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Screening Assessment for the Challenge

Benzenamine, 4,4′-[(1-methylethylidene)bis(4,1-phenyleneoxy)]bis-

(BAPP)

Chemical Abstracts Service Registry Number 13080-86-9

Environment and Climate Change Canada
Health Canada

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Synopsis

Pursuant to section 74 of the *Canadian Environmental Protection Act, 1999* (CEPA), the Minister of the Environment and the Minister of Health have conducted a screening assessment of benzenamine, 4,4'-[(1-methylethylidene)bis(4,1-phenyleneoxy)]bis, hereinafter referred to as BAPP. The Chemical Abstracts Service Registry Number (CAS RN[1]) for BAPP is 13080-86-9. This substance was identified as a priority for assessment as it met categorization criteria under subsection 73(1) of CEPA.

BAPP is not naturally occurring in the environment. In 2006, 250 kg of BAPP were imported into Canada for use mainly as an additive in a corrosion-inhibiting structural adhesive bonding primer for aerospace applications. In 2010, the quantity of BAPP in commerce in Canada was approximately 500 kg.

According to reported use patterns and certain assumptions, most of the substance (66.5%) is sprayed onto aircraft parts and is chemically transformed after subsequent curing. Some proportions that do not reach aircraft parts are estimated to be released to sewer following treatment at a hazardous waste treatment facility (4.5%), to air (1.5%) and to landfill/incineration (27.5%). BAPP has low solubility in water, negligible volatility and a tendency to partition to particles because of its hydrophobic nature. For these reasons, this substance is expected to ultimately be found mostly in sediments or in soil depending on the medium to which it is released. It is not expected to be significantly present in the other media. It is also not expected to be subject to long-range atmospheric transport.

On the basis of the results of structure-activity relationship predictions, BAPP is not expected to degrade quickly in the environment. It persists in water, soil and sediments. This substance also has the potential to accumulate in organisms and may biomagnify in trophic food chains. In addition, modelled acute and chronic aquatic toxicity values indicate that the substance is highly hazardous to aquatic organisms. It has also been identified as having a strong estrogenic receptor binding potential.

Given the small amount of BAPP imported into Canada, its use patterns and the handling and disposal practices currently in place, ecological exposure to this substance in Canada resulting from commercial activity is expected to be very low. Considering all available lines of evidence presented in this screening assessment, there is low risk of harm to organisms and the broader integrity of the environment from BAPP. It is concluded that BAPP does not meet the criteria under paragraphs 64(*a*) or (*b*) of CEPA

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as it 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.

Very little empirical health effects information was identified for BAPP. The outputs of quantitative structure-activity relationship predictions indicate potential hazardous properties (i.e., genotoxicity, carcinogenicity). Exposure of the general population to BAPP through environmental media and food is expected to be negligible. General population exposure to BAPP from use of products available to consumers is not expected. As exposure to the general population through environmental media in Canada is expected to be negligible, the risk to human health is considered to be low. On the basis of the information presented in this screening assessment, it is concluded that BAPP does not meet the criteria under paragraph 64(*c*) of CEPA as it is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

It is concluded that BAPP does not meet any of the criteria set out in section 64 of CEPA.

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1. Introduction

The *Canadian Environmental Protection Act, 1999* (CEPA) (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.

On the basis of 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 on the basis of 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, benzenamine, 4,4'-[(1-methylethylidene)bis(4,1-phenyleneoxy)]bis, was identified as a priority for assessment as it met categorization criteria under subsection 73(1) of CEPA (ECCC, HC [modified 2007]). The Challenge for this substance was published in the *Canada Gazette* on December 26, 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.

Screening assessments focus on information critical to determining whether a substance meets the criteria as set out in section 64 of CEPA. Screening assessments

examine scientific information and develop conclusions by incorporating a weight-of-evidence approach and precaution.[2]

This 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, and stakeholder research reports and from literature searches up to October 2010 for both the ecological and health sections of the screening assessment. In February 2017, a rapid search of the literature did not identify any significant new information that could influence the outcome of this assessment. Key studies were critically evaluated, and modelling results were also used to reach conclusions.

When available and relevant, information presented in hazard assessments from other jurisdictions was considered.

This screening assessment was prepared by staff in the Existing Substances Programs at Health Canada and Environment and Climate Change Canada and incorporates input from other programs within these departments. The ecological portion of this assessment has undergone external written peer review/consultation. Approaches used in the screening assessments under the Challenge have been reviewed by an independent Challenge Advisory Panel. Additionally, the draft of the screening assessment was subject to a 60-day public comment period. No external comments were received in the draft screening assessment. The final content and outcome of the screening assessment remain the responsibility of Health Canada and Environment and Climate Change Canada.

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

[2] A determination of whether one or more of the criteria of section 64 of CEPA are met is based on 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 products available to consumers. A conclusion under CEPA is not relevant to, nor does it preclude, an assessment against the hazard criteria for WHMIS that are specified in the *Hazardous Products Regulations,* which are part of the regulatory framework for the Workplace Hazardous Materials Information System for products intended for workplace use. Similarly, a conclusion based on the criteria contained in section 64 of CEPA does not preclude actions being undertaken under other sections of CEPA or other acts.

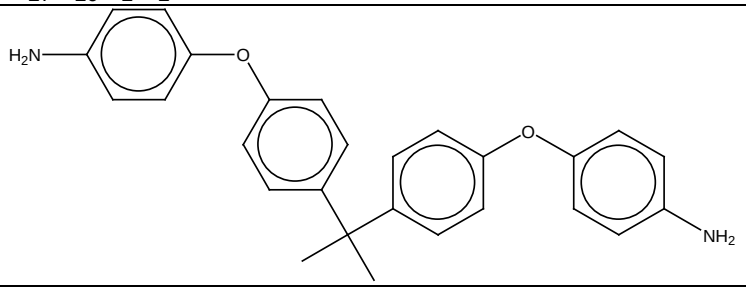
2. Substance identity

2.1 Substance name

For the purposes of this document, this substance will be referred to as BAPP, a common name used in the scientific literature.

Table 2-1. Substance identity for BAPP

Chemical Abstracts Service Registry Number (CAS RN)	**13080-86-9**
DSL[a] name	**Benzenamine, 4,4'-[(1-methylethylidene)bis(4,1-phenyleneoxy)]bis-**
National Chemical Inventories (NCI) names[b]	*Benzenamine, 4,4'-[(1-methylethylidene)bis(4,1-phenyleneoxy)]bis-* (TSCA, ASIA-PAC, NZIoC) *4,4'-[isopropylidenebis(4,1-phenyleneoxy)]dianiline* (REACH, EINECS) *4,4'-[Isopropylidenebis(4,1-phenyleneoxy)]bis[aniline]* (ENCS)
Other names	*2,2'-Bis[4-(4-aminophenoxy)phenyl]propane* *2,2-Bis[4-(4-aminophenoxy)phenyl]propane* *2,2-Bis[p-(4-aminophenoxy)phenyl]propane* *4,4'-[(1-Methylethylidene)bis(4,1-phenyleneoxy)]bisbenzenamine* *4,4'-[Isopropylidenebis(1,4-phenylene)dioxy]dianiline* *Aniline, 4,4'-[isopropylidenebis(p-phenyleneoxy)]di-* *BAPP* *Bisphenol A bis(4-aminophenyl) ether* *Bis[4-(4-aminophenoxy)phenyl]dimethyl methane* *Cheminox CLP 5250* *CLP 5250* *4,4'-[Isopropylidenebis(4,1- phenylenoxy)]dianiline*

Chemical group (DSL Stream)	Discrete organics
Major chemical class or use	Low-molecular carbo-polycyclic organic compounds
Major chemical sub-class	Bisphenol A compounds; benzenamines; phenyleneoxy compounds
Chemical formula	$C_{27}H_{26}N_2O_2$
Chemical structure	
SMILES[c]	O(c(ccc(c1)C(c(ccc(Oc(ccc(N)c2)c2)c3)c3)(C)C)c1)c(ccc(N)c4)c4
Molecular mass	410.52 g/mol

[a] Domestic Substances List (DSL).
[b] National Chemical Inventories (NCI). 2010: ASIA-PAC (Asia-Pacific Substances Lists); EINECS (European Inventory of Existing Commercial Chemical Substances); ENCS (Japanese Existing and New Chemical Substances); NZIoC (New Zealand Inventory of Chemicals); REACH (Registration, Evaluation, Authorisation & Restriction of Chemicals); and TSCA (Toxic Substances Control Act Chemical Substance Inventory).
[c] Simplified Molecular Input Line Entry System.

3. Physical and chemical properties

Table 3-1 contains experimental and modelled physical and chemical properties of BAPP that are relevant to its environmental fate.

Models based on quantitative structure-activity relationships (QSAR) were used to generate data for some of the physical and chemical properties of BAPP. A model input summary table is available in Appendix A. These models (except WSKOWWIN 2008) are based mainly on fragment addition methods, i.e., they rely on the structure of a chemical. Since most of these models only accept the neutral form of a chemical as input (in SMILES form), the modelled values shown in Table 3-1 are for the neutral form of BAPP. Given its pK_a value (see Table 3-1), the substance is expected to be mostly in its neutral form at environmentally relevant pH (6–9).

Since few empirical data were available for BAPP, a “read-across” approach was used to identify experimental data from suitable analogue substances that could be used for further modelling and lines of evidence in this assessment. An analogue is a chemical that is structurally similar to the substance under assessment and is therefore expected to have similar physical and chemical properties, similar behaviour in the environment, and/or similar toxicity. The modelled log K_{ow} value for BAPP presented in Table 3-1 was determined using the experimental value adjustment (EVA) option in KOWWIN. This approach estimates log K_{ow} for a queried chemical (in this case BAPP) by comparing its structure to that of a suitable analogue chemical that has an empirical log K_{ow} value, in this case bisphenol A (BPA). The empirical log K_{ow} value for the analogue is

quantitatively adjusted on the basis of the influence of structural differences on log K_{ow} when the two chemicals are compared. BAPP and bisphenol A are considered suitable analogues, as both substances contain a bisphenol functional group. It should be noted that BPA is considered adequate for use as an analogue for the determination of the log K_{ow} of BAPP, but not in the ecological and health effects characterization, as they are not toxicologically similar.

Table 3-1. Physical and chemical properties for neutral form of BAPP

Property	Type	Value[a]	Temperature (°C)	Reference
Physical state	N/A	White powder	N/A	Sigma-Aldrich 2010
Melting point (ºC) (neutral form)	Experimental	127–130	-	Sigma-Aldrich 2010
Melting point (ºC) (neutral form)	Modelled	246	-	MPBPWIN 2008
Boiling point (ºC) (neutral form)	Modelled	571	-	MPBPWIN 2008
Density (kg/m^3)	Experimental	N/A	-	-
Vapour pressure (Pa) (neutral form)	Modelled	2.18 x 10^{-10} (1.64 x 10^{-12} mmHg)	25	MPBPWIN 2008
Henry's law constant (Pa·m^3/mol) (neutral form)	Modelled	5.12 x 10^{-9} (5.05 x 10^{-14} atm·m^3/mole)	-	HENRYWIN 2008
log K_{ow} (octanol-water partition coefficient) (dimensionless) (neutral form)	Modelled	6.6[b*]	-	KOWWIN 2008

Property	Type	Value[a]	Temperature (°C)	Reference
log K_{oc} (organic carbon-water partition coefficient) (dimensionless) (neutral form)	Modelled	4.6[c]	-	KOCWIN 2008
Water solubility (mg/L) (neutral form)	Modelled	6.6×10^{-3}[c]	25	WSKOWWIN 2008
Water solubility (mg/L) (neutral form)	Modelled	2.2×10^{-3}	25	WATERNT 2008
pK_a (acid dissociation constant) (dimensionless)	Modelled	pK_a 1 = 5.16 pK_a 2 = 4.54	–	ACD/pKaDB 2005
Maximum diameter (nm)	Modelled	1.4–2.2 (mean 1.8)	–	CPOPs 2008

Abbreviations: N/A, not-applicable; K_{oc}, organic carbon-water partition coefficient; K_{ow}, octanol–water partition coefficient; '-', no information.

[a] Values in parentheses represent the original ones as reported by the authors or as estimated by the models.

[b] This value was modelled using the "experimental value adjustment method" of KOWWIN (2008), which estimated the log K_{ow} of the substances on the basis of an experimental log K_{ow} value of 3.32 for the analogue bisphenol A (CAS RN 80-05-7) (Howard 1989; Hansch et al. 1995).

[c] log K_{ow} value of 6.6 was used as input to generate this result.

* indicates selected value for modelling.

4. Sources

BAPP does not occur naturally in the environment.

Information was collected through industry surveys conducted for the years 2005 and 2006 under *Canada Gazette* notices issued pursuant to section 71 of CEPA (Canada 2006c, 2009b). These notices requested data on the Canadian manufacture and import quantities of the substances. In the notice for the year 2006, data were also requested on the use quantity of BAPP.

There was no manufacture of BAPP in Canada above the reporting threshold of 100 kg/year for the 2006 calendar year. One company imported 250 kg of BAPP, present in an industrial structural adhesive bonding primer at a concentration of 3% to 6%, in 2006 (Environment Canada 2010a). More recent information shows that the quantity of BAPP in commerce in Canada has increased, as indicated by a use quantity of 500 kg by the same company in 2010 (2011 personal communication from the industrial user to Environment Canada; unreferenced).

During the 1984 to 1986 calendar years, the quantity reported as having been manufactured, imported or in commerce in Canada was 5000 to 25 000 kg, with fewer than four notifiers.

In the United States, BAPP is listed on the *Toxic Substances Control Act* (TSCA) inventory. The national aggregated production volume in the United States is less than 500 000 lb (~230 000 kg) (US EPA 2006).

5. Uses

Information on uses for the 2006 calendar year was gathered in response to a CEPA section 71 notice (Canada 2009b). In 2006, one company reported using BAPP as an additive in a structural adhesive bonding primer for aircraft parts (Environment Canada 2010a). More specifically, BAPP is an additive in corrosion inhibiting primer used in an epoxy adhesive bonding system in the aeronautic industry (Cytec 2001; Environment Canada 2010a). Following application, the primer coating is cured for one hour at 120 C to obtain a surface that is scratch resistant and that will withstand more than 20 wipes with a shop towel saturated with methyl ethyl ketone (M.E.K. resistance) (Cytec 2001). It is assumed that nearly all of the BAPP that ends up on airplane parts is chemically transformed following curing.

During the 1984 to 1986 calendar years, the DSL use code identified for BAPP was chemical intermediate- inorganic, organometallic.

A review of the available scientific and technical information indicates that BAPP has been identified for use as an organic intermediate in the chemical synthesis of polyester-type new materials, where it acts as a solidifying agent (Suzhou Yinsheng Chemical Co. Ltd 2003). It is used in low concentrations (< 6%) as a reactant or reagent in the manufacture of aromatic polyimides, polyamides or benzoxazine resins (Chuang et al. 2001; Ghosh and Mittal 1996; Kong et al. 2006; Lin et al. 2008). These thermosetting resins are polymers that display high thermo-oxidative stability as well as outstanding mechanical and electrical properties (Gosh and Mittal 1996; Lin et al. 2008). BAPP improves resin flexibility, solubility into organic solvents, and resin workability in moulding (Seika Group 2010). BAPP-containing thermoplastic polyimides are used extensively in the electronic industry because of their excellent film-forming characteristics and resistance to common solvents (Chuang et al. 2001).

BAPP is also used as an organic dyestuff and pigment intermediate (Xia and Miley 2002) and as a reagent for high-performance polymer research (TCI America 2010). It is not used as a dye and pigment intermediate in the Canadian textile industry, but there is insufficient information to determine whether it is present in imported products (2010 personal communication from Products Division, Environment and Climate Change Canada, to Existing Substances Risk Assessment Bureau, Health Canada; unreferenced).

BAPP was not notified as an ingredient in cosmetic products in Canada (CNS 2010) and is not listed in the Cosmetic Ingredient Hotlist, Health Canada's administrative list of ingredients that are intended to be prohibited or restricted for use in cosmetics in Canada (Health Canada 2010). BAPP is not currently registered in Canada as a formulant in pesticide products (PMRA 2007) nor is it listed in the lists of permitted food additives as an approved food additive under the *Food and Drugs Act* (Canada 1978) and associated marketing authorizations (Health Canada, 2013). BAPP was not identified in food packaging applications or in formulations of incidental additives (2010 personal communication from Food Directorate, to Risk Management Bureau, Health Canada; unreferenced).

BAPP is not listed in the Drug Product Database (DPD), the Therapeutic Products Directorate's internal Non-Medicinal Ingredients Database, the Natural Health Products Ingredients Database (NHPID) or the Licensed Natural Health Products Database (LNHPD) as a medicinal or a non-medicinal ingredient present in final pharmaceutical products, natural health products or veterinary drugs (DPD 2010; NHPID 2010; LNHPD 2010; 2010 personal communication from Therapeutic Products Directorate, Natural Health Products Directorate and Veterinary Drugs Directorate, Health Canada, to Risk Management Bureau, Health Canada; unreferenced).

6. Releases to the environment

A method has been developed by Environment and Climate Change Canada to estimate a substance's losses during different stages of its life cycle, including its fate within a finished product or article (Environment Canada 2008). This method, referred to as mass flow, consists of a life-cycle analysis and a spreadsheet tool (Mass Flow Tool or MFT) that integrates information on the manufacturing, importation and use data available for the substance. Starting with an identified mass of the substance, each life-cycle stage is evaluated until all of the mass is accounted for. Relevant factors are considered, uncertainties are recognized, and assumptions may be made during each stage, depending on information available. The estimated losses represent the complete mass balance of the substance over the life cycle of the substance and include releases to wastewater and other receiving compartments (land, air), chemical transformation, transfer to recycling activities, and transfer to waste disposal sites (landfill, incineration). However, unless specific information on the rate or potential for release of the substance from landfills and incinerators is available, the method does not quantitatively account for releases to the environment from disposal.

In general, releases of a substance to the environment depend on various losses from its manufacture, industrial use, and/or consumer/commercial use. These losses can be grouped into seven types: (1) discharge to wastewater; (2) emission to air; (3) loss to land; (4) chemical transformation; (5) disposal to landfill; (6) loss to incineration; and (7) disposal through recycling (i.e., recycling is deemed a loss and not considered further). Losses are estimated using regulatory survey data, industry data, and data published by various organizations. In this case, discharge to wastewater refers to release to a wastewater treatment system[3] after primary and secondary treatment at a specialized hazardous waste treatment facility. Loss via chemical transformation refers to changes in a substance's identity that may occur within the manufacture, industrial use, and consumer/commercial use stages, but excludes those during waste management operations such as incineration and wastewater treatment. Loss to land includes unintentional transfer or leakage to soil or paved/unpaved surfaces during the substance's use and service life (e.g., from the use of agricultural machinery or automobiles). However, it does not include transfers subsequent to a substance's use and service life (e.g., land application of biosolids and atmospheric deposition).

The estimated losses of BAPP over its life cycle (based on conservative assumptions) are presented in Table 6-1 (Environment Canada 2010b). Given that BAPP is not manufactured in Canada above the reporting thresholds, the estimated losses are based on the industrial application of BAPP reported by the company importing the substance in 2006.

Table 6-1. Estimated losses of BAPP during its life cycle

Type of loss	Proportion (%)	Pertinent life cycle stages
Wastewater	4.5	Industrial use
Air emission	1.5	Industrial use
Land	0	-
Chemical transformation	66.5	Industrial use
Landfill	9.4	Industrial use
Incineration	18.1	Industrial use
Recycling	0	-

'-': not available or not calculated.

BAPP is estimated to be released to air at 1.5%, to sewer at 4.5% and to landfill/incineration at 27.5% during the industrial use stage.

[3] In this assessment, the term "wastewater treatment system" refers to a system that collects domestic, commercial and/or institutional household sewage and possibly industrial wastewater (following discharge to the sewer), typically for treatment and eventual discharge to the environment. Unless otherwise stated, the term wastewater treatment system makes no distinction of ownership or operator type (municipal, provincial, federal, indigenous, private, partnerships). Systems located at industrial operations and specifically designed to treat industrial effluents will be identified by the terms "on-site wastewater treatment systems" and/or "industrial wastewater treatment systems".

Following shipping of the adhesive primer to an industrial facility, the primer containing BAPP is sprayed onto aircraft parts in a downdraft spray booth. During discharge, overspray droplets are removed from the air by dry filter systems. The filters are disposed of in landfill after use. The primer containing BAPP not captured by the filtering system and which settles down onto the floor is cleaned up using a floor scrubber. The liquid effluent is then collected into a wastewater tank where the solid fraction (sludge) will settle at the bottom of the tank. The wastewater and sludge are typically sent off-site to a specialized hazardous waste treatment facility. Following treatment, the wastewater is sent via sewer system to the regional wastewater treatment facility. The sludge is sent to a specialized facility for incineration.

Assumptions made during the industrial use stage include 3% shipping container residue loss, 2% process equipment cleaning loss, 70% spray efficiency, 75% air dry filters efficiency, and 79.6% secondary wastewater treatment removal modelled using ASTreat (2006). The majority of the proportion of BAPP applied to aircraft parts (66.5%) is estimated to be chemically transformed following the curing of the applied coating. Of the waste disposal component (27.5%), the majority is estimated to be incinerated (66%) and a smaller proportion landfilled (34%).

The above loss estimates indicate that BAPP has a potential for release to the environment. However, given current use patterns, quantities estimated to be released are low.

7. Environmental fate

On the basis of the results of Level III fugacity modelling (Table 6-1) performed using the physical and chemical properties of BAPP (Table 3-1), the substance is expected to predominantly reside in soil or sediment, depending on the compartment of release (see Appendix A for the model input summary table).

Table 7-1. Results of the Level III fugacity modelling (EQC 2003) (% of substance partitioning into each compartment)

Substance released to:	Air	Water	Soil	Sediment
Air (100%)	0.4	0.4	82.4	16.8
Water (100%)	0	2.3	0	97.7
Soil (100%)	0	0	99.9	0.1

The Level III fugacity modelling results represent the partitioning of the substance in a hypothetical evaluative environment resulting from intermedia partitioning and loss by both advective transport (out of the modelled region) and degradation/transformation processes. The partitioning values shown in Table 7-1 represent the net effect of these processes under conditions of continuous release when a non-equilibrium “steady state” has been achieved.

If released to water, BAPP is expected to strongly adsorb to suspended solids and sediment given its high log K_{oc} value of ~4.6. Volatilization from water surfaces is expected to be an unimportant fate process considering this compound's estimated Henry's law constant (5.12 x 10^{-9} Pa·m^3/mol). Thus, if water is a receiving medium, little BAPP will remain in water, and most of the substance (~97.7%) will be expected to partition to sediment (see Table 7-1).

If released to air, a small amount of the substance is expected to reside in air (see Table 7-1 above). With its negligible modelled vapour pressure of 2.18 x 10^{-10} Pa and Henry's law constant of 5.12 x 10^{-9} Pa·m^3/mol, BAPP is non-volatile. Therefore, if released solely to air, it will tend to be deposited to soil (~82.4%) and, to a lesser degree, to sediment (16.8%) (see Table 7-1).

Given its estimated log K_{oc}, BAPP is expected to be immobile if released to soil. Volatilization from moist and dry soil surfaces seems to be an unimportant fate process because of its low vapour pressure. The Level III fugacity modelling also suggests that BAPP will partition to soil (see Table 7-1).

The relatively high acid dissociation constant (pK_a) of 5.2 for the acidic functional group indicates that half of the chemical will be dissociated at pH 5.2. In water bodies at environmentally relevant pH (6 to 9), almost all will be undissociated, indicating that biotic exposure to BAPP will be from the neutral form. The relatively low proportion of the dissociated chemical also indicates that partitioning behaviour as predicted using the log K_{ow} and log K_{oc} is appropriate.

In conclusion, while releases of BAPP are expected to occur to the aquatic environment and air, results from fugacity modelling indicate that BAPP released to air, if not oxidized, will ultimately be deposited to soil, while BAPP released to water will find its way to the sediment compartment.

7.1 Environmental persistence

No experimental degradation data for BAPP have been identified for any media. Given the ecological importance of the water compartment and the fact that BAPP is expected to be released to wastewater, persistence in water was primarily examined using predictive QSAR models for biodegradation. BAPP does not contain functional groups expected to undergo hydrolysis. Table 7-2 summarizes the results of available QSAR models for degradation in various environmental media (see Appendix A for the model input summary table).

Table 7-2. Modelled data for degradation of BAPP

Fate process	Type	Model and model basis	Model result and prediction	Extrapolated half-life (days)

Fate process	Type	Model and model basis	Model result and prediction	Extrapolated half-life (days)
Atmospheric oxidation	Abiotic	AOPWIN 2008[a]	$t_{1/2}$ ~ 0.053 days	< 2
Ozone reaction	Abiotic	AOPWIN 2008[a]	N/A[b] a[b]	-
Hydrolysis	Abiotic	HYDROWIN 2008[a]	N/A[b] a[b]	-
Biodegradation (aerobic)	Primary	BIOWIN 2008[a] Sub-model 4: Expert Survey (qualitative results)	3.04[c] "may biodegrade fast"	<= 182
Biodegradation (aerobic)	Ultimate	BIOWIN 2008[a] Sub-model 3: Expert Survey (qualitative results)	1.69[c] "biodegrades slowly"	>= 182
Biodegradation (aerobic)	Ultimate	BIOWIN 2008[a] Sub-model 5: MITI linear probability	-0.23[d] biodegrades very slowly"	>= 182
Biodegradation (aerobic)	Ultimate	BIOWIN 2008[a] Sub-model 6: MITI non-linear probability	0.0[d] "biodegrades very slowly"	>= 182
Biodegradation (aerobic)	Ultimate	TOPKAT 2004 Probability	0.02[d] "biodegrades very slowly"	>= 182
Biodegradation (aerobic)	Ultimate	CATABOL 2004–2008: % BOD (biological oxygen demand)	% BOD =5.1 "biodegrades very slowly"	>= 182

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

All BAPP molecular fragments are included in the training set for TOPKAT. These model results are therefore considered reliable despite being outside the optimum prediction space (OPS) limits. It is noted that 6.45% of BAPP molecular fragments are not covered in CATABOL.

In air, a predicted atmospheric oxidation half-life value of 0.053 days (see Table 7-2) demonstrates that BAPP 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 BAPP. With a half-life of 0.053 days via reactions with hydroxyl radicals, BAPP is considered not to persist in air.

The biodegradation results from Table 7-2 indicate that all five ultimate biodegradation models (BIOWIN 3, 5, 6, TOPKAT and CATABOL) suggest that biodegradation is very slow and that the half-life in water is greater than 182 days. Results for the primary biodegradation model (BIOWIN Sub-model 4) indicate potential for fairly rapid primary degradation, but since the identity of the degradation products is not known, this result is given less weight. The ultimate survey model (BIOWIN 3) result of 1.69 may be equated to a half-life value of 180 to 240 days assuming first order-rate kinetics (Aronson et al. 2006). Similarly, probability results from BIOWIN sub-models 5 and 6 are both well below the suggested threshold for persistence (less than 0.3), clearly suggesting that the substance persists in this medium. The overall conclusion from BIOWIN (2000) is that BAPP is not readily biodegradable. Other ultimate degradation models (TOPKAT and CATABOL) predict that BAPP does not undergo mineralization in a 28-day timeframe with probability or extent of biodegradation in the range of very persistent chemicals. TOPKAT, which simulates the Japanese MITI 28-day biodegradation test, predicted a probability of 0.02, which is far below the suggested cut-off for persistent substances in this model (less than 0.3). (It should be noted that 0.7 is suggested for non-persistent chemicals) (TOPKAT 2004). CATABOL predicted only 5.1% biodegradation on the basis of the OECD 301 ready biodegradation test (%BOD) which has been suggested as meaning the compound is likely to have a half-life in water of greater than 182 days (Aronson and Howard 1999).

Using an extrapolation ratio of 1:1:4 for water: soil: sediment biodegradation half-lives (Boethling et al. 1995), the half-life in soil is also greater than 182 days and the half-life in sediments is greater than 365 days. This indicates that BAPP is expected to persist in soil and sediment.

7.2 Potential for bioaccumulation

Since experimental bioaccumulation factor (BAF) and/or bioconcentration factor (BCF) data for species in any media were not available for BAPP, a predictive approach was applied using available BAF and BCF models for the aquatic environment as shown in Table 7-3 below (see Appendix A for the model input summary table). Predictions for aquatic-dwelling organisms will be used as surrogates for sediment- and soil-dwelling organisms. The log K_{ow} value of 6.6 generated using the EVA method was used as input in all models when possible in order to yield more accurate predictions. Measures of BAF are the preferred metric for assessing the 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} values greater than ~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 tracks the mass balance of a substance in an organism and allows for uptake and elimination parameter correction, provided the log K_{ow} of the substance is within the domain of the model.

BCF and BAF estimates, corrected for potential biotransformation, were generated using the BCFBAF model (EPI Suite 2000–2008). Metabolic rate constants were

derived using structure-activity relationships described further in Arnot et al. (2008a, 2008b, 2009). Since metabolic potential can be related to body weight and temperature (Hu and Layton 2001; Nichols et al. 2007), the BCFBAF model further normalizes the k_M for a 10-g 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. After normalization routines, the median k_M for a 184-g fish is 0.012 (1/days).

Table 7-3. Model data for bioaccumulation for BAPP

Test organism	Model and model basis	Endpoint	Value wet weight (L/kg)	Reference
Fish	BCFBAF Sub-model 1: linear regression	BCF	9892	BCFBAF 2008
Fish	BCFBAF Sub-model 2: mass balance	BCF	6913	BCFBAF 2008
Fish	BCFBAF Sub-model 3: Gobas - mass balance	BAF	296 100	BCFBAF 2008
Fish	OASIS Forecast 2005 (with mitigating factors considered)	BCF	1091	Dimitrov et al. 2005
Fish	Baseline BCF Model (BCF Max)	BCF	31 623	Dimitrov et al. 2005

Metabolism-corrected BCF and BAF values for BAPP according to the BCFBAF model are 6913 L/kg and 296 100 L/kg, respectively. Having an uncomplicated structure, BAPP is well within the structural domain of this model and, as a neutral chemical with log K_{ow} of 6.6, it is expected to be taken up via passive diffusion and is thus also considered to be within the mechanistic and physical/chemical property domain (global parameter domain) of the models. The metabolism-corrected BCF value according to the OASIS model is 1091 L/kg (Dimitrov et al. 2005). However, as only ~52% of the substance's molecular fragments are covered by the model, this value is outside of the total domain of the model and is therefore not considered as reliable as the BCFBAF predictions.

Recent investigations relating fish BCF data and molecular size parameters (Dimitrov et al. 2002; Dimitrov et al. 2005; BBM 2008) suggest that the probability of a molecule crossing cell membranes as a result of passive diffusion declines significantly with

increasing maximum diameter (D_{max}). The probability of passive diffusion falls appreciably when a maximum diameter is greater than ~1.5 nm and falls more significantly when molecules have a maximum diameter of greater than 1.7 nm. Sakuratani et al. (2008) have also investigated the effect of cross-sectional diameter on passive diffusion in a test set of about 1200 new and existing chemicals. They observed that substances that do not have a very high bioconcentration potential (BCF less than 5000) often have a D_{max} of greater than 2.0 nm and an effective cross-sectional diameter (D_{eff}) of greater than 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. Arnot et al. (2010) pointed out that 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.

BAPP has a molecular weight of 410.52 g/mol and a D_{max-} = 2.2 nm, indicating a potential for a slightly reduced uptake rate from water and reduced *in vivo* bioavailability of the substance compared to model predictions. However, while the D_{max} of BAPP may be greater than 2.0 nm ($D_{max-mean}$ = 1.8 nm), its molecular weight is less than 450 g/mol, which indicates that BAPP has a BCF of greater than 5000.

The available evidence indicates that BAPP is expected to have high bioaccumulation potential because of its physical and chemical properties (i.e., high log K_{ow}, medium molecular weight, or low water solubility). Metabolism-corrected BCF and BAF values indicate that BAPP has a BCF of greater than 5000, with the exception of the metabolism-corrected OASIS modelled value.

8. Potential to cause ecological harm

8.1 Ecological effects assessment

There are no experimental data available for toxicity for this substance. Modelled data for the aquatic environment were therefore used to estimate the potential toxicity of BAPP. Table 8-1 contains predicted ecotoxicity values that were considered reliable and used in the QSAR weight-of-evidence approach for aquatic toxicity (Environment Canada 2007b). A model input summary table is available in Appendix A.

Since BAPP is expected to be undissociated at environmentally relevant pH (6 to 9), aquatic toxicity predictions were done for the neutral form of BAPP. The EVA log K_{ow} value of 6.6 was used as a correction factor in models when permitting, in order to yield more accurate predictions. The predicted concentrations associated with toxicity for

aquatic organisms may have an additional source of uncertainty when these concentrations exceed the solubility of the chemical in water. Given that modelled concentrations for water solubility are often uncertain, toxicity values that exceeded solubility estimates by up to a factor of 10 were considered to be acceptable.

Table 8-1. Modelled data for aquatic toxicity

Test organism	Type of test	Endpoint	Value (mg/L)	Reference
Fish	Acute (96 hours)	LC_{50}[a]	0.041^	ECOSAR 2008 (neutral organic SAR)
Fish	Acute (96 hours)	LC_{50}[a]	0.021	TOPKAT 2004
Fish	Acute (96 hours)	LC_{50}[a]	9.22*	AIEPS 2003–2007
Fish	Chronic	ChV[b]	0.003	ECOSAR 2008 (neutral organic SAR)
Daphnia	Acute (48 hours)	LC_{50}[a]	0.041^	ECOSAR 2008 (neutral organic SAR)
Daphnia	Acute (48 hours)	LC_{50}[a]	0.244*	TOPKAT 2004
Daphnia	Acute (48 hours)	LC_{50}[a]	2.44*	AIEPS 2003–2007
Daphnia	Chronic	ChV[b]	0.008	ECOSAR 2008 (neutral organic SAR)
Algae	Acute (96 hours)	EC_{50}[c]	0.12*	ECOSAR 2008 (neutral organic SAR)
Algae	Acute (96 hours)	EC_{50}[c]	1.82*	AIEPS 2003–2007
Algae	Chronic	ChV[b]	0.097*	ECOSAR 2008 (neutral organic SAR)

[a] LC50 – The concentration of a substance that is estimated to be lethal to 50% of the test organisms.
[b] ChV – Chronic toxicity value - the concentration of a substance that will cause chronic effects.
[c] EC50 – The concentration of a substance that is estimated to cause some effect on 50% of the test organisms.
* No effects at saturation are predicted for this organism since the toxicity value exceeds the water solubility (0.0066 mg/L) by more than a factor of 10.
^ This prediction is considered unreliable as the substance log K_{ow} exceeds the log K_{ow} cut-off value of 5.

A range of aquatic toxicity predictions were also obtained from the various QSAR models (Table 8-1). When reliable, these results indicate that the substance is potentially highly hazardous to aquatic organisms. More specifically, the TOPKAT 96-h LC_{50} of 0.021 mg/L for fish and the ECOSAR ChV values of 0.003 mg/L and 0.008 mg/L for fish and daphnids indicate that BAPP will cause acute and chronic effects to these organisms at low concentrations.

Despite using a calculated log K_{ow} of 5.89, which is slightly below the BAPP selected log K_{ow} value of 6.6, the TOPKAT fish 96-h LC_{50} prediction is considered reliable, as all molecular fragments are covered by the model database. ECOSAR indicates that BAPP may have an aromatic amine mode of action in addition to a neutral organic structure-activity relationship (SAR) (baseline toxicity). However, most ECOSAR predictions for the aromatic amine mode of action are considered unreliable above a log K_{ow} of 4.3, or exceed the modelled BAPP water solubility value of 0.0066 mg/L. While the cut-off log K_{ow} value for the ECOSAR acute baseline toxicity fish and *Daphnia* predictions is exceeded by the BAPP log K_{ow} value of 6.6, the fish and *Daphnia* chronic toxicity estimates (ChV) are considered reliable on the basis of a reliability prediction cut-off value of log K_{ow} = 8.

The weight of evidence regarding modelled data for BAPP indicates that this substance is expected to cause acute and chronic harm to aquatic organisms at low concentrations.

In addition, the OECD QSAR Toolbox was used as a profiling tool to determine BAPP estrogen receptor (ER) binding potential, a molecular initiating event much like protein binding (Schultz et al. 2006) that may lead to a series of adverse outcomes (OECD 2009). Binding potency is related to the presence of specific functional groups as well as the size and shape of the molecule, which can be grossly measured using its molecular weight (OECD 2009). With a molecular weight (410.52 g/mol) that falls within the optimum molecular weight range for ER binders (200 to 500 g/mol) and the presence of two aromatic structures with an unhindered amino-group, BAPP is considered to have a strong binding ER potential.

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

8.2 Characterization of ecological risk

BAPP is expected to persist in water, sediment and soil, and to have a high bioaccumulation potential. It is also considered to have high toxicity to aquatic organisms and potential for estrogen receptor binding.

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.

Nevertheless, given the small quantity of BAPP imported into Canada, its use pattern, and the handling and disposal practices known to be in place for its current use, releases to the environment and exposure to this substance are expected to be very

low. Therefore, it is concluded that BAPP is not currently causing ecological harm in Canada.

While exposure of the environment to BAPP is not of concern at current levels, this substance is considered to have an environmental effect of concern because of its high toxicity to aquatic organisms, potential for estrogen receptor binding and high bioaccumulation potential. Therefore, there may be a concern for the environment if exposures were to increase.

8.3 Uncertainties in evaluation of ecological risk

The predicted concentrations associated with toxicity for aquatic organisms may have an additional source of uncertainty when these concentrations exceed the solubility of the chemical in water. Given that modelled concentrations for water solubility are often uncertain, toxicity values that exceeded solubility estimates by up to a factor of 10 were considered to be acceptable.

9. Potential to cause harm to human health

9.1 Exposure assessment

9.1.1 Environmental media

Empirical data on concentrations of BAPP in environmental media in Canada were not identified. Environmental concentrations of BAPP were estimated using ChemCAN (2003), a Canada-specific level III fugacity model employed to estimate average concentrations in various media on the basis of the annual release of a substance.

Annual releases were calculated using a total quantity in commerce of approximately 500 kg in 2010 (2011 personal communication from the industrial user to Aerospace, Automotive and Transportation – Chemical Sector, Environment Canada; unreferenced). The loss percentages predicted by the Mass Flow Tool (see Table 6-1) were applied to this quantity (500 kg) and were used to derive conservative upper-bounding daily intakes of BAPP for the general population in Canada. This resulted in a total upper-bounding estimate of exposure from environmental media of less than 1 nanogram per kg-bw (kilogram of body weight) per day. Accordingly, the potential for exposure of the general population to BAPP through environmental media in Canada is expected to be negligible.

BAPP is not expected to be found in food or beverages.

9.1.2 Products available to consumers

BAPP is present as an additive in adhesive bonding primer used for aircraft structural parts at a concentration of 3% to 6% by weight (Environment Canada 2010a). As the use of this product is considered to occur in industrial settings only, exposure of the general population of Canada to BAPP from use of products available to consumers is not expected.

9.2 Health effects assessment

Available empirical data for BAPP were on acute health effects only (Appendix B). The acute toxicity of BAPP after dermal exposure appeared to be low given that the lowest dermal median lethal dose (LD_{50}) was greater than 8000 mg/kg in male and female rats. The lowest oral LD_{50} was 308 mg/kg in female rats (NTIS 1992a). BAPP was not irritating to rabbit skin, but it induced transient irritation in 1 of 6 tested eyes in rabbits (NTIS 1992a).

Since limited empirical health effects information was available for BAPP, relevant information on analogue substances was also considered. Two analogues were identified on the basis of chemical similarity and availability of empirical hazard data: benzenamine, 4,4'-[1,4-phenylenebis(oxy)]bis- (CAS RN 3491-12-1) and bisaniline A (CAS RN 2479-47-2). The degree of structural similarity was quantified using the

Tanimoto association coefficient in SciFinder; this coefficient was 76% and 74% between BAPP and its analogues, benzenamine, 4,4'-[1,4-phenylenebis(oxy)]bis- and bisaniline A, respectively. The structures of these analogues are presented in Appendix C.

A summary of the available hazard data for the two identified analogues is presented below.

For 1,4-phenylenebis(oxy)]bis- (CAS RN 3491-12-1), *in vitro* genotoxicity bioassays were mixed, with a positive result for mutation in bacteria (Shimizu et al. 1982) and a negative result for unscheduled DNA synthesis in hepatocyte primary cultures (Mori et al. 1988).

Bisaniline A was mutagenic in Ames test strain TA100 and TA98 in the presence of metabolic activation. Without metabolic activation, a positive mutagenic response was observed towards test strain TA100, but not TA98 (NTIS 1992b). In a carcinogenicity study, 1 of 3 dogs treated with Bisaniline A for 6 years at a dose of 15.03 mg/kg-bw per day developed bladder tumours. No gross anatomical changes were observed in the other 2 dogs, but all 3 dogs tested positive for hematuria (NTIS 1992c). No other empirical health effects data were available for the identified analogues.

The outputs of predictive QSAR models for BAPP were considered using four different models—DEREK, TOPKAT, CASETOX and Leadscope Model Applier—which generated mixed results for carcinogenicity, genotoxicity, developmental toxicity and reproductive toxicity (DEREK 2008; TOPKAT 2004; CASETOX 2008; Leadscope 2005-2008). A summary of the model outputs are shown in Appendix D. Model Applier and Multicase Casetox generated positive predictions for mouse and rat carcinogenicity endpoints. Genotoxicity predictions by Model Applier and Multicase Casetox were positive for several endpoints in *in vivo* bioassays, including chromosomal aberrations, micronucleus, and gene mutation in *Drosophila melanogaster*, and in *in vitro* bacterial mutation bioassays in *Salmonella typhimurium*. For developmental toxicity endpoints, there were positive predictions on weight decrease and post implantation loss in rats by Model Applier, and a positive prediction on teratogenicity by Multicase Casetox. Multicase Casetox also generated positive predictions for reproductive endpoints in mice and rats.

The confidence in the health effects database on BAPP is considered to be very low. Only acute toxicity and irritation empirical data were available. For the identified analogues, only *in vitro* genotoxicity data and a very limited carcinogenicity study were available. The predictive QSAR models generated mixed results for genotoxicity, carcinogenicity, and developmental and reproductive toxicity.

9.3 Characterization of risk to human health

Very little empirical health effects information was identified for BAPP. The outputs of quantitative structure-activity relationship predictions indicate potential hazardous

properties (i.e., genotoxicity, carcinogenicity). Exposure of the general population to BAPP through environmental media and food is expected to be negligible. General population exposure to BAPP from use of products available to consumers is not expected. As exposure to the general population through environmental media in Canada is expected to be negligible, the risk to human health is considered to be low.

9.4 Uncertainties in evaluation of risk to human health

Uncertainty in the exposure characterization is high because no empirical data on environmental concentrations of BAPP were available and quantities in commerce for the year 2006 calendar were used to predict environmental concentrations. In addition, there is uncertainty because of the assumptions used in the model. As the maximum value of the quantity in commerce was used in the modeling, it is likely that the modeled outputs are overestimates of actual concentrations of BAPP in environmental media. Confidence in the environmental exposure estimate for BAPP is low.

Because of the limited empirical health effects data on BAPP and its analogues and the use of qualitative structure-activity relationship models, confidence in the health effects database is low.

10. Conclusion

Considering all available lines of evidence presented in this screening assessment, there is low risk of harm to organisms and the broader integrity of the environment from BAPP. It is concluded that BAPP does not meet the criteria under paragraphs 64(*a*) or 64(*b*) of CEPA as it 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.

On the basis of limited hazard information, principally on the QSAR results for BAPP, it cannot be precluded that BAPP may be associated with potential genotoxicity and carcinogenicity. However, exposure of BAPP to the general Canadian population is negligible. Therefore, on the basis of the information presented in this screening assessment, it is concluded that BAPP does not meet the criteria under paragraph 64(*c*) of CEPA as it is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

It is concluded that BAPP does not meet any of the criteria set out in section 64 of CEPA.

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Appendices

Appendix A. PBT model input summary tables

Table A-1. PBT model input summary table for physical-chemical models

Model input parameters	**EPI Suite™ (all models, including AOPWIN, KOCWIN, BCFBAF, BIOWIN and ECOSAR)**
SMILES code	O(c(ccc(c1)C(c(ccc(Oc(ccc(N)c2)c2)c3)c3)(C)C)c1)c(ccc(N)c4)c4
Molecular weight (g/mol)	-
Melting point (°C)	--
Boiling point (°C)	--
Data temperature (°C)	-
Vapour pressure (Pa)	--
Henry's Law constant ($Pa \cdot m^3/mol$)	--
Logl K_{aw} (dimensionless)	-
Logl K_{ow} (dimensionless)	6.6
K_{ow} (dimensionless)	-
Logl K_{oc} (L/kg)	-
Water solubility (mg/L)	-
Logl K_{oa} (dimensionless)	-

Abbreviations: K_{aw}, air–water partition coefficient; K_{oa}, octanol–air partition coefficient; K_{oc}, organic carbon–water partition coefficient; K_{ow}, octanol–water partition coefficient; SMILES, simplified molecular input line entry system; '-', not applicable

Table A-2 PBT model input summary table for fate modelling

Model input parameters	**Models for wastewater treatment removal[e]**	**EQC[i]**	**Arnot-Gobas BCF/BAF Model**
SMILES code	-	-	-
Molecular weight (g/mol)	410.52[f,g,h]	410.52 [j]	-
Melting point (°C)	-	246 [j]	-
Boiling point (°C)	-	-	-
Data temperature (°C)	-	20 [j]	-
Density (kg/m^3)	1.44[g]	-	-
Vapour pressure (Pa)	2.18×10^{-10} [f,h]	2.18×10^{-10}	-

Model input parameters	**Models for wastewater treatment removal[e]**	**EQC[i]**	**Arnot-Gobas BCF/BAF Model**
Henry's law constant (Pa·m^3/mol)	5.1 x 10^{-9} [h]	-	-
log K_{aw} (dimensionless)	x [g]	-	-
log K_{ow} (dimensionless)	6.9 [f]	6.6 [j]	6.6
K_{ow} (dimensionless)	7 585 776 [g,h]	-	-
log K_{oc} (L/kg)	-	-	-
Water solubility (mg/L)	0.003 [f,h]	6.0 x 10^{-3} [j]	-
log K_{oa} (dimensionless)	-	-	-
Soil–water partition coefficient (L/kg)[a]	-	-	-
Sediment–water partition coefficient (L/kg)[a]	-	-	-
Suspended particles–water partition coefficient (L/kg)[a]	135 021[g]	-	-
Fish–water partition coefficient (L/kg)[b]	-	-	-
Aerosol–water partition coefficient (dimensionless)[c]	-	-	-
Vegetation–water partition coefficient (dimensionless)[a]	-	-	-
Enthalpy (K_{ow})	-	-	-
Enthalpy (K_{aw})	-	-	-
Half-life in air (days)	-	0.641 hr [j]	-
Half-life in water (days)	-	182 [j]	-
Half-life in sediment (days)	-	728	-
Half-life in soil (days)	-	182 [j]	-
Half-life in vegetation (days)[d]	-	-	-
Metabolic rate constant (1/day)	-	-	-
Biodegradation rate constant (1/h) – specify	0.031	-	-
Biodegradation rate constant (1/day) – specify	0.74	-	-
Biodegradation half-life in primary clarifier ($t_{½\text{-}p}$) (h)	22.4[f]	-	-
Biodegradation half-life in aeration vessel ($t_{½\text{-}s}$) (h)	22.4[f]	-	-
Biodegradation half-life in settling tank ($t_{½\text{-}s}$) (h)	22.4[f]	-	-

Abbreviations: BCF, bioconcentration factor; K_{aw}, air–water partition coefficient; K_{oa}, octanol–air partition coefficient; K_{oc}, organic carbon–water partition coefficient; K_{ow}, octanol–water partition coefficient; SMILES, simplified molecular input line entry system

[a] Derived from log K_{oc}.
[b] Derived from BCF data.
[c] Default value.
[d] Derived from half-life in water.

[e] Wastewater treatment removal models include STP, ASTreat and SimpleTreat. Required inputs are different, depending on the model.
[f] Input for STP.
[g] Input for ASTreat.
[h] Input for Simpletreat.
[i] Required inputs for EQC are different if Type I vs. Type II chemical.
[j] EQC input for Type I chemical.

Table A-3 Table A-3. PBT model input summary table for PBT profiling and ecotoxicity

Model input parameters	CPOPs (including CATALOGIC, BCF Mitigating Factors Model, OASIS Toxicity Model)	AIES / DS TOPKAT/ ASTER
SMILES code	-	-
Molecular weight (g/mol)	-	-
Melting point (°C)	-	-
Boiling point (°C)	-	-
Data temperature (°C)	-	-
Density (kg/m^3)	-	-
Vapour pressure (Pa)	-	-
Henry's Law constant (Pa·m^3/mol)	-	-
Log K_{aw} (dimensionless)	-	-
Log K_{ow} (dimensionless)	6.6	-
K_{ow} (dimensionless)	-	-
Log K_{oc} (L/kg)	-	-
Water solubility (mg/L)	-	-
Log K_{oa} (dimensionless)	-	-

Abbreviations: AIES, Artificial Intelligence Expert System; K_{aw}, air–water partition coefficient; K_{oa}, octanol–air partition coefficient; K_{oc}, organic carbon–water partition coefficient; K_{ow}, octanol–water partition coefficient; SMILES, simplified molecular input line entry system; '-' not applicable

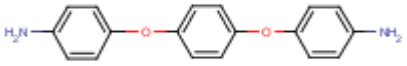
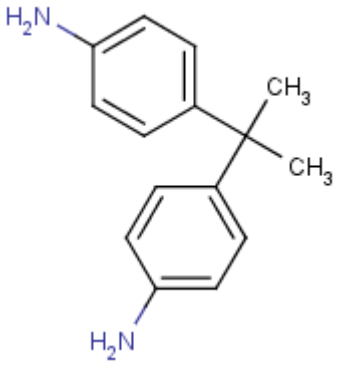
Appendix B. Summary of health effects information for BAPP

Endpoint	Lowest effect levels/Results
Acute toxicity	Lowest inhalation LD_{50} not specified, 6.0 hours of exposure (at unknown concentration) killed 0 of 5 rabbits (NTIS 1992a). Lowest oral LD_{50} = 308 mg/kg-bw in female rats (NTIS 1992a). Lowest dermal LD_{50} > 8000 mg/kg-bw in male and female rats (0 mortality in 14 days) (NTIS 1992a). [No additional acute studies identified]
Short-term repeated-dose toxicity	[No studies identified]
Subchronic toxicity	[No studies identified]
Chronic toxicity/carcinogenicity	*Bisaniline A (CAS RN 2479-47-2)* Three dogs exposed to Bisaniline A orally in capsule at a dose of 52.63 mg/kg-bw (0.3 g per dog, converted on the basis of bw = 5.7 g per dog (Calabrese and Kenyon [1991]) twice a week (equivalent to 15.03 mg/kg-bw per day, i.e., 52.6 mg/kg-bw × 2 days/7 days per week) for 6 years. Bladder tumours (Grade II papillary carcinoma) were noted in one dog. Kidneys of the dog with tumours showed marked fibrosis of cortex. No gross anatomical changes were observed in the other two dogs. Positive hematuria (i.e., presence of red blood cells in urine) were observed in all three dogs. Non-neoplastic effect LOEL = 15.03 mg/kg-bw per day, based on hematuria observed in all of the three dogs (NTIS 1992c). [No studies identified for BAPP]
Developmental toxicity	[No studies identified]
Reproductive toxicity	[No studies identified]
Genotoxicity and related endpoints: *in vivo*	[No studies identified]
Genotoxicity and related endpoints:	*Bisaniline A (CAS RN 2479-47-2)*

Endpoint	Lowest effect levels/Results
in vitro	Ames test Positive: *Salmonella typhimurium* strains TA98, TA100, 10 mg/plate, with S9 (NTIS 1992b). Positive: *Salmonella typhimurium* strain TA100, 10 mg/plate, without S9 (NTIS 1992b). Negative: *Salmonella typhimurium* strain TA98, 10 mg/plate, without S9 (NTIS 1992b). *1,4-phenylenebis(oxy)]bis- (CAS RN 3491-12-1)* Mutation in bacteria Positive: *Salmonella* typhimurium strain and concentration unknown (Shimizu et al. 1982) Unscheduled DNA synthesis Negative: hepatocyte primary cultures, washed and exposed to 10 µCi/mL test compounds for 20 hours (Mori et al. 1988) [No studies identified for BAPP]
Irritation	Skin irritation Not irritating: rabbit (NTIS 1992a). Eye irritation Irritating (transient): 1 of 6 tested eyes in rabbits, minor conjunctival irritation from 100 mg per eye (5 eyes healed at 24 hours, all healed at 48 hours) (NTIS 1992a).

Abbreviations: kg-bw, kilograms of body weight; LD_{50}, median lethal dose; LOEL, lowest-observed-effect level

Appendix C. Structures and data for BAPP analogues considered in the Health Section of this assessment

Name / CAS RN	Structure	Molecular weight (g/mol)	Analogue identification method (% similar)
Benzenamine, 4,4'-[1,4-phenylenebis(oxy)]bis- / 3491-12-1		292.336	SciFinder (76)
Bisaniline A /2479-47-2		226.321	ChemID (74.03)

Appendix D. Summary of QSAR results for BAPP

Table D-1. QSAR predictions on carcinogenicity

Model/ Species	Male Mice	Female Mice	Male Rat	Female Rat	Rat	Mice	Rodent	Mammal
Model Applier	N	P	P	N	N	N	N	-
Multicase Casetox	IC*	IC*	P	P	-	-	-	-
TOPKAT	ND	IC*	N	ND	-	-	-	-
Derek	-	-	-	-	-	-	-	NR

Abbreviations: '-' – No model available in QSAR suite; IC* – inconclusive (unreliable prediction, based on user-defined model specific criteria other than the models' applicability domain); N – Negative; ND – Not in domain; NR – Nothing to report; P – Positive.

Table D-1. QSAR predictions on carcinogenicity

Model/endpoints	Model Applier	Multicase Casetox	TOPKAT
Chromosomal aberrations	P	P	-
Chromosomal aberrations - other rodent	P	-	-
Chromosomal aberrations - rat	ND	-	-
Micronucleus mice	N	P	-
Micronucleus rodent	P	-	-
Drosophila	N	P	-
Drosophila heritable translocations	N	-	-
Drosophila SLRL	N	-	-
Mam. mutation	N	-	-
Mam. mutation dominant lethal	N	-	-
UDS	N	IC	-
UDS human lymphocytes	ND	-	-
UDS rat hepatocytes	N	-	-
Mouse lymphoma mut	N	N	-
S. cerevisiae	N	-	-
Yeast	N	-	-
HGPRT	N	-	-
E. coli	N	-	-
E. coli w	N	-	-
Microbial	N	-	-

Model/endpoints	Model Applier	Multicase Casetox	TOPKAT
Salmonella	N	P	IC*

Abbreviations: '-' – No model available in QSAR suite; IC* – inconclusive (unreliable prediction, based on user-defined model specific criteria other than the models' applicability domain); N – Negative; ND – Not in domain; NR – Nothing to report; P – Positive.

Table D-3. QSAR predictions on developmental toxicity - Model Applier

Endpoint/ Species	Mice	Rabbit	Rat	Rodent
Retardation	ND	ND	N	N
Weight decrease	ND	ND	P	N
Fetal death	ND	ND	N	N
Post-implantation loss	ND	ND	P	N
Pre-implantation loss	ND	ND	N	N
Structural	ND	ND	N	N
Visceral	ND	-	N	N

Abbreviations: '-' – No model available in QSAR suite; N – Negative; ND – Not in domain; P – Positive.

Table D-4. QSAR predictions on developmental toxicity – Multicase Casetox

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

Abbreviations: '-' – No model available in QSAR suite; N – Negative; P – Positive.

Appendix E. QSAR predictions on reproductive toxicity

Table E-1. QSAR predictions on reproductive toxicity – Model Applier

Model/ Endpoint /Species	Female Mice	Female Rat	Female Rodent	Male Mice	Male Rat	Male Rodent
Repro	ND	ND	ND	ND	ND	ND
Sperm	-	-	-	ND	ND	ND

Abbreviations: ND – not in domain; '-' – no model available in QSAR suite.

Table E-2. QSAR predictions on reproductive toxicity – Multicase Casetox

Mice	Rat	Rabbit	Human
P	P	N	N

Abbreviations: N – Negative; P – Positive.