identified for PEDA (CAS RN 41556-26-7) and bis-TMPS (analogue, CAS RN 52829-07-9).

Endpoint	Lowest effect levels[1]/Results
Genotoxicity and related endpoints: *in vitro*	**PEDA (CAS RN 41556-26-7)** **Negative:** *Salmonella typhimurium* (strains not specified) with and without metabolic activation (European Commission 2000). **Tinuvin 123 (analogue, CAS RN 122586-52-1)** **Negative:** *Salmonella typhimurium* (TA98, TA100, TA1535 and TA1537 strains) and *Escherichia coli* (WP2uvrA strain) with or without activation (Ciba–Geigy 1990a). **bis-TMPS (analogue, CAS RN 52829-07-9)** **Negative:** *Salmonella typhimurium* strains TA100, TA1535, TA98 and TA 1537 with and without metabolic activation (OECD 2008). **Negative:** Chromosomal aberration test with human lymphocytes was negative with and without metabolic activation (OECD 2008).
Sensitization	**PEDA (CAS RN 41556-26-7)** Humans Closed-patch test was carried out with 2 male and 8 female human volunteers using a mixed test material involving unknown amount of PEDA; test material applied on the right arm of test subjects; 4 days per week for 4 weeks followed by a challenge phase (4 days per week for 1 week, patch was removed 2 hours following application). Intense responses typical of allergic contact dermatitis were noted in all ten subjects (TSCAT 1992). In skin sensitisation tests, when guinea pigs **were** exposed to various concentrations of TK 12576 (contains 70-80% of CAS RN 41556-26-7 and 15-25% of CAS RN 82919-37-7)), positive reaction, including erythema, edema and allergic reactions were reported. TK 12576 was concluded as a strong sensitizer (Ciba–Geigy 1992a, b).
Irritation	**PEDA (CAS RN 41556-26-7)** **Skin irritation:** 0.5 mL of mixed test material containing an unknown amount of PEDA was applied on two test sites of the skin of six New Zealand Rabbits. After 24 and 72 hours application, severe irritations (erythema and edema) were observed, ulcers and blanching (loss of skin colour) were also reported. Test article was considered as a "primary dermal irritant" (Eastman Kodak 1992). **Eye irritation:** 0.1 mL of mixed test material containing an unknown amount of PEDA was applied to one eye of each New Zealand White rabbits (9 animals tested). Iritis to a lesser degree corneal opacity and conjunctivitis were observed. Test article was considered as a "mild ocular irritant" (Eastman Kodak 1992).
Human	

Endpoint	**Lowest effect levels[1]/Results**
No other effects in humans were identified for PEDA or its analogues.	

[1] LC_{50}, median lethal concentration; LD_{50}, median lethal dose; LOAEL, lowest-observed-adverse-effect level; LOEL, lowest-observed-effect level; NOEL, no-observed-effect level.
[2] High-dose group changed from 8000 to 5000 ppm starting at week 7.