Phenol, 4,4'-(1-methylethylidene)bis-: Environment tier II assessment

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Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted 4 years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has 3 tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit: www.nicnas.gov.au.

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Acronyms & Abbreviations

Rationale

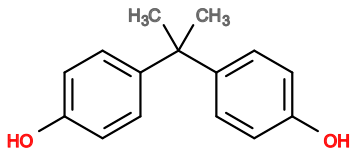
This Tier II assessment considers the environmental risks associated with the industrial uses of phenol, 4,4'-(1-methylethylidene)bis-, more commonly known as bisphenol A or BPA. This chemical is produced in very high volumes globally for use as a monomer feedstock for the manufacture of industrially important polymers, such as polycarbonates and epoxy resins. BPA also has significant non-monomer uses in thermal paper and as an additive stabiliser in polyvinyl chloride (PVC) plastics.

BPA has been reviewed by some international regulatory agencies due to its ability to mimic (o)estrogen in *in vitro* endocrine activity testing. The chemical has been listed on a number of international lists of suspected or identified endocrine-active or endocrine disrupting chemicals. In some international jurisdictions, restrictions on or voluntary cessation of the use of BPA and BPA-derived polymers has occurred for applications which potentially result in direct human exposure. Some examples of restricted applications include use in baby bottles and pacifiers, cosmetics, food packaging such as metal can linings and water bottles, and point-of-sale receipt paper.

BPA is frequently identified as a contaminant in the environment in Australia and internationally. This assessment will focus on the risks associated with exposure to BPA at environmentally relevant concentrations in Australia.

Chemical Identity

Synonyms	bisphenol A (BPA)
Structural Formula	



Molecular Formula	$C_{15}H_{16}O_2$
Molecular Weight (g/mol)	228.29
SMILES	Oc1ccc(cc1)C(c2ccc(O)cc2)(C)C

Physical and Chemical Properties

The measured physical and chemical property data below were retrieved from the databases contained in the OECD QSAR Toolbox 3.3 (LMC, 2013), the risk assessment of BPA conducted by the European Chemicals Bureau (ECB, 2003), and the registration dossier for BPA submitted under the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) legislation in Europe (REACH, 2019):

Physical Form	solid
Melting Point	155°C
Boiling Point	360°C (decomposition)
Vapour Pressure	4.12×10^{-7} Pa (25°C)
Water Solubility	300 mg/L
Ionisable in the Environment?	no
log K_{ow}	3.4

BPA is moderately soluble in water and very slightly volatile. The chemical is a weak acid which has an ionisation constant (pK_a) in water of 10.1 (LMC, 2013). This indicates that the phenolic groups in BPA are unlikely to be dissociated and that the chemical will not be ionised in the environment.

Import, Manufacture and Use

Australia

According to previous mandatory and/or voluntary calls for information, the chemical has uses in adhesives (binding agents) and as a stabiliser in the plastics industry. The total volume of BPA introduced into Australia in 2004/2005 was in the range of 100–1000 tonnes (NICNAS, 2016).

A significant additional source of BPA introduction is likely to be through import of thermal paper and PVC articles.

International

BPA is a high volume industrial chemical, with global use volumes in excess of 1 000 000 tonnes per year. BPA volume data are available from a number of jurisdictions. BPA is used in the European Union (EU) at 100 000–1 000 000 tonnes per year (ECHA, 2019b). Data from the US Chemical Data Reporting rule indicate that in 2012–2015 the total annual import/manufacture volume in the USA was in the range of 1–5 billion pounds (0.454–2.27 million tonnes) (US EPA, 2016). The annual manufacture and import volumes for Japan from 2012–2017 are in the range of 387 000–492 000 tonnes (NITE, 2017).

The main uses of BPA by volume are as an intermediate in the manufacture of polycarbonate and epoxy resin polymers (ECB, 2008; US EPA, 2010). Comparatively minor volumes of BPA are used in the manufacture of phenoplast resins, unsaturated polyester/polyacrylate resins, polysulfone resins and other specialty polymers (ECB, 2010).

BPA is also used in its unbound form in thermal paper, and as an additive stabiliser/antioxidant in polyvinyl chloride (PVC). Data from the EU in 2008 indicate that these two uses account for approximately 0.4% of the total volume of BPA used (ECB, 2010). BPA may also be used as a polymerisation retarder in PVC manufacture, but this use has been phased out in the EU (ECB, 2010).

Environmental Regulatory Status

Australia

The use of BPA is not subject to any specific national environmental regulations.

BPA-containing polycarbonate baby bottles are not generally available in Australia following a voluntary industry phase-out in 2010 (FSANZ, 2019).

BPA concentrations in recycled water for drinking water augmentation are recommended to not exceed 200 micrograms per litre (µg/L) (NHMRC, 2008). This guideline was derived from a tolerable daily intake value of 0.05 milligrams per kilogram body-weight per day (mg/kg bw/day).

Default guideline values for BPA in fresh and marine water are in development under the National Water Quality Management Strategy (Water Quality Australia, 2018).

United Nations

BPA is not currently identified as a Persistent Organic Pollutant (UNEP, 2001), ozone depleting substance (UNEP, 1987), or hazardous substance for the purpose of international trade (UNEP & FAO, 1998).

OECD

A SIDS initial assessment profile on BPA was agreed upon in 2002 at the 14th Screening Information Dataset (SIDS) Initial assessment Meeting (SIAM 14) (OECD, 2012b). The screening profile concluded that the chemical was a candidate for further work. Specific further work was recommended to clarify effects on aquatic snails and on spermatogenesis in fish, to generate toxicity data for soil organisms, to conduct further research on effects of BPA on mammalian reproductive development, and that further information gathering on water compartment exposure may be considered for regional risk assessments. This document identified use in thermal paper and PVC industries as the main sources of BPA emissions to the environment.

Canada

BPA is listed on the Canadian Domestic Substances List (DSL) (ECCC, 2019b). During the Categorization of the DSL in 2006, this substance was categorized as not Persistent (not P), not Bioaccumulative (not B), and Inherently Toxic to the Environment (iT_E) (ECCC, 2019a).

BPA has been subject to assessment and risk management measures conducted under the *Canadian Environmental Protection Act, 1999* (CEPA). BPA was included in Batch 2 of the Canadian Challenge program (Government of Canada, 2010a), with the subsequent screening assessment published in 2008 (ECCC, 2008). This assessment concluded that, based on a precautionary approach, BPA is entering or may be entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity. Following this assessment, BPA was added to the Schedule 1 List of Toxic Substances in 2010 (Government of Canada, 2010b). In 2010, a notice requiring the preparation and implementation of pollution prevention plans with respect to bisphenol A in industrial effluents was published, which required facilities manufacturing or using BPA in quantities greater than 100 kg/year to develop and implement plans to maintain a BPA concentration of 1.75 µg/L or lower in facility effluent (Government of Canada, 2012).

Canadian federal environmental quality guidelines for BPA were released in 2018. These included a water concentration of 3.5 µg/L, sediment concentration of 25 micrograms per kilogram dry weight (µg/kg dw), and dietary concentrations of 660 micrograms per kilogram wet weight (µg/kg ww) of food for mammalian wildlife and 110 µg/kg ww food for avian wildlife (ECCC, 2018).

BPA is listed on the Cosmetic Ingredient Hotlist, prohibiting its use in cosmetic products (Health Canada, 2018).

Polycarbonate baby bottles containing bisphenol A were prohibited in Canada in 2010 by addition of BPA to Schedule I of the *Hazardous Products Act* (Government of Canada, 2010c).

European Union

BPA is registered under the REACH legislation (ECHA, 2019c). It is also identified as a Substance of Very High Concern (SVHC) (ECHA, 2019d) due to its endocrine disrupting properties for human health and the environment, and for its reproductive toxicity. BPA is listed on Annex XVII (the Restriction list), which will prohibit the sale of thermal paper containing BPA at a concentration of 0.02% or more by weight in the EU when it comes into effect in January 2020 (ECHA, 2016). In addition, in October 2019 the European Chemicals Agency recommended that BPA be added to Annex XIV (the Authorisation list), which would require industry to seek authorisation for use of BPA in non-polymer applications (ECHA, 2019e).

This substance was previously prioritised for assessment under the superseded Existing Substances Regulation (ESR), with a risk assessment report published by the European Chemicals Bureau in 2003 followed by an addendum published in 2008 (ECB, 2003; 2008). A combined document containing the original report and the addendum was published in 2010 (ECB, 2010). BPA was subsequently assessed through the Community Rolling Action Plan (CoRAP) and Risk Management Option Analysis (RMOA) processes under the REACH legislation for its human health and environmental risk profile. These assessment efforts resulted in the listings of BPA on the SVHC list and the Restriction list (ECHA, 2019a).

Bisphenol A is listed on Annex II of the EU Cosmetics Directive, prohibiting its use in cosmetics in the EU (EC, 2019).

United States of America

BPA is listed as ‘active’ on the United States Environmental Protection Agency Chemical Substance Inventory, indicating that it has recently been manufactured, imported or processed by industry in the USA (US EPA, 2019b).

BPA is a US EPA Action Plan chemical (US EPA, 2011), and was added to the TSCA Work Plan list in 2014 (US EPA, 2014b). The chemical is not currently a candidate for the High-Priority Chemical Substances list for review by the US EPA after amendment of TSCA in 2016 (US EPA, 2019a).

BPA is not approved for use in baby bottles, sippy cups and infant formula packaging following amendments to food additive regulations in 2012 and 2013 (FDA, 2014). This regulatory action was not a risk management measure, but rather due to market abandonment of the use of BPA in these applications.

Association of Southeast Asian Nations (ASEAN)

BPA is on the ASEAN Cosmetic Directive Annex II Part 1 (ACA, 2019). BPA may not form part of cosmetic products in ASEAN countries.

Environmental Exposure

Use of unbound BPA in PVC is expected to be a major source of diffuse emissions of BPA, while paper recycling mills may be significant point emission sources for the chemical.

The primary uses of BPA by volume (>90%) are as intermediates in the manufacture of polycarbonate and epoxy resin polymers (ECB, 2010; US EPA, 2010). BPA is also used in aryl polyesters, polysulfones, and phenoplast resin manufacture. Despite the high use volume, these uses are not expected to result in high emissions to the environment as they result in BPA irreversibly bound within a polymer matrix. The European Chemicals Bureau completed a detailed exposure assessment for BPA in 2008 (ECB, 2010). The quantities of residual unreacted BPA in polycarbonate products were reported to be < 25 parts per million (ppm), with maximum residual amounts in the 100–150 ppm range. Release of BPA from the ongoing use of BPA-based polymers was generally low. Calculations for annual releases of BPA from epoxy resin and polycarbonate articles in Europe returned cumulative BPA emissions low enough that this emission pathway was disregarded in the final exposure assessment.

Uses of BPA in applications which do not result in BPA covalently bound within an article generally have higher potential for emissions to the environment. The most important of these for environmental exposure are uses in thermal paper and in PVC.

BPA is used in PVC as an additive stabiliser/antioxidant, where it is generally a stabiliser for the other unbound additives such as plasticisers rather than for the polymeric material itself. As BPA is not irreversibly bound within the PVC matrix, it can be released to the environment through migration of the chemical onto the polymer surface, as well as from abrasion and wear of these articles during their normal use (ECB, 2010). BPA migration from articles can contribute to BPA in indoor dust, where it is a common contaminant (Healy, et al., 2015). Dust-borne contaminants may be released to the environment through the washing of surfaces and fabrics (OECD, 2011). The exposure assessment by the ECB concluded that releases from PVC articles accounted for more than 90% of BPA emissions to European surface waters (ECB, 2010).

BPA is used as a developer in thermal paper for receipts, tickets and labels (US EPA, 2014a). Paper recycling mills often de-ink paper waste, which results in high removal of BPA and emission to waste streams (ECB, 2010). Solid paper mill sludge waste may be disposed of to landfill or applied to land as a soil improver. Insufficient treatment of aqueous waste streams may result in high BPA concentrations in effluent.

Environmental exposure to BPA is expected to be primarily through diffuse emissions from PVC articles, with the possibility of point source emissions to wastewater and soil from paper recycling mills. These exposure pathways are considered in this assessment.

Environmental Fate

Partitioning

BPA is generally expected to partition to the soil and water compartments.

BPA is a neutral organic chemical that is moderately soluble in water. The calculated Henry’s Law constant for the partitioning of BPA between air and water is 0.0003 Pa m^3/mol (US EPA, 2008), indicating that the chemical is only very slightly volatile from

water and moist soil.

Experimentally determined organic carbon normalised soil adsorption coefficients (K_{oc}) for BPA in several Australian soils indicate that the chemical will have medium to low mobility in soil (log K_{oc} = 2.4–3.2) (Ying and Kookana, 2005). These K_{oc} values are consistent with those used in international assessments (ECB, 2010; ECCC, 2008)

Calculations with a standard multimedia partitioning (fugacity) model assuming equal and continuous distributions to air, water and soil compartments (Level III approach) predict that this chemical will mainly partition to the soil and water compartments (53% and 47% respectively) (US EPA, 2008).

Degradation

BPA is not persistent. Under aerobic conditions, BPA will fully degrade in water, sediment and soil. Minimal abiotic or anaerobic degradation is expected in these compartments.

Abiotic degradation of BPA is unlikely to be a major dissipation pathway. Hydrolysis under aqueous conditions is expected to be negligible based on the lack of hydrolysable functional groups; corroborating this, BPA degradation studies in sterilised water, sediment and soil showed no degradation over extended time periods (Kang and Kondo, 2005; Ying and Kookana, 2003; 2005). BPA is likely to be rapidly degraded by reactions with hydroxyl radicals in the atmosphere (US EPA, 2008), but as the chemical has very low volatility this is not likely to account for a significant fraction of the dissipation of BPA that occurs in the environment.

BPA is readily biodegradable according to standard aerobic biodegradation screening tests. The chemical passed the ready biodegradability criteria with 75–81% and 89% biodegradation over 28 days in two separate OECD Test Guideline (TG) 301F (manometric respirometry) tests (ECB, 2008; ECCC, 2008).

Aerobic biodegradation of BPA has also been demonstrated in tests simulating environmental media, including riverwater, seawater, sediment and soil. In one study, primary degradation half-lives in the range of 2–3 days at 30°C were found for BPA in river water sampled from three different Japanese rivers (Kang and Kondo, 2002). In another study, 28-day aerobic degradation tests were conducted using river water sampled from seven rivers in Europe and the USA (Klečka, et al., 2001). After lag periods of 2–8 days, BPA degraded rapidly in tests with the different river water samples, with calculated BPA primary degradation half-lives (excluding the lag phase) in the range of 0.5–2.6 days. Addition of 10% by weight sediment sampled from the same location to a riverwater degradation test gave a primary degradation half-life of approximately 2.5 days, without any visible lag period. In both the riverwater and sediment/riverwater systems, mineralisation of BPA was observed without the production of recalcitrant metabolites (Klečka, et al., 2001).

Aerobic degradation studies indicate that BPA will degrade in seawater, but with substantially longer lag periods. Seawater sampled from Hyuga Bay in Japan was used to conduct 60 day degradation tests at a range of temperatures (Kang and Kondo, 2005). At 25°C, negligible degradation was observed for the first 30 days, followed by approximately 80% primary degradation over the remaining 30 days. In another study using seawater sampled from the coast near Adelaide in South Australia, a similar acclimation period of 35 days with minor BPA degradation preceded 65–70% primary degradation over 7 days in an aerobic degradation test (Ying and Kookana, 2003).

Ying and Kookana (2005) conducted degradation studies on BPA in loam soil sampled from agricultural land in South Australia. BPA underwent rapid primary degradation without any initial lag period, giving a calculated half-life of 7 days in soil under aerobic conditions.

Many of the studies discussed above also conducted experiments under anaerobic conditions, generally as controls for the aerobic degradation tests. Minimal degradation of BPA was observed under anaerobic conditions in riverwater, seawater, soil and marine sediment over periods of up to 70 days (Kang and Kondo, 2002; 2005; Ying and Kookana, 2003; 2005).

Bioaccumulation

BPA is not bioaccumulative.

BPA has low potential to bioconcentrate in fish. Rice fish (*Oryzias latipes*) were exposed to 15 or 150 µg/L BPA under flow-through conditions for 6 weeks with HCO-40 (a fatty acid ethoxylate) used as an emulsifier (NITE, 2019). The maximum measured bioconcentration factor for BPA during the test was 68 L/kg, which is well below the categorisation threshold for a bioaccumulative chemical (BCF ≥ 2000 L/kg).

Heinonen, et al. (2002) tested the bioconcentration potential of BPA in freshwater clams (*Pisidium amnicum*) at a number of temperatures. Clams were exposed to 1 µg/L BPA under semi-static conditions for a total period of 8 days, followed by a depuration period of 4 days. The maximum BCF measured in this study was 144 L/kg at 8°C.

BPA is biotransformed in organisms across a wide range of trophic levels, including mammals, fish, amphibians, crustaceans, bacteria, fungi, and plants (Canesi and Fabbri, 2015; Michałowicz, 2014; Suzuki, et al., 2004). This is likely to limit the bioaccumulation potential of BPA. In mammals, BPA may be conjugated to form sulfate, glucuronide or glutathione derivatives, or alternately undergo a number of possible hydroxylation or oxidation reactions on the phenol rings or at the linking methylethylidene group (Michałowicz, 2014). Bacterial degradation pathways appear to begin with oxidation or hydroxylation at the linking group followed by rearrangement, further oxidation, and finally cleavage into a variety of monophenolic compounds (Suzuki, et al., 2004).

Transport

Based on its low potential to partition to the atmosphere and predicted rapid degradation in the troposphere by indirect photo-oxidation, the chemical is not expected to undergo long-range transport.

Predicted Environmental Concentration (PEC)

A PEC for BPA in river water of 200 nanograms per litre (ng/L) (0.2 µg/L) was estimated based on the range of available measured BPA concentrations in effluents from sewage treatment plants (STPs) and in riverine receiving waters in Australia. BPA is generally efficiently removed by secondary sewage treatment.

The highest BPA concentrations in the Australian environment identified for this assessment were those reported by French, et al. (2015), who conducted organic contaminant monitoring at three STP outfall sites and other sites in Darwin Harbour in 2010–2011. The highest BPA concentrations were consistently detected in the outfall from the Buffalo STP, a secondary treatment plant which treats most of the sewage from the northern suburbs of Darwin. Seasonal variation of flow rate due to rainfall was also apparent during the year. The highest BPA concentrations in the Buffalo STP effluent were 150 ng/L in October 2010 (late dry season), which increased to 1000 ng/L (1 µg/L) in March 2011 (wet season). The concentration decreased to 24 ng/L in July 2011 (dry season). The highest concentrations at other sites were also during the March 2011 wet season, with an STP effluent concentration of 600 ng/L, and a surface water concentration of 560 ng/L taken in front of a stormwater discharge point near an industrial site.

BPA concentrations measured at other sites in Australia were generally somewhat lower. Monitoring at five sites in southeast Queensland found BPA at concentrations in surface waters in the range of <10–106 ng/L (Scott, et al., 2018). A median BPA effluent concentration of 21.5 ng/L was obtained from a survey of 11 STPs in Queensland, South Australia and the ACT (Williams, et al., 2007). Monitoring at the Wodonga STP in Wodonga, Victoria, which employs a tertiary treatment process, found BPA at only trace amounts in effluent and in surface waters near the STP outfall (Kumar, et al., 2012).

BPA is generally efficiently removed during secondary sewage treatment. One secondary STP in southeast Queensland had a notably high influent BPA concentration of 3000 ng/L, which was reduced to 37 ng/L in effluent (Tan, et al., 2007). Other STPs sampled in this study had effluent BPA concentrations of 12–87 ng/L. A survey of endocrine-active compounds in 13 Australian STPs found influent BPA concentrations up to 670 ng/L, which was generally removed to below 100 ng/L after secondary treatment, with a maximum effluent concentration of 145 ng/L (Leusch, et al., 2006).

BPA emissions in STP effluent are not the only significant source of BPA found in surface waters. At the Wetalla secondary STP in Towoomba, Queensland, the BPA concentration measured in surface waters adjacent to the STP outfall was 314 ng/L (Kumar, et al., 2012). However, the BPA concentration in water samples taken upstream of this STP outfall was 141 ng/L. It was noted in the report that the STP itself was downstream of the urban area it serviced, and that diffuse emissions from this urban area were likely the source of the BPA measured upstream. In another study, BPA concentrations in effluent from 5 STPs in northeast Queensland were in the range of 13–44 ng/L (Ying, et al., 2009). Receiving water concentrations, including upstream, outfall, and downstream of these STP outfalls were in the range of 4–59 ng/L, suggesting that other sources apart from the related STP contribute to the environmental concentrations.

Measured levels of BPA in the Australian environment are generally comparable with those found internationally. Monitoring in Canada indicated that most surface water concentrations were in the range of 10–100 ng/L, with a highest value of 12 µg/L (ECCC, 2018). Monitoring in the US gave a median concentration of 140 ng/L in samples from US streams collected in 1999–

2000 (US EPA, 2010), with concentrations generally not exceeding 1 µg/L. Monitoring in freshwater in the EU conducted between 1997 and 2005 found a median concentration of 10 ng/L and a mean concentration of 130 ng/L (ECB, 2010). Maximum concentrations generally did not exceed 1 µg/L.

No studies quantifying BPA concentrations in Australian sediment were found. Freshwater sediment BPA concentrations up to 1.63 mg/kg dry weight were found in a survey of studies conducted across European countries. However, most maximum measured concentrations were below 0.4 mg/kg dw, and median concentrations reported in these studies were generally below 0.2 mg/kg dw (ECB, 2010).

A survey of biosolids from 13 Australian STPs found BPA concentrations in the range of <0.01–1.47 mg/kg, with an average of 0.47 mg/kg dry weight (Langdon, et al., 2011). This is below a global average of 1.22 mg/kg dw calculated by the same authors in an earlier study (Langdon, et al., 2010).

Environmental Effects

Effects on Aquatic Life

BPA is very toxic to fish and aquatic invertebrates. There is a large difference between the acute and chronic toxicity of BPA suggesting that the chemical may exert chronic effects through a specific mode of toxic action.

Acute toxicity

BPA has moderate acute toxicity. The following measured median effect concentration (EC50) and median lethal concentration (LC50) data were retrieved from the REACH registration dossier for BPA and from the scientific literature (Alexander, et al., 1988; REACH, 2019):

Taxon	Endpoint	Method
Fish	96 h LC50 = 4.6 mg/L	*Pimephales promelas* (fathead minnow) – freshwater fish OECD TG 203 Mortality
Invertebrates	48 h LC50 = 10.2 mg/L	*Daphnia magna* E07-04, ASTM E-35.21 – freshwater invertebrate Mortality
	96 h LC50 = 1.1 mg/L	*Americamysis bahia* (mysid shrimp) E07-04 – marine invertebrate Mortality
Algae	96 h EC50 = 1.1 mg/L	*Skeletonema costatum* (marine diatom) EPA 560/6-82-002 Cell count

Taxon	Endpoint	Method
	96 h EC50 = 2.73 mg/L	*Pseudokirchneriella subcapitata* (freshwater green algae) EPA 560/6-82-002 Cell count

Chronic toxicity

BPA has high chronic toxicity to fish and invertebrates. The following lowest-observed-effect-concentration (LOEC) and no-observed-effect-concentration (NOEC) values are summarised in the table below (Alexander, et al., 1988; Brennan, et al., 2006; Keiter, et al., 2012; REACH, 2019; Sieratowicz, et al., 2011):

Taxon	Endpoint	Method
Fish	90 d LOEC = 0.01 mg/L	*Danio rerio* (zebrafish) Flow-through multigenerational study Growth rate (F1 generation) (Keiter, et al., 2012)
Invertebrates	21 d LOEC = 0.2 mg/L	*Daphnia magna* ISO 10706 Mortality (F1 generation) (Brennan, et al., 2006)
Algae	96 h EC10 = 1.36 mg/L	*Pseudokirchneriella subcapitata* EPA 560/6-82-002 Cell count (Alexander, et al., 1988; REACH, 2019)

Developmental and reproductive effects are among the most common reported endpoints, with several studies reporting increased susceptibility to BPA-induced toxic effects following chronic exposure between generations in vertebrates and invertebrates. Relevant details from the studies summarised in the table above and from additional studies are discussed further below:

A freshwater fish multigenerational BPA exposure study with zebrafish was conducted, starting with fertilised zebrafish eggs (Keiter, et al., 2012). This study gave a 30 and 90 day growth LOEC of 10 µg/L in the second generation; this was the lowest test concentration and the 90 d NOEC is, therefore, < 10 µg/L. Two generations of zebrafish were exposed to BPA from 2–4 hours post fertilisation, with continual exposure for 180 days. Sampling at 30, 90 and 180 days exposure time revealed significantly decreased fish weight and length within early stage (30–90 d), but not late stage (180 d) development in fish from the second generation at 10 µg/L BPA. The second generation therefore appeared to be more sensitive to BPA-induced growth inhibition compared to the first generation.

In a freshwater fish multigenerational study, fathead minnow were exposed to BPA, with a hatching success LOEC of 160 µg/L for eggs produced by the second generation (NOEC = 16 µg/L) (Staples, et al., 2011). The hatching success LOEC for eggs

produced by the first generation was 640 µg/L, demonstrating that later generations were more sensitive to this BPA-induced adverse reproductive effect after chronic multigenerational exposure.

A two-generation *Daphnia magna* (freshwater) exposure study (Brennan, et al., 2006), found a 21 d mortality LOEC of 0.2 mg/L in the second generation. In comparison, the first generation 21 d LOEC was 0.6 mg/L, again demonstrating increasing sensitivity to BPA between generations following chronic multigenerational exposure.

A BPA exposure study with a marine invertebrate, *Americamysis bahia* (mysid shrimp) according to US EPA OPPTS guideline 850.1350, resulted in a 28 day reproduction NOEC of 0.17 mg/L (Mihaich, et al., 2018).

Sediment

There are relatively few studies on the toxicity of BPA exposed through sediment. The available studies indicate that BPA has moderate toxicity, with a lowest sediment NOEC of 12 mg/kg dw BPA.

Several sediment ecotoxicity tests were conducted according to standardised test guidelines, using BPA-spiked sediment in mixed sediment-water systems with freshwater and estuarine/marine benthic organisms (Staples, et al., 2016). In each case, calculated concentrations of BPA were also supplemented in the overlying water to maintain constant concentrations of the chemical in sediment. BPA concentrations in the test sediment were measured periodically during each test so that actual exposure concentrations could be verified.

A freshwater midge toxicity test according to OECD TG 218 using *Chironomus riparius* returned a 28 day emergence NOEC of 54 mg/kg dry weight (dw) BPA. A freshwater worm toxicity test according to OECD TG 225 using *Lumbriculus variegatus* (blackworm) returned a 28 day biomass NOEC of 22 mg/kg dw BPA. An estuarine/marine amphipod toxicity test according to US EPA method EPA/600/R-01/020 using the burrowing amphipod, *Leptocheirus plumulosus*, returned a 28 day amphipod mass NOEC of 12 mg/kg dw BPA.

Effects on Terrestrial Life

The effects of BPA on terrestrial model organisms has been addressed in the IMAP Human health tier II assessment of BPA (NICNAS, 2016). Critical health effects identified include systemic long-term reproductive toxicity at high dose levels, and general toxicity to the liver and kidney in mice and rats.

Endocrine Effects

BPA may induce effects in biota through an endocrine-mediated mode of action. A detailed examination of this mode of action is beyond the scope of this assessment; however, summary findings from a small selection of relevant peer-reviewed scientific studies are presented below. A comprehensive examination of the available literature on this topic was recently published by ECHA in support of the listing of BPA as a SVHC for environmental concerns (ECHA, 2017).

BPA is known to act as an (o)estrogen receptor agonist in *in vitro* tests (ECHA, 2017). This indicates the potential for BPA to induce endocrine-mediated effects at the organism level. However, *in vitro* responses are not necessarily directly indicative of *in vivo* effects due to pharmacokinetic considerations. This assessment will therefore focus on *in vivo* studies.

A number of fish vitellogenin induction studies indicate that BPA has *in vivo* (o)estrogenic potential in fish. Increased concentrations of biomarkers such as the egg yolk precursor protein, vitellogenin (VTG), in fish blood serum is commonly considered to be diagnostic of endocrine activity in *in vivo* studies (OECD, 2004; 2012a). In the same multigenerational fathead minnow study as discussed in the chronic toxicity section above (Staples, et al., 2011), induction of serum VTG levels was seen at 160 µg/L BPA in male fish for both F0 and F1 generations. In a separate long-term fish study, induction of VTG synthesis was seen at 160 µg/L BPA after 71 days exposure (Sohoni, et al., 2001). In a relatively short-term fish study, a significant increase in the vitellogenin levels in male carp exposed to 1000 µg/L BPA was seen after 14 days exposure time (Mandich, et al., 2007). In addition, the numbers of male carp that could be grouped in to ‘non-vitellogenic’, ‘vitellogenic’ and ‘highly vitellogenic’ groups was biased in favour of the ‘vitellogenic’ and ‘highly vitellogenic’ groups in a dose-dependent manner with increasing BPA concentration from 1–1000 µg/L, supporting a causal association after 14 days exposure time.

Two studies examining fish gonad histopathology indicate that BPA causes effects that are generally considered diagnostic or strongly indicative of an endocrine-related response. The observed diagnostic gonad histopathological endpoints include the presence of testicular oocytes and increased spermatogonia, while other observed endpoints such as oocyte atresia and testicular degeneration changes are generally indicative of endocrine effects, though they may have other causes (Mandich, et al., 2007; OECD, 2010; 2012a; Sohoni, et al., 2001).

The first study found significant increases in spermatogonia cells present in male fathead minnow testes at exposure concentrations of 640 and 1280 µg/L BPA after 164 days (Sohoni, et al., 2001). Concurrently, decreases in mature spermatozoa cells were seen at exposure concentrations from 16 to 1280 µg/L BPA, further supporting a causal association. This effect was more pronounced at higher BPA concentrations, with only 10% of sampled males in the 1280 µg/L exposure group containing any mature spermatozoa at all. These two effects, specifically a decrease in mature sperm cell count and an increase in immature sperm cell count, indicate that BPA may inhibit spermatogenesis in fish.

The second study found a number of gonad histological alterations in common carp after 2 weeks BPA exposure (Mandich, et al., 2007). At the highest exposure concentration of 1000 µg/L BPA, 27% of the male carp had intersex gonads, showing previtellogenic oocytes alongside both normal and degenerating testicular tissue. Female carp were also affected, with oocyte atresia observed in increasing proportions of the test group alongside increasing BPA concentrations from 10–1000 µg/L. At 1000 µg/L BPA, 57% of females exhibited oocyte atresia. These observed effects are indicative of an endocrine mode of action, and are notable for the short time-frame of exposure leading to significant effects.

In BPA exposure studies with *Xenopus laevis* (African clawed frog) tadpoles during metamorphosis, a significant change in male:female sex ratio compared to the control group was seen at 23 µg/L BPA (Levy, et al., 2004). Tadpoles exposed to 23 µg/L BPA throughout metamorphosis had a 31% prevalence of males based on gross gonad morphology, compared to the 56% male population in the control group. These exposure conditions were repeated in a second experiment, finding a 30% male population in the BPA-dosed group and a 52% male population in the control. However, exposure at lower (2.3 µg/L) and higher (230 µg/L) concentrations did not induce any effect on the sex ratio. Intersex gonads did not occur at a significant rate. This study indicates that BPA may affect sexual differentiation, though potentially with a biphasic dose-response curve.

A number of field studies have tested for (o)estrogenic activity in Australian surface waters or STP effluent based on *in vivo* biomarkers such as vitellogenin induction or specific morphological change-type effects (Scott, et al., 2018). Several of these studies detected (o)estrogenic effects. Most of these studies did not attempt to quantify the chemicals present in the sampled waters. However, detected (o)estrogenic effects are often suggested to be caused by a number of natural and synthetic (o)estrogens such as estrone, 17β-estradiol (E2), estriol (E3), and 17α-ethinylestradiol (EE2), and phenolic compounds such as nonylphenols, octylphenols, and BPA.

One of these studies found (o)estrogenic activity in marine waters receiving STP effluent from the Burwood beach STP in Newcastle, New South Wales (Andrew-Priestley, et al., 2012). Effluent from this plant is released approximately 500 metres offshore through underwater diffusers. Sydney rock oysters placed at different depths at two sites less than 50 metres and 100–150 metres from this outfall had higher vitellogenin levels and a higher proportion of mature female gonad developmental stages compared to a reference location after 6 weeks exposure time. An increased proportion of females was found at one depth at the < 50 metres site.

BPA was present in combination with other endocrine-active chemicals at this marine site, making it difficult to attribute endocrine effects exclusively to BPA (or any specific chemical). Natural and synthetic (o)estrogens concentrations in water samples were below 1 ng/L each for estrone, E2 and EE2, and 3 ng/L for E3. Phenolic compound concentrations were 5 and 6 ng/L for nonylphenols and octylphenols respectively, while BPA was quantified at 62 ng/L. While BPA was present at a relatively high concentration, the other chemicals present included those with relatively potent (o)estrogenic potential.

Predicted No-Effect Concentration (PNEC)

The PNEC for BPA is 0.1 µg/L (100 ng/L).

The zebrafish growth LOEC value of 0.01 mg/L was used to derive the PNEC for this chemical. A conservative assessment factor of 100 was used based on evidence of increasing sensitivity to BPA after intergenerational exposure in multiple studies over multiple trophic levels.

Categorisation of Environmental Hazard

The categorisation of the environmental hazards of BPA according to domestic environmental hazard thresholds is presented below (EPHC, 2009):

Persistence

Not Persistent (Not P). Based on multiple studies demonstrating rapid degradation in a variety of environmental media, BPA is categorised as Not Persistent.

Bioaccumulation

Not Bioaccumulative (Not B). Based on low measured bioconcentration factors (BCF) in fish and clams, and evidence of biotransformation over multiple trophic levels, BPA is categorised as Not Bioaccumulative.

Toxicity

Toxic (T). Based on high chronic toxicity to fish, BPA is categorised as Toxic.

Summary

Phenol, 4,4'-(1-methylethylidene)bis- is categorised as:

- Not P
- Not B
- T

Risk Characterisation

BPA has high chronic aquatic toxicity and can cause adverse effects on growth and reproduction. Monitoring data indicate that BPA is a ubiquitous contaminant in Australian surface waters, with contributing sources including STP outfall emissions as well as diffuse emissions from urban areas. Due to the high water solubility of BPA, surface waters are expected to be the compartment of concern.

Based on the PEC and PNEC values determined above, the following Risk Quotient (RQ = PEC ÷ PNEC) has been calculated for release of BPA into surface water:

Compartment	PEC (µg/L)	PNEC (µg/L)	RQ
Freshwater	0.2 µg/L	0.1 µg/L	2

The RQ value for BPA in freshwater is 2, which suggests a marginal risk to aquatic life in rivers. The main risk driver is considered to be the possibility of adverse effects occurring at concentrations lower than those used in most ecotoxicity studies due to cumulative sensitisation of aquatic organisms following intergenerational exposure.

BPA is not infrequently detected at higher concentrations than the PNEC of 0.1 µg/L in surface waters and STP effluent in Australia. As rainwater runoff from urban areas appears to be a significant source of BPA, seasonal variations in exposure concentrations in surface waters may be expected. In addition, potential point emission sources such as paper recycling facilities

may contribute to high localised emissions of BPA to sewage treatment plants, which may in turn lead to increased emissions to surface waters despite the generally efficient removal of this chemical in secondary sewage treatment plants.

Acute and chronic BPA toxicity data for marine organisms reviewed in this report generally indicate slightly higher toxicity than for freshwater organisms of the same trophic level, though there are fewer reliable studies available. In addition, there are insufficient Australian monitoring data to derive a predicted environmental concentration for the marine aquatic environment. In lieu of these data, the freshwater risk quotient is considered to be indicative of the risk posed to the marine environment. However, it is noted that while toxicity may be slightly higher and the degradation half-life slightly longer in the marine environment, emissions of BPA are less likely to be a concern outside the immediate vicinity of the release point where discharge occurs into well-mixed marine waters.

BPA can cause adverse effects in aquatic vertebrates through an endocrine-mediated mode of action. However, many of the specific endocrine-related effects occur at concentrations well in excess of what has been detected in the Australian environment. In addition, the specific effects of BPA in the Australian environment are difficult to distinguish from effects caused by other known (o)estrogenic chemicals in STP effluent and surface waters, including natural and synthetic (o)estrogens. These effects are nonetheless of concern as, being related in particular to reproductive success in aquatic organisms, there are clear connections to potential population-level adverse outcomes in the environment.

Key Findings

BPA is a chemical with a high global volume of use. The main sources of emission to the environment are likely to be due to its use in PVC articles, and releases due to recycling of BPA-containing thermal paper. Uses of BPA that result in it irreversibly bound within a polymer matrix generally result in very low emission rates, and are not expected to be significant sources of emission of the chemical to the environment.

Monitoring of Australian surface waters and STP effluent indicate that BPA is present at levels which are generally below 200 ng/L. However, seasonal variation of BPA emissions in urban rainwater runoff may contribute to higher concentrations of the chemical in surface waters near urban areas. Australian fresh and marine water default guideline values for BPA are currently in development.

BPA is toxic, with adverse effects related to development identified at very low concentrations. Intergenerational exposure appears to cause an increased sensitivity to BPA-induced adverse effects in aquatic organisms. In addition, BPA is an endocrine active chemical, which may cause effects mediated through an endocrine-related mode of action.

BPA is assessed as posing a marginal risk to the Australian riverine and marine environment at current exposure levels.

The chemical is not a PBT substance according to domestic environmental hazard criteria.

Recommendations

It is recommended that BPA be added to the list of organic contaminants that are routinely monitored in sewage treatment effluent and surface waters in Australia.

Further assessment may be required if reliable studies become available demonstrating adverse intergenerational effects of BPA on aquatic life at current exposure concentrations in the Australian environment.

Environmental Hazard Classification

In addition to the categorisation of environmental hazards according to domestic environmental thresholds presented above, the classification of the environmental hazards of phenol, 4,4'-(1-methylethylidene)bis- according to the third edition of the United Nations' Globally Harmonised System of Classification and Labelling of Chemicals (GHS) is presented below (UNECE, 2009):

Hazard	GHS Classification (Code)	Hazard Statement

Hazard	GHS Classification (Code)	Hazard Statement
Acute Aquatic	Category 2 (H401)	Toxic to aquatic life
Chronic Aquatic	Category 1 (H410)	Very toxic to aquatic life with long lasting effects

These classifications have been made based on the ecotoxicity data presented in this assessment.

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