An Australian Government Initiative

Australian & New Zealand
GUIDELINES FOR FRESH & MARINE WATER QUALITY

Toxicant default guideline values for aquatic ecosystem protection

Bisphenol A in freshwater

Technical brief

July 2023

Water Quality Guidelines is a joint initiative of the Australian and New Zealand governments, in partnership with the Australian states and territories.

Cataloguing data
This publication (and any material sourced from it) should be attributed as: ANZG 2023, *Toxicant default guideline values for aquatic ecosystem protection: bisphenol A in freshwater*. Australian and New Zealand Guidelines for Fresh and Marine Water Quality. CC BY 4.0. Australian and New Zealand Governments and Australian state and territory governments, Canberra, ACT, Australia.

This publication is available at waterquality.gov.au/anz-guidelines/guideline-values/default/water-quality-toxicants/toxicants.

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Acknowledgements
These default guideline values (DGVs) were derived by Naomi Cooper, Kirsten Broadgate, Clare Papaleo and Carolyn Brumley of Golder Associates, Melbourne, Australia. The DGVs were peer reviewed by two anonymous reviewers and by two contracted technical advisors, Dr Rick van Dam and Alicia Hogan. The DGVs were also reviewed and approved by jurisdictional technical and policy oversight groups and a National Water Reform Committee prior to being published.

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Summary

The default guideline values (DGVs) and associated information in this technical brief should be used in accordance with the detailed guidance provided in the Australian and New Zealand Guidelines for Fresh and Marine Water Quality website (www.waterquality.gov.au/anz-guidelines).

Bisphenol A (BPA) is a widely used, high production volume industrial chemical. Major uses of BPA are as an intermediate compound in the manufacturing of polycarbonate plastic and epoxy resins, which are used as coatings to line the inside of food containers and beverage cans (Staples et al. 1998, ECB 2003, EC & HC 2008, OEHHA 2009, NCBI 2020).

In the environment, BPA mainly partitions to water, with lesser amounts partitioning to soil and sediment (ECB 2003, OEHHA 2009). Following an initial lag period, degradation of BPA in water appears to be rapid (ECB 2003, EC & HC 2008, NCBI 2020). However, under anaerobic conditions, such as in anoxic or anaerobic sediment, BPA degradation can be slow, and long half-lives have been reported (Kang et al. 2007, EC & HC 2008).

With its widespread use, BPA has been detected in the environment in fresh, marine and estuarine surface water, groundwater, sediment, soil, leachates from landfill sites, and waste effluents from municipal and industrial waste treatment plants (EC & HC 2008, OEHHA 2009, Flint et al. 2012, NCBI 2020). Although BPA has been detected in fish, crabs, clams, mussels, squid and snails, it has a low-to-moderate potential to bioaccumulate in aquatic organisms (ECB 2003, Tsai 2006, EC & HC 2008).

BPA is a nonsteroidal xenoestrogen and endocrine disruptor that exhibits both oestradiol and anti-androgen activity (Kang et al. 2007, Flint et al. 2012). There is evidence that low level exposure to BPA, particularly at sensitive life cycle stages, can lead to permanent alterations in hormonal, developmental and reproductive capacities. Multigenerational effects of BPA exposure have been reported in fish and aquatic invertebrates (Sohoni et al. 2001, ECB 2003, Kang et al. 2007, EC & HC 2008, OEHHA 2009).

Very high reliability default guideline values (DGVs) were derived using chronic EC10, NOEC, LOEC, LC50 and IC50 data for 19 species from 10 taxonomic groups, with a good fit of the distribution to the toxicity data. The DGVs for 99%, 95%, 90% and 80% species protection are 0.78 µg/L, 6.8 µg/L, 18 µg/L, and 52 µg/L, respectively. The 95% species protection level for BPA is recommended for adoption in the assessment of slightly-to-moderately disturbed ecosystems.

1 Introduction

Bisphenol A (BPA) (CASRN 80-05-7), also known as 4,4'-isopropylidenediphenol, is a widely used, high production volume industrial chemical (ECB 2003, EC & HC 2008) with the chemical formula $(CH_3)_2C(C_6H_4OH)_2$. BPA is composed of two phenol rings connected by a methyl bridge, with two methyl functional groups attached to the bridge (Kang et al. 2007, NCBI 2020). Major uses of BPA are as:

- an intermediate compound in the manufacturing of polycarbonate plastic (used in a wide variety of products including water bottles)
- an intermediate compound in epoxy resins, which are used as coatings to line the inside of some food containers and beverage cans (Staples et al. 1998, ECB 2003, EC & HC 2008, OEHHA 2009, NCBI 2020).

Other products containing BPA include adhesives, powder paints, automotive lenses, protective window glazing, building materials, compact disks, optical lenses, thermal paper, and paper coatings. BPA is also produced through the biological reductive dehalogenation of tetrabromobisphenol A (TBBPA), a widely used brominated flame retardant (Kang et al. 2007, Flint et al. 2012).

The annual global production of BPA has increased significantly since the 1960s (Chen et al. 2002, Flint et al. 2012). In 2006, global production of BPA was reported to be 4 million tonnes, approximately one-third of which was manufactured in the United States, and one quarter in Europe (Tsai 2006, EC & HC 2008). Global consumption of BPA in 2011 was predicted to exceed 5.5 million tonnes (Flint et al. 2012). BPA can enter the environment during production and processing, via various waste streams and spills, and during the use and disposal of products containing BPA. Flint et al. (2012) reported that, in 2008, over 500 tonnes of BPA was released to the environment from manufacture and processing, with another 1 300 tonnes released via incineration or wastewater treatment plants in the United States alone.

Under ambient conditions, BPA is a white solid, usually in the form of flakes or a powder (ECB 2003, NCBI 2020). If released to air, a vapour pressure of 4.0×10^{-8} mmHg at 25°C indicates BPA will exist in both the vapour and particulate phases (NCBI 2020). BPA is short-lived in the atmosphere and is unlikely to be transported a long distance from its point of emission (ECB 2003).

In the environment, BPA mainly partitions to water, with lesser amounts partitioning to soil and sediment. Reported water solubility for BPA at ~25°C ranges from 120 mg/L to 300 mg/L, while reported log K_{OC} values range from 2.0 to 4.64 (ECB 2003, Tsai 2006, EC & HC 2008, NCBI 2020). In natural waters, BPA is not expected to volatilise, based on an estimated Henry's Law constant of 4.0×10^{-11} atm-m^3/mol. As BPA lacks functional groups that hydrolyse under environmental conditions, it is not expected to undergo hydrolysis (ECB 2003, EC & HC 2008, NCBI 2020). Sensitised photo-oxidation may be an important fate process for BPA in sunlit natural waters (NCBI 2020).

Although some studies and screening tests show that BPA is non-biodegradable, other studies have found that BPA is readily biodegradable or inherently biodegradable. However, biodegradation appears to require an acclimation period to allow for the development of a microbial community capable of degrading BPA (ECB 2003, EC & HC 2008, NCBI 2020). Aerobic degradation of BPA in water appears to be rapid, often following the acclimation lag time, although trace amounts of BPA may

persist in water over time (Kang et al. 2007, EC & HC 2008). Half-lives in surface water have been reported to range from 1 day to 15 days (ECB 2003, EC & HC 2008, NCBI 2020), with faster rates of photo-degradation in the presence of dissolved organic matter and reactive oxygen species (Kang et al. 2007, OEHHA 2009). Under anaerobic conditions in water, limited biodegradation of BPA occurs (Kang et al. 2007, EC & HC 2008).

Primary biodegradation of BPA in an activated sludge treatment system with acclimated microbial populations has been reported to remove up to 99% of the BPA (EC & HC 2008, NCBI 2020). Reduction rates in sewage treatment plants range from <1% to 99%, depending on whether secondary treatment is used (EC & HC 2008, NCBI 2020). The range in reduction rates likely reflects whether microbial organisms are acclimated to BPA. Major degradation products of BPA include 4-hydroxyacephenone and 4-hydroxybenzoic acid, which rapidly degrade to carbon dioxide and water (NCBI 2020). Although BPA can be rapidly degraded in biological waste treatment systems, detectable concentrations of BPA have been found in wastewater due to incomplete BPA removal during treatment from paper and plastic production plants and domestic sewage treatment plants (Kang et al. 2007, EC & HC 2008).

The primary route of BPA contamination to the aquatic environment is via effluent from wastewater treatment plants and leaching from landfill sites (Kang et al. 2007, EC & HC 2008). BPA has been detected in fresh, marine and estuarine surface water, sediment, groundwater and soil, and municipal and industrial waste treatment streams (Crain et al. 2007, EC & HC 2008, OEHHA 2009, Flint et al. 2012, NCBI 2020). In fresh surface water, concentrations of BPA range from below the limits of reporting to 21 µg/L, although most concentrations were reported below 0.5 µg/L (ECB 2003, Tsai 2006, Kang et al. 2007, OEHHA 2009, NCBI 2020). Other reported concentrations of BPA in water, sediment and other media are as follows:

- up to 2.47 µg/L, with most concentrations at or below 0.2 µg/L, in marine water (Tsai 2006, Crain et al. 2007, OEHHA 2009)
- from <0.5 µg/kg to 1 630 µg/kg in freshwater sediment (ECB 2003, Kang et al. 2007)
- from <0.5 µg/kg to 53 µg/kg in marine sediment (Tsai 2006).
- from 15 µg/L to 5 400 µg/L prior to treatment, and from 0.5 µg/L to 5.1 µg/L after treatment, in leachates from landfills (Kang et al. 2007).

BPA has a low-to-moderate potential to bioaccumulate in aquatic organisms, with log K_{OW} values ranging from 2.2 to 4.16 (ECB 2003, Tsai 2006, EC & HC 2008). Bioconcentration factors (BCFs) in fish have been reported from 3.5 L/kg to 5.5 L/kg for rainbow trout (*Oncorhynchus mykiss*), 67.7 L/kg for carp (*Cyprinus carpio*) and 73.4 L/kg for medaka (*Oryzias latipes*) (ECB 2003, EC & HC 2008, NCBI 2020). Higher BCFs of 94–182 L/kg have been measured in salmon (*Salmo salar* m. *sebago*) yolk-sac fry, suggesting greater accumulation of BPA in early life stages (Honkanen et al. 2004). BCFs of 110–144 L/kg and 131–147 L/kg have been reported in freshwater clams (*Pisidium amnicum*) and frogs (*Rana temporaria*), respectively (ECB 2003, EC & HC 2008). Concentrations of BPA in whole freshwater biota and individual organs have been reported up to concentrations of 0.075 mg/kg (dry weight) in fish liver and 0.011 mg/kg in snails (OEHHA 2009).

2 Aquatic toxicology

2.1 Mechanism of toxicity

BPA is a nonsteroidal xenoestrogen and endocrine disruptor that exhibits both oestradiol and anti-androgen activity in aquatic organisms following chronic exposures. BPA also has an active, but poorly understood, involvement in steroidal sex hormones in plant development and growth processes (Speranza 2010). Thus, the mode of action of BPA is known to affect both plants and animals (Speranza 2010).

2.2 Toxicity

A literature review of the effects of BPA on aquatic organisms found the following effects in either marine water and freshwater.

- Effects reported for fish include: inhibition of gonadal growth in males and females, vitellogenin induction, induction of apoptosis in testis cells, inhibition of spermatogenesis and reduced percentage of spermatocytes, embryonic deformities, and intersex.
- Effects reported for invertebrates include: premature metamorphosis of larvae, developmental inhibition, delayed larval emergence, altered sex ratios, reducing feeding behaviour, super-feminisation and imposex, oviduct rupture and morphological deformities (Kang et al. 2007, OEHHA 2009, Flint et al. 2012).

BPA is acutely toxic to aquatic organisms and adversely affects growth and development (Chen et al. 2002, Kang et al. 2007, EC & HC 2008, NCBI 2020). There is evidence that low level exposure to BPA, particularly at sensitive life stages, can lead to permanent alterations in hormonal, developmental or reproductive capacities (ECB 2003, EC & HC 2008). These data indicate that endocrine disruption may be the most sensitive endpoint of BPA, with many of the lowest effect concentrations for reproductive endpoints (e.g. vitellogenin induction, gonad development, sex ratios) occurring in the range of 1 µg/L to 1 mg/L in fish, aquatic invertebrates and frogs (Sohoni et al. 2001, ECB 2003, Kang et al. 2007, EC & HC 2008, OEHHA 2009). Vitellogenin is a precursor of egg-yolk proteins, and vitellogenin induction is one of the most widely studied biomarkers of BPA exposure (Kang et al. 2007).

As with other compounds that affect reproductive hormones, BPA can produce adverse effects in aquatic organisms following prolonged exposure at levels below those that usually elicit effects in standard toxicity tests for apical endpoints such as survival, reproduction and growth. Effects can also become apparent later in the life cycle following brief, low dose exposure at sensitive developmental stages, and on filial generations following parental exposure (EC & HC 2008).

Standard duration aquatic toxicology tests have limited capacity to assess the hazards of chemicals that have bioaccumulative, endocrine disrupting, and/or multigenerational effects. A limited number of multigenerational studies (Minghong et al. 2011, Staples et al. 2011, Keiter et al. 2012) with freshwater fish exposed to BPA have been published. These studies reported reproductive-related effects (such as changes in sex cell types in testis, vitellogenin induction, reduced hatching of eggs, and reduced growth of F1 and F2 generations), providing supporting evidence of adverse effects in the subsequent generations of adults exposed to BPA.

The available chronic toxicity data indicate that fish are the most sensitive taxonomic group to BPA exposure, with macrophytes the least sensitive. This trend may be due, in part, to the availability of long-term and multigenerational fish studies for BPA.

In the literature reviewed, fish studies with long exposure durations typically reported the lowest effect concentrations. Chronic negligible effect concentrations reported for four fish species were 10 µg/L for the zebrafish *Danio rerio* (90 day growth NOEC) (Keiter et al. 2012), 16 µg/L for the fathead minnow *Pimephales promelas* (164 day F2 generation reproduction NOEC) (Staples et al. 2011), and 20 µg/L for *Carassius auratus* (90 day growth and sperm density NOEC) (Hatef et al. 2012) and 60 µg/L for the Japanese medaka *Oryzias latipes* (44-day reproduction NOEC) (Sun et al. 2014). Partial life cycle chronic exposure tests on fish typically had higher no or low effect concentrations, such as 6 250 µg/L for *Oryzias latipes* (14 day reproduction LOEC) (Ishibashi et al. 2005).

Chronic exposures for amphibians included a 14 day mortality NOEC for *Rhinella arenarum* of 1 800 µg/L and a 90 day mortality NOEC for *Xenopus laevis* of 500 µg/L (Pickford et al. 2003).

For macrophytes, the chronic duration studies ranged from 7 days to 28 days. A 28 day study for the mangrove species *Bruguiera gymnorhiza* reported an LC50 of 39 970 µg/L (Saiyood et al. 2013). A NOEC of 7 800 µg/L (frond density and growth rate) was reported for the duckweed *Lemna gibba* after 7 days of exposure (Mihaich et al. 2009). For microalgae, a 4 day growth EC10 of 1 360 µg/L and NOEC of 4 000 µg/L were reported for *Raphidocelis subcapitata* (Alexander & Dill 1988) and *Chlorolobion braunii* (Gattullo et al. 2012), respectively.

Chronic effects were identified for a variety of freshwater macroinvertebrate organisms, including crustaceans, molluscs, an insect, a sponge and a rotifer. Chronic NOECs included: 20 µg/L for reproduction of the snail *Potamopyrgus antipodarum* (Sieratowicz et al. 2011); 100 µg/L for reproduction of two snail species (*Marisa cornuarietis* and *Physa acuta*) (Schirling et al. 2006, Sanchez-Arguello et al. 2012) and for growth of the insect *Chironomus riparius* (Watts et al. 2003); 1 600 µg/L for reproduction for the sponge *Heteromyenia* sp. (Hill et al. 2002); and 1 800 µg/L for growth for the rotifer *Brachionus calyciflorus* (Mihaich et al. 2009).

Numerous acute toxicity studies were available, assessing mortality and some sub-lethal responses due to BPA exposure. These studies included laboratory tests undertaken on fish and invertebrates, including freshwater daphnids, amphipods, cnidarians, and mysids. A summary of the representative aquatic toxicity effects is as follows.

- 2–4 day LC50 values ranged from 4 700 µg/L for the fathead minnow *P. promelas* (Alexander & Dill 1988) to 12 800 µg/L for the daphnid *D. magna* (Hirano et al. 2004).
- A 4 day LC50 of 6 900 µg/L was reported for the cnidarian *Hydra vulgaris* (Hill et al. 2002).
- A 10 day LC50 of 1 500 µg/L was reported for the amphipod *Gammarus pulex* (Watts et al. 2001).
- In terms of acute sub-lethal effects, a 4 day IC50 (egg hatching) of 9 000 µg/L was reported for the medaka *O. latipes* (Kashiwda et al. 2002), while a 2 day EC50 (immobilisation) of 10 000 µg/L was reported for the daphnid *D. magna* (Chen et al. 2002).

A mesocosm study undertaken by de Kermoysan et al. (2013) assessed effects of three concentrations (1, 10 and 100 µg/L) of BPA on macrophytes (*Nasturtium officinale, Callitriche platycarpa, Myriophyllum spicatum* and *Spyrogyra* sp.), a community of macroinvertebrates, a snail

(*Radix balthica*), and a fish (*Gasterosteus aculeatus*) in 20 m long lotic systems for 165 days. Numerous effects were reported at 100 µg/L as follows: reduced volume in two of the macrophytes tested (*M. spicatum* and *Spyrogyra* sp.), community structure changes in macroinvertebrates, and increased snail and fish abundance. Additionally, a reduction in gonad size was recorded at 10 ug/L for *G. aculeatus*, although this endpoint was considered to not be ecologically relevant. Other endpoints assessed for which there was no effect included snail length, snail reproduction (egg mass abundance), fish length and weight, fish sex ratio and developmental status of males.

3 Factors affecting toxicity

Data indicate that BPA may persist longer in marine water compared to freshwater (Sajiki & Yonekubo 2003, Kang & Kondo 2005), which may have an influence on its toxicity. The available toxicity data suggest that BPA may be less toxic to freshwater species compared to marine species. Effects for several marine species have been reported at concentrations below 1 µg/L (Marcial et al. 2003, Liu et al. 2011, Laufer et al. 2012), whereas there have been no effects for freshwater species reported below 1 µg/L (ECCC 2017). This is despite the fact that the marine toxicity data are based on shorter duration, partial life cycle studies (albeit for early life stages), whereas the freshwater data are mostly based on studies of chronic duration, including multigenerational exposures. Currently, there is no empirical evidence of abiotic factors, such as salinity, affecting the toxicity of BPA, and more data are required to determine whether BPA is generally less toxic to freshwater species than to marine species and whether there are any key toxicity modifying factors.

4 Default guideline value derivation

The DGVs were derived in accordance with the method described in Warne et al. (2018) and using Burrlioz 2.0 software.

4.1 Toxicity data used in derivation

A summary of the toxicity data (one value per species), including any associated data conversions, used to calculate the DGVs for BPA in freshwater is provided in Table 1. Further details on the data that passed the screening and quality assessment, including those used to derive the single species values used to calculate the DGVs, are presented in Appendix A: Toxicity data that passed the screening and quality assessment and were used to derive the default guideline values. Details of the data quality assessment and the data that passed the quality assessment are provided as supporting information.

Where only one acceptable toxicity value was available for a species, that value was selected for the final dataset used to derive the DGVs. For species with more than one acceptable toxicity value available, the value selected for the final dataset was in accordance with Warne et al. (2018). Overall, chronic toxicity data for 20 species passed the quality assessment process. Data for the goldfish *C. auratus* were rejected because the study assessed two exposure concentrations that were greater than 10-fold different (0.2 µg/L and 20 µg/L) and reported no significant effects on body mass or growth (Hatef et al. 2012). Data for the mudsnail *Potamopyrgus antipodarum* were also rejected (NOEC growth of 40 µg/L) (Stange et al. 2012) because only one BPA concentration was assessed,

and a concentration–response relationship could not be determined. Data from de Kermoysan et al. (2013) were not used for the DGVs derivation due to (i) inability to demonstrate the ecological

Table 1 Summary of single chronic toxicity values, all species used to derive the default guideline values for BPA in freshwater

Taxonomic group	Species	Life stage	Duration (days)	Toxicity measure [a] (test endpoint)	Toxicity value (µg/L)	Estimated chronic value (µg/L)
Amphibian	*Xenopus laevis*	Larva	90	NOEC (Survival)	500	500 [b]
	Rhinella arenarum	Egg	14	NOEC (Survival)	1 800	1 800 [b]
Crustacean	*Daphnia magna*	Neonate	21	LC50 (Survival)	600	120 [d]
	Hyalella azteca	8 d old	42	NOEC (Reproduction)	490	490 [b]
Fish	*Danio rerio*	Egg/Embryo, F2 generation	90	LOEC (Growth)	10	4 [c]
	Pimephales promelas	Egg–adult	164	NOEC (Reproduction – F2)	16	16 [b]
	Oryzias latipes	Embryo	44	NOEC (Reproduction)	60	60 [b]
Insect	*Chironomus riparius*	Egg	20	NOEC (Growth)	100	100 [b]
Macrophyte	*Lemna gibba*	–	7	NOEC (Growth)	7 800	7 800 [b]
	Bruguiera gymnorhiza	–	28	LC50 (Survival)	39 970	7 990 [d]
Microalga	*Raphidocelis subcapitata*	–	4	EC10 (Population)	1 360	1 360 [b]
	Chlorolobion braunii	–	4	NOEC (Growth)	4 000	4 000 [b]
Micro-invertebrate	*Brachionus calyciflorus*	Newly hatched (<2 h)	2	NOEC (Population)	1 800	1 800 [b]
Micro-organism (protozoa)	*Paramecium trichium*	–	5	IC50 (Growth)	182	36.4 [d]
	Paramecium caudatum	–	5	IC50 (Growth)	2 462	492 [d]
Mollusc	*Potamopyrgus antipodarum*	Adult	28	NOEC (Reproduction)	20	20 [b]
	Marisa cornuarietis	Embryo	14	NOEC (Reproduction)	50	50 [b]
	Physa acuta	Egg	21	LOEC (Survival)	500	200 [b]
Sponge	*Heteromyenia* sp.	Gemmule	6	NOEC (Reproduction)	1 600	1 600 [b]

Note: Estimated chronic values are reported to no more than three significant figures.
a The measure of toxicity being estimated/determined: EC/IC/LCx: x% effect/lethal concentration; NOEC: no observed effect concentration; LOEC: lowest observed effect concentration.
b Actual chronic NOEC/EC10.
c Default conversion from chronic LOEC to chronic negligible effect (NOEC/EC10) concentration: chronic LOEC ÷ 2.5 = chronic NOEC.
d Default conversion from chronic EC50 or IC50 to chronic negligible effect (NOEC/EC10) concentration: chronic LC50 ÷ 5 = chronic NOEC.

relevance of some endpoints, including the sensitive fish gonad development endpoint (as per guidance in Warne et al. 2018) and (ii) various confounding factors including significant differences in

environmental parameters (dissolved oxygen, pH and conductivity) between the control and experimental concentrations. However, this mesocosm study was used as a form of validation of the DGVs (Section 4.3).

There were sufficient chronic EC10 and NOEC data (for 13 species from nine taxonomic groups) to attain the minimum species and taxonomic representation of five species and four taxonomic groups without using chronic LOEC and IC50/LC50 data. However, some of the chronic LOEC and IC50/LC50 data resulted in relatively low values once converted to negligible effect equivalents (EC10/NOEC), including the lowest available value: a LOEC of 10 µg/L for *D. rerio*. To increase the likelihood of the DGVs achieving appropriate protection, the chronic LOEC and IC50/LC50 data (converted to negligible effect concentrations) were included; this was sufficient to attain the minimum species and taxonomic representation without using acute data.

Some data selections involved the need for professional judgment, as follows.

- The 2 day NOEC of 1 800 µg/L for the rotifer *B. calyciflorus* was classified as a chronic study given this organism may undergo a full life cycle within 2 days, and was reported to have had, on average, six offspring during the experimental period (Mihaich et al. 2009).
- Although the 90 day F2 generation LOEC of 10 µg/L for *D. rerio* (Keiter et al. 2012) was performed using a greater than 10-fold increase in exposure concentration, it was considered sufficiently important to warrant inclusion. The study is a long-term, second generation (F2) exposure for a toxicant noted to cause reproductive and development effects at low exposures, particularly in fish, frogs and invertebrates in multigenerational studies, as discussed in Section 2. The toxicity value was at the lower end of the effects range, indicating sensitivity to BPA, and was consistent with another long-term fish exposure study (*P. promelas* 164 days F2 generation reproduction NOEC of 16 µg/L) (Staples et al. 2011).
- A study using the arthropod *C. riparius* (Watts et al. 2003) was also included for similar reasons to the *D. rerio* study. Although the *C. riparius* study used greater than 10-fold increases in test concentrations, the exposure was long-term (20 days) at a sensitive live stage (eggs), and was from a taxonomic group that would not be represented if the study was excluded. Additionally, the toxicity value (100 µg/L growth NOEC) (Watts et al. 2003) was at the lower end of the effects range, indicating sensitivity to BPA.

Thus, the final dataset used to derive the DGVs comprised chronic toxicity values for 19 species from 10 taxonomic groups (Table 1). These species included: three fish, two amphibians, two crustaceans, three molluscs, two protozoans, two macrophytes, two green algae, an insect, a sponge, and a rotifer. Of the toxicity data used for these 19 species, one was a chronic EC10 value, 11 were chronic NOEC values, two were chronic IC50 values, two were chronic LOEC values, and two were chronic LC50 values. The effect concentrations for these species span three orders of magnitude. Modality checks on the dataset were performed according to the method specified in Warne et al. (2018), with the details of the assessment provided in Appendix B: Modality assessment for bisphenol A. The weight of evidence assessment concluded that the dataset was not bimodal or multimodal and, hence, supported use of the data for 19 species for derivation of the DGVs.

4.2 Species sensitivity distribution

The cumulative frequency (species sensitivity) distribution (SSD) of the 19 chronic BPA freshwater toxicity data reported in Table 1 is shown in Figure 1. The model was judged to provide a good fit to the data.

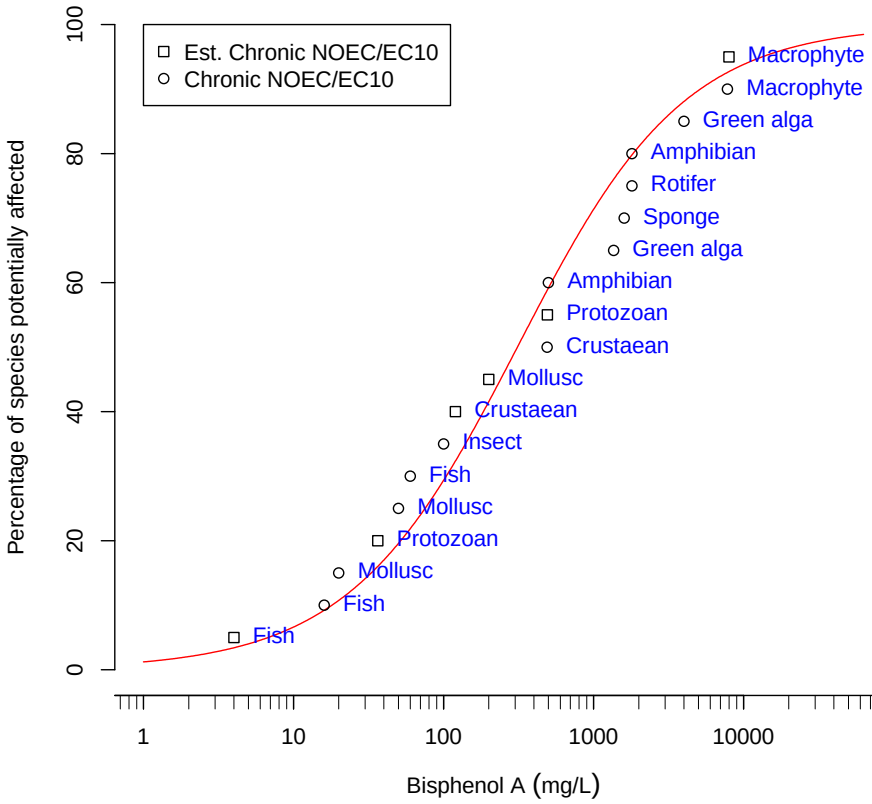

Figure 1 Species sensitivity distribution, BPA in freshwater

4.3 Default guideline values

It is important that the DGVs (Table 2) and associated information in this technical brief are used in accordance with the detailed guidance provided in the Australian and New Zealand Guidelines for Fresh and Marine Water Quality website (ANZG 2018).

The DGVs for 99%, 95%, 90% and 80% species protection are shown in Table 2. Measured log K_{OW} and BCF values for BPA are below the threshold at which secondary poisoning must be considered (i.e. log K_{OW} or log BCF values > 4) (Warne et al. 2018). Therefore, the DGVs for BPA do not need to account for secondary poisoning and, as such, the 95% species protection DGV of 6.8 µg/L is recommended for application to slightly-to-moderately disturbed ecosystems.

Table 2 Toxicant default guideline values, BPA in freshwater, very high reliability

Level of species protection (%)	DGV for BPA in freshwater (µg/L) [a]
99	0.78
95	6.8
90	18

Level of species protection (%)	DGV for BPA in freshwater (μg/L) [a]
80	52

a The DGVs were derived using the Burrlioz 2.0 software, and have been rounded to two significant figures.

The DGVs were compared to the raw chronic toxicity data that passed the quality assessment and were compiled from the literature review (i.e. 49 chronic values for 19 species). The theoretical protection offered by the DGVs for 99%, 95%, 90% and 80% species protection is considered to be adequate. The DGVs were also compared with the results of the 165-day mesocosm study reported by De Kermoysan et al. (2013). No significant ecologically relevant effects were reported from the mesocosm experiment at or below 10 μg/L, suggesting that the 99% and 95% species protection DGVs are protective of effects. Numerous significant effects were observed at 100 μg/L, but the lack of exposure concentrations between 100 and 10 μg/L made it difficult to assess the 90% and 80% species protection DGVs.

4.4 Reliability classification

The BPA freshwater DGVs have a very high reliability classification (Warne et al. 2018) based on the outcomes for the following three criteria:

- Sample size—19 (preferred)
- Type of toxicity data—chronic
- SSD model fit—good (Burr Type III).

Glossary

Term	Definition
acute toxicity	A lethal or adverse sub-lethal effect that occurs as the result of a short exposure period to a chemical relative to the organism's life span.
chronic toxicity	A lethal or sub-lethal adverse effect that occurs after exposure to a chemical for a period of time that is a substantial portion of the organism's life span or an adverse effect on a sensitive early life stage.
default guideline value (DGV)	A guideline value recommended for generic application in the absence of a more specific guideline value (e.g. a site-specific guideline value) in the Australian and New Zealand Guidelines for Fresh and Marine Water Quality. Formerly known as 'trigger values'.
EC50 (median effective concentration)	The concentration of a substance in water or sediment that is estimated to produce a 50% change in the response being measured or a certain effect in 50% of the test organisms relative to the control response, under specified conditions.
ECx	The concentration of a substance in water or sediment that is estimated to produce an x% change in the response being measured or a certain effect in x% of the test organisms, under specified conditions.
endpoint	The specific response of an organism that is measured in a toxicity test (e.g. mortality, growth, a particular biomarker).
guideline value	A measurable quantity (e.g. concentration) or condition of an indicator for a specific community value below which (or above which, in the case of stressors such as pH, dissolved oxygen and many biodiversity responses) there is considered to be a low risk of unacceptable effects occurring to that community value. Guideline values for more than one indicator should be used simultaneously in a multiple lines of evidence approach. (Also refer to default guideline value and site-specific guideline value.)
IC50	The concentration of a substance in water or sediment that is estimated to produce a 50% inhibition of the response being measured in test organisms, relative to the control response, under specified conditions.
ICx	The concentration of a substance in water or sediment that is estimated to produce an x% inhibition of the response being measured in test organisms relative to the control response, under specified conditions.
K_{OC} (soil adsorption coefficient)	Measures the amount of chemical substance adsorbed onto soil per amount of water.
LC50 (median lethal concentration)	The concentration of a substance in water or sediment that is estimated to be lethal to 50% of a group of test organisms, relative to the control response, under specified conditions.
lowest observed effect concentration (LOEC)	The lowest concentration of a material used in a toxicity test that has a statistically significant adverse effect on the exposed population of test organisms as compared with the controls.
macrophyte	A member of the macroscopic plant life of an area, especially of a body of water; large aquatic plant.
no observed effect concentration (NOEC)	The highest concentration of a material used in a toxicity test that has no statistically significant adverse effect on the exposed population of test organisms as compared with the controls.
site-specific guideline value	A guideline value that is relevant to the specific location or conditions that are the focus of a given assessment or issue.
species (biological)	A group of organisms that resemble each other to a greater degree than members of other groups and that form a reproductively isolated group that will not produce viable offspring if bred with members of another group.

Term	Definition
species sensitivity distribution (SSD)	A method that plots the cumulative frequency of species' sensitivities to a toxicant and fits a statistical distribution to the data. From the distribution, the concentration that should theoretically protect a selected percentage of species can be determined.
toxicity	The inherent potential or capacity of a material to cause adverse effects in a living organism.
toxicity test	The means by which the toxicity of a chemical or other test material is determined. A toxicity test is used to measure the degree of response produced by exposure to a specific level of stimulus (or concentration of chemical) for a specified test period.

Appendix A: Toxicity data that passed the screening and quality assessment and were used to derive the default guideline values

Table A 1 Summary, chronic toxicity data that passed the screening and quality assurance processes, BPA in freshwater

Taxonomic group	Species	Life stage	Exposure duration (days)	Toxicity measure [a] (test endpoint)	Test medium	Temperature (°C)	Salinity (µS/cm)	pH	Concentration (µg/L)	Reference
Amphibian	*Xenopus laevis*	Larva	90	NOEC (Survival)	Dechlorinated water	22 ± 1	212–237	7.19–7.79	500 [b]	Pickford et al. 2003
	Rhinella arenarum	Egg	14	NOEC (Survival)	AS solution	20 ± 2	–	–	1 800 [b]	Wolkowicz et al. 2014
Crustacean	*Daphnia magna*	Neonate	21	LC50 (Survival)	Fresh culture medium as per ISO guidelines	20 ± 1	–	–	600 [c]	Brennan et al. 2006
	Hyalella azteca	8-d old	42	NOEC (Reproduction)	-	22–24	150–180	7.4–7.8	490 [b]	Mihaich et al. 2009
Fish	*Pimephales promelas*	Egg–adult	164	NOEC (Reproduction – F2)	Dechlorinated tap water	24.1–25.8	–	7.1–8.0	16 [b]	Staples et al. 2011
	Oryzias latipes	Embryo	44	NOEC (Reproduction)	Reconsituted water	25 ± 1	–	–	60 [b]	Sun et al. 2014
	Danio rerio	Egg/embryo, F2 generation	90	LOEC (Growth)	Deionised and tap water	26 ± 1	–	8.25–8.75	10 [d]	Keiter et al. 2012
Insect	*Chironomus riparius*	Egg	20	NOEC (Growth)	Dechlorinated tap water	20 ± 1	221–236	6.9–7.3	100 [b]	Watts et al. 2003

Taxonomic group	Species	Life stage	Exposure duration (days)	Toxicity measure [a] (test endpoint)	Test medium	Temperature (°C)	Salinity (µS/cm)	pH	Concentration (µg/L)	Reference
Macrophyte	*Lemna gibba*	–	7	NOEC (Growth)	Algal assay procedure medium	22–26	–	7.4–8.6	7 800 [b]	Mihaich et al. 2009
	Bruguiera gymnorhiza	–	28	LC50 (Survival)	Distilled water	–	–	6.3–6.5	39 970 [c]	Saiyood et al. 2013
Microalga	*Raphidocelis subcapitata*	–	4	EC10 (Population)	Algal assay Medium	24 ± 2	–	–	1 360 [b]	Alexander et al. 1988
	Chlorolobion braunii	–	4	NOEC (Growth)	FW04 growth medium	22	–	8.3	4 000 [b]	Gattullo et al. 2012
Microinvertebrate	*Brachionus calyciflorus*	Newly hatched (<2 h)	2	NOEC (Population)	Fortified well water	23 ± 1	290	8	1 800 [b]	Mihaich et al. 2009
Micro-organism (protozoa)	*Paramecium caudatum*	–	5	IC50 (Growth)	Lettuce infusion	23 ± 1	–	–	2 462 [c]	Miyoshi et al. 2003
	Paramecium trichium	–	5	IC50 (Growth)	Lettuce infusion	23 ± 1	–	–	182 [c]	Miyoshi et al. 2003
Mollusc	*Potamopyrgus antipodarum*	Adult	28	NOEC (Reproduction)	Reconstituted water	16		7.5–8.5	20	Sieratowicz et al. 2011
	Marisa cornuarietis	Embryo	14	NOEC (Reproduction)	Distilled water	26 ± 0.5	–	50	50 [b]	Schirling et al. 2006
	Physa acuta	Egg	21	LOEC (Survival)	Reconstituted water	20	–	–	500 [d]	Sanchez-Arguello et al. 2012
Sponge	*Heteromyenia* sp.	Gemmule	6	NOEC (Reproduction)	Spring water	22	–	–	1 600 [b]	Hill et al. 2002

a The measure of toxicity being estimated/determined: EC/IC/LCx: the concentration resulting in a x% effect, inhibition or lethality relative to the control response; NOEC: no observed effect concentration; LOEC: lowest observed effect concentration.

b Value included in the dataset to derive the DGVs, as is.

c Value included in the dataset to derive the DGVs, after application of a default chronic EC50 to NOEC/EC10 conversion factor of 5.

d Value included in the dataset to derive the DGVs, after application of a default chronic LOEC to NOEC/EC10 conversion factor of 2.5.

Appendix B: Modality assessment for bisphenol A

A modality assessment was undertaken for BPA toxicity to freshwater species according to the four questions stipulated in Warne et al. (2018). These questions and their answers are listed as follows.

Is there a specific mode of action that could result in taxa-specific sensitivity?
BPA is a nonsteroidal xenoestrogen and endocrine disruptor that exhibits both oestradiol and anti-androgen activity in aquatic organisms following chronic exposures. BPA also has an active, but poorly understood, involvement in steroidal sex hormones in plant development and growth processes (Speranza 2010). Therefore, based on mode of action alone, there was no clear reason to suspect large differences in taxa-specific sensitivity.

Does the dataset suggest bimodality?
Visual representation of the data, calculation of the bimodality coefficient (BC), and consideration of the range in the effect concentrations are recommended lines of evidence for evaluating whether bimodality or multimodality of the dataset is apparent. This is discussed as follows.

- The histogram of the raw effect concentration SSD data (Figure B 1) could be interpreted as positively right skewed typical of concentration-based data (Warne et al. 2018). The log-transformed histogram appears to show left skewed data (Figure B 1).
- Data that span large ranges (>4 orders of magnitude) indicate potential for underlying bimodality or multimodality (Warne et al. 2018); the BPA data span three orders of magnitude.
- When the BC is greater than 0.555, it indicates that the data do not follow a normal distribution and may be bimodal; the BC of the log-transformed data is 0.39, which does not support bimodality.

Based on these lines of evidence, the distribution of the log-transformed dataset does not follow a normal distribution, although the data do not appear to be bimodal.

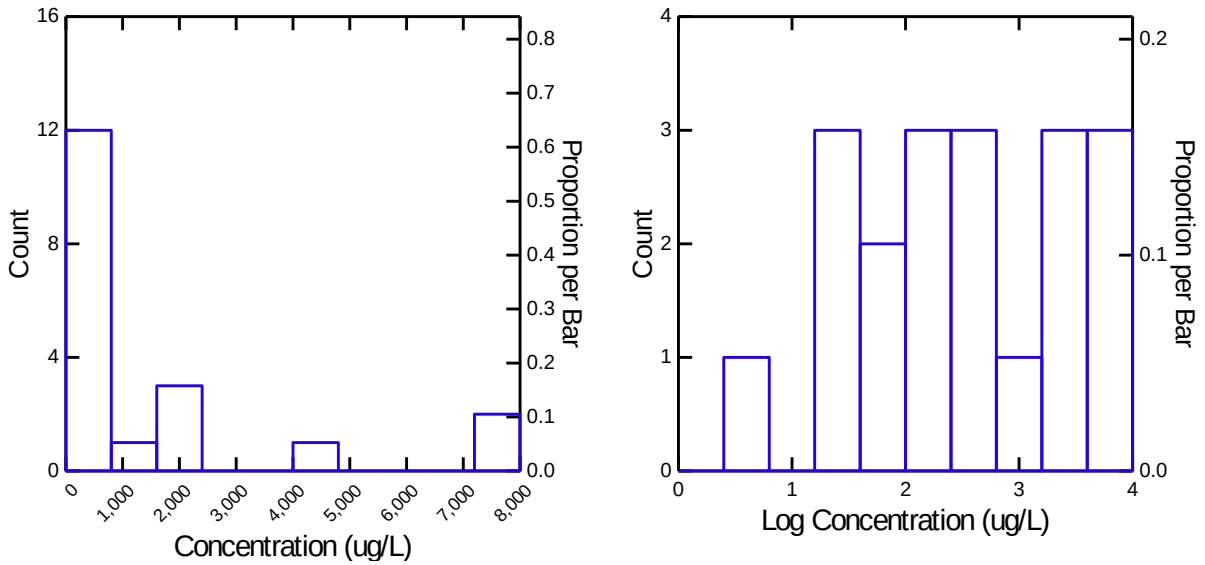

Figure B 1 Histogram, raw (left) and log-transformed (right) data

Do data show taxa-specific sensitivity (i.e. through distinct groupings of different taxa types)?
The mode of action of BPA is known to affect both plants and animals (Speranza 2010); the potential for taxa-specific sensitivity in the data was examined using box plots of the SSD data with the grouping variable phyla and major organism types.

As shown in Figure B 2, heterotrophs appear to be the most sensitive group. However, there are only four species in the autotroph grouping, compared to 15 heterotrophs, which makes it difficult to draw robust conclusions.

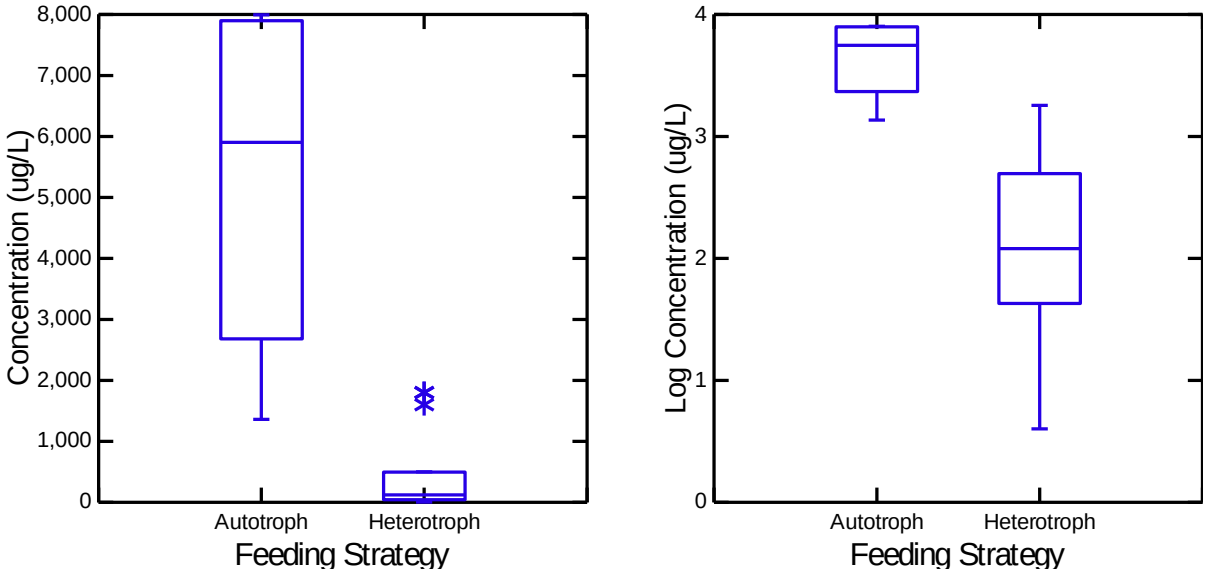

Figure B 2 Box plots, raw (left) and log-transformed (right) data grouped by feeding strategy

Is it likely that indications of bimodality or multimodality or distinct clustering of taxa groups are not due to artefacts of data selection, small sample size, test procedures, or other reasons unrelated to a specific mode of action?
Due to the small sample size, it is not possible to discern trends in the data and if such trends are artefacts of data selection, test procedures, or other reasons unrelated to a specific mode of action. Nevertheless, based on the weight of evidence, the dataset does not appear to be bimodal or multimodal, which supports the use of all 19 species identified in preparation of the SSD.

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