RESEARCH ARTICLES

Comparison of Four Species Sensitivity Distribution Methods to Calculate Predicted No Effect Concentrations for Bisphenol A

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ABSTRACT

Bisphenol A (BPA, CAS RN 80-05-7) is a high production volume chemical used as an intermediate in the production of polycarbonate plastic and epoxy resins. During its manufacture and use, some emissions to surface waters are anticipated. Chronic predicted no effect concentrations (PNECs) for aquatic systems are used to support the assessment of potential risks to aquatic organisms in receiving waters. PNECs for a compound are considered protective of populations, communities, and ecosystems. Traditionally, PNECs are derived by taking the lowest no-observed effect concentration (NOEC) from a set of toxicity studies and dividing by an assessment factor (e.g., 10 to 1000). This traditional approach is appropriate for substances with few data, but may not be necessary for substances with many valid studies. For well-studied substances, statistical approaches (i.e., development of Species Sensitivity Distribution or SSD methods) can be used to calculate a PNEC that makes use of the full distribution of available NOEC values. Bisphenol A has an extensive set of aquatic toxicity studies covering diverse taxa including algae, hydra, rotifers, mollusks, crustaceans (both benthic and pelagic), insects, annelids, fish, and amphibians. The full chronic data set was used to calculate PNEC values using four SSD methods: (1) the Hazard Concentration (HC5) approach developed by The Netherlands National Institute of Public Health and the Environment (RIVM), (2) the U.S. Environmental Protection Agency's water quality criteria procedure, (3) SigmaPlot (Systat 2000) commercial software that calculates percentile values, and (4) a distributional method consistent with that used by Environment Canada. Using these approaches, PNEC values for BPA range from 11 to 71 µg/L. Literature studies suggest that application of
an additional assessment factor is unwarranted if an SSD-based PNEC is based on chronic data. SSD-derived PNEC values and the traditionally derived PNEC value of 1.6 μg/L are then compared to concentrations of BPA that have been measured in North American and European surface waters. Adverse risks to aquatic organisms are not anticipated from measured concentrations of BPA in North American and European surface waters.

Key Words: no observed effect concentration (NOEC), Final Chronic Value (FCV), hazard concentration (HC5), hazard quotient (HQ), PNEC.

INTRODUCTION

Bisphenol A (BPA, also 4,4'-isopropylidene diphenol, CAS Registry No. 80-05-7) is primarily used as an intermediate in the production of polycarbonate plastics and epoxy resins. Lower volume applications include use as additives to polyvinyl chloride (PVC) and other plastics, and other miscellaneous monomeric applications. Small amounts of BPA enter the environment from production and processing facilities, sewage treatment plants, and following disposal of PVC materials. Cousins et al. (2002) identified the aqueous compartment as one of the main compartments into which BPA may be found following release into the environment.

To conduct a risk assessment for a chemical entering the environment, estimates of both the hazard (available toxicity data for potentially exposed organisms) and the estimated or measured exposure concentrations are required. For the purposes of this article, the general term Predicted No Effect Concentration (PNEC) was adopted to describe the estimated threshold concentration below which communities of organisms can be chronically exposed without adverse consequences. PNEC values are frequently used to describe the hazard component of ecological risk assessments.

A simple deterministic approach for toxicity assessment relies on single, usually worst case values and is widely used in North America and Europe, particularly if data are limited (USEPA 1984; CEPA 1997; EC 2003). A criticism of this approach for PNEC determination is that an assessment factor (AF) is applied to the most sensitive acute LC50 or chronic NOEC value and the full dataset is not used to characterize potential toxicity. Assessment factors are a precautionary means of addressing perceived uncertainties in a set of toxicity studies. This method therefore produces a single criterion concentration that is assumed to be cautious and protective in terms of adverse environmental effects but which actually may best serve as a screening tool because it provides little information on the likelihood of impact and provides no expression of its uncertainty. In contrast, probabilistic modeling approaches evaluate and compare complete distributions (i.e., the distribution of chemical toxicity to a range of species can be compared to the distribution of exposure concentrations). The result is a distribution of potential outcomes that can be used to examine the probability or likelihood of certain results occurring, versus a single result with deterministic techniques. For any given compound, the distribution of toxicity values for a set of species is often referred to as a species sensitivity distribution (SSD).

It has long been recognized that species of organisms within a community have differing sensitivities to a toxic substance. A distribution of species responses would be
expected to occur rather than a single response value. In addition, SSDs that include a number of studies across a range of species increases the confidence in SSD-derived PNECs. For these reasons, SSDs are increasingly recommended to either complement or replace the use of deterministic criteria in the risk assessment of chemicals in the United States and in Europe (Posthuma et al. 2002). For example, the SSD concept has been formally incorporated into ecological risk assessment frameworks at the USEPA (ECOFRAM 1999; http://www.epa.gov/oppefedl/ecorisk/) and within the Organization for Economic Cooperation and Development (OECD 1992). The USEPA has also used the SSD technique to derive water quality criteria for several decades (USEPA 1985).

The assumed goal of a traditionally derived PNEC calculated using the single lowest acute or chronic toxicity value of any taxa and an AF is an attempt to protect all individuals of all species. As Suter (1993) notes, the reproducing population is the smallest ecological unit that can be meaningfully protected. Further, populations require a community of organisms of which the population is a part. In contrast to the traditional AF approach, SSD-derived PNECs reflect the concentration at which a significant risk to the community of species is reached. It is acknowledged that the selection of the appropriate level of protection is a risk management or policy decision, not the decision of the risk assessor. The most common policy-based protection threshold is 5%, that is, effects on more than 5% of species are unacceptable (Postuma et al. 2002). Thus, SSD-based PNECs will be derived at the 5% threshold.

The focus of this article is on the hazard definition of BPA in the aquatic environment, in particular the development of PNEC values needed for risk assessment. To give results that are as comparable as possible, the lower-bound 5th percentile concentrations were taken from all SSD approaches, even though some of the SSD models can generate toxicity values of other percentiles (e.g., the 10th percentile). PNEC values for BPA from four SSD methods will be compared and contrasted with each other and with the traditional assessment factor (AF) approach. To demonstrate the use of SSD-based PNEC values, all PNEC values will be compared to measured aquatic BPA concentrations in surface waters in the United States and Europe.

CHRONIC AQUATIC TOXICITY OF BISPHENOL A

Study Quality Assessment

As an initial step, the available chronic ecotoxicity studies were critically reviewed for suitability for use in risk assessment following the criteria and procedures outlined in the European Union (EU) Technical Guidance Document (EC 2003). These procedures are presented and refined in Staples et al. (2002). Only studies designated as "valid without restriction" are used in this aquatic hazard assessment. Studies designated as "use with care" or "not valid" are not used. Many of the studies used in this paper were previously evaluated by Staples et al. (2002) in a weight-of-evidence analysis of the aquatic toxicity of BPA. Studies that were conducted after the publication of Staples et al. (2002) are discussed later. Specific note is made of studies for which there is some controversy as to their acceptability and where additional work
Recent Chronic Aquatic Studies with BPA

Fish

As presented in Staples et al. (2002), two valid partial life-cycle studies report the effects of BPA on medaka fish. One study measured growth and sexual development over 100 days using adult fish (Metcalfe et al. 2001), reporting a NOEC of 120 µg/L. The second study is a 60-day partial life cycle study that measured survival, growth and development with a NOEC of 355 µg/L (Yokota et al. 2000). Subsequently, the Japanese government (Japan MOE 2004) reported the results of a multigeneration study with medaka. Although all experimental details of this study are not yet widely available, it is known that the BPA results are part of a series of studies sponsored by the Japanese government that are being used to inform their regulatory management decisions on endocrine modulation-related issues. In this latter study, newly hatched F0 eggs were exposed to BPA until they reached maturity. F0 adults were bred, F1 eggs were hatched, and hatchlings were exposed to BPA until they reached maturity. Endpoints related to survival, growth and development, and reproduction are reported. An overall NOEC of 247 µg/L was reported that is based on F0 survival as the most sensitive endpoint. NOEC for growth, development, and reproduction were similar or less sensitive, and range from 247 to 1179 µg/L. For the PNEC calculations, the NOEC of 247 µg/L based on survival of the F0 generation was taken as the most sensitive endpoint from the longest duration valid medaka study available (Japan MOE 2004).

Caunter and colleagues (1998, 2000) conducted two studies with BPA using fathead minnows. The studies were conducted using flow-through exposures to BPA following standard guidelines and conducted in accordance with Good Laboratory Practices (GLP). An NOEC of 640 µg/L based on survival and growth was determined in a 35-day early life stage test. An NOEC of 16 µg/L based on hatchability of F2 eggs was determined in a multigeneration test (overall 451 days) with fathead minnows. Sohoni et al. (2001) reported the results from the F1 exposure through day 164 and includes observations of an apparent effect on spermatogenesis in male fish at concentrations lower than effects reported for mortality, growth, and development, and reproduction endpoints. A third-party pathology review found the gametogenic cell counts reported by Sohoni et al. (2001) to be questionable (Experimental Pathology Laboratories, Inc 2005). The study reported by Sohoni et al. (2001) was designed to examine effects on growth, reproduction, and hatchability, but was not optimally designed for quantitative examination of gonadal cell types as a supplemental endpoint. In addition, a number of critical inadequacies related to the histological analyses were identified, specifically with respect to the number of fish sampled from each exposure level, methods of tissue collection, procedures used in preparation of slides for histopathological analysis, and the procedures used for quantitative analysis including the identification and number of cells counted in each sample.

To clarify the potential for effects from BPA on spermatogenesis in fathead minnows, a follow-up study sponsored by the Polycarbonate/BPA Global Group was

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Table 1. Studies used for calculation of PNECs for bisphenol A using four different Species Sensitivity Distribution methods. All concentrations in µg/L.

<table>
<thead>
<tr>
<th>Family</th>
<th>Species</th>
<th>Endpoint: NOEC (LOEC)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fam. 1 Salmonids</td>
<td>Rainbow trout  Oncorhynchus mykiss</td>
<td>28-day, juvenile growth test</td>
<td>Bayer (1999)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Growth: 3640 (11,000)</td>
<td></td>
</tr>
<tr>
<td>Fam. 2 Other fish family</td>
<td>Medaka fish  Oryzias latipes</td>
<td>Multi-generation**</td>
<td>Japan Ministry of Environment (2004)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mortality: 247 (1179)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Growth: 247 (1179)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reproduction: 1179</td>
<td></td>
</tr>
<tr>
<td>Fam. 2 Other fish family</td>
<td>Medaka fish  Oryzias latipes</td>
<td>60-d** Mortality: 1820</td>
<td>Yokota et al. (2000)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Growth: 355 (1820)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reproduction: 355 (1820)</td>
<td></td>
</tr>
<tr>
<td>Fam. 2 Other fish family</td>
<td>Medaka fish  Oryzias latipes</td>
<td>100-d post-hatch**</td>
<td>Metcalfe et al. (2001)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Growth: 120</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reproduction: 120</td>
<td></td>
</tr>
<tr>
<td>Fam. 2 Other fish family</td>
<td>Fathead minnow  Pimephales promelas</td>
<td>35-d ELS assay</td>
<td>Caunter et al. (1998)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mortality: 640 (1280)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Growth: 640 (1280)</td>
<td></td>
</tr>
<tr>
<td>Fam. 2 Other fish family</td>
<td>Fathead minnow  Pimephales promelas</td>
<td>Multi-generation</td>
<td>Caunter et al. (2000)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mortality: 640</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Growth: 640</td>
<td></td>
</tr>
<tr>
<td>Fam. 2 Other fish family</td>
<td>Fathead minnow  Pimephales promelas</td>
<td>164-day partial life cycle</td>
<td>Rhodes et al. (2007)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mortality: 160 (640) (males only)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Growth: 640 (males and females)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Reproduction: 640 (males and females)</td>
<td></td>
</tr>
<tr>
<td>Fam. 2 Other fish family</td>
<td>Guppy  Poecilia reticulata</td>
<td>50-d</td>
<td>Kinnberg and Toft (2003)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mortality: 500 (5000)</td>
<td></td>
</tr>
<tr>
<td>Fam. 3 Third phyla in Chordates</td>
<td>African clawed frog Xenopus laevis</td>
<td>90-d Mortality: 500</td>
<td>Pickford et al. (2000)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Growth: 500</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sexual differentiation: 500</td>
<td>Pickford et al. (2003)</td>
</tr>
<tr>
<td>Fam. 4 Planktonic crustacean</td>
<td>Water flea  Daphnia magna</td>
<td>21-d</td>
<td>Caspers (1998)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mortality: 3160</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reproduction: 3160</td>
<td></td>
</tr>
<tr>
<td>Fam. 5 Benthic crustacean</td>
<td>Amphipod  Hyalella azteca</td>
<td>Survival, growth, reproduction</td>
<td>Carafella (2005)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mortality: 1000</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Growth: 1000</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reproduction: 490 (1000)</td>
<td></td>
</tr>
<tr>
<td>Fam. 6 Aquatic insect</td>
<td>Midge Chironomus riparius</td>
<td>Growth and development</td>
<td>Watts et al. (2003)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moultng delay: 100 (1000)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Growth: 100 (1000)</td>
<td></td>
</tr>
<tr>
<td>Fam. 7 Family from non- Chordata/ Arthropoda</td>
<td>Rotifers Brachionus calycifloris</td>
<td>Life cycle, intrinsic rate of population increase</td>
<td>Sayers (2003)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Population growth: 1800 (3600)</td>
<td></td>
</tr>
</tbody>
</table>

(Continued on next page)
Table 1. Studies* used for calculation of PNECs for bisphenol A using four different Species Sensitivity Distribution methods. All concentrations in µg/L. (Continued)

<table>
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<tr>
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<th>Species</th>
<th>Endpoint: NOEC (LOEC)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fam. 8 Other insect or other phylum</td>
<td>Prosobranch mollusks <em>Marisa cornuarietis</em></td>
<td>84-d adult survival and reproduction; hatchability and 90-d juvenile growth trials (25°C)</td>
<td>Forbes et al. (2007b)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mortality: 640</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reproduction: 640</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hatching and juvenile growth: 640</td>
<td></td>
</tr>
<tr>
<td>Fam. 8 Other insect or other phylum</td>
<td>Prosobranch mollusks <em>Marisa cornuarietis</em></td>
<td>181-d adult survival and reproduction; hatchability and 90-d juvenile growth trials (25°C)</td>
<td>Warbritton et al. (2007a)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mortality: 640</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Reproduction: 640</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hatching and juvenile growth: 640</td>
<td></td>
</tr>
<tr>
<td>Fam. 8 Other insect or other phylum</td>
<td>Hydra <em>Hydra vulgaris</em></td>
<td>Mortality, growth and development</td>
<td>Pascoe et al. (2002)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mortality: 42 (460)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Growth: 460</td>
<td></td>
</tr>
<tr>
<td>Fam. 8 Other insect or other phylum</td>
<td>Poriferan Sponge <em>Heteromyenia sp.</em></td>
<td>9-d</td>
<td>Hill et al. (2002)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Growth: 1600 (16,000)</td>
<td></td>
</tr>
<tr>
<td>Fam. 9 Algae</td>
<td>Green algae <em>Selenastrum capricornutum</em></td>
<td>4-d</td>
<td>Alexander (1988)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EC10 Growth: 1360</td>
<td></td>
</tr>
<tr>
<td>Fam. 10 Aquatic macrophyte</td>
<td>Duckweed <em>Lemma gibba</em></td>
<td>7-d</td>
<td>Putt (2003)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Growth: 7800 (20,000)</td>
<td></td>
</tr>
</tbody>
</table>

*All studies used to derive the PNECs have been screened for study quality according to the procedures described in Staples et al. (2002). Concentrations presented here are either nominal or mean measured as reported in each study.

**The longest duration medaka study was used for this species (NOEC = 247 µg/L).

conducted (Rhodes 2007). Preliminary work developed and optimized the histopathology techniques (Wolf et al. 2004). A range finding test was performed to develop the optimal design for the definitive test, including a power analysis to determine the appropriate number of replicates and appropriate statistical methods (Cautner et al. 2006). The definitive study followed the general design of that reported by Sohoni et al. (2001), while using a four-fold higher replication per concentration to improve statistical power. Results for survival, growth, and reproduction are similar to those reported by Sohoni et al. (2001) with NOEC of 160 µg/L and higher being determined, depending on the specific endpoint. In contrast, the results of the gonadal histopathology analysis were markedly different than reported...
SSD-Derived Predicted No Effect Concentrations for Bisphenol A by Sohoni et al. (2001). Delay in gametogenesis was found at 640 and 160 µg/L, but not at 64 µg/L. BPA for males. Thus for fathead minnows, a NOEC of 16 µg/L will be used for the PNEC calculations, based on the F2 hatchability endpoint originally observed in the multigeneration study as reported by Caunter et al. (2000).

Two additional fish studies with BPA have been reported, but were considered not valid. Bowmer and Gimeno (2001) measured the effects from BPA exposure on gonadal development of common carp over a 49-day test. Segner et al. (2003) reported an EC50 for reproductive success in a life-cycle test with zebrafish. Both of these studies suffer from incomplete description of experimental design and results, and were not considered fully valid for use in deriving an SSD-based PNEC.

Kinnberg and Toft (2003) examined the effects on survival, male reproductive behavior, secondary sex characteristics, sperm count, and gonadosomatic indices in guppy fish. After exposure to BPA for 30 days at concentrations up to 5,000 µg/L, survival was affected at the highest concentration with a NOEC of 500 µg/L. In addition, some effects on testes structure were reported but apparently no other developmental or reproductive effects were found at any exposure concentration. Based on these results a NOEC of 500 µg/L for survival will be used for PNEC calculations.

**Amphibians**

Kloas and colleagues reported that BPA has an effect on the sex ratio of the African clawed frog, *Xenopus laevis* (Kloas et al. 1999; Levy et al. 2004). Upon critical review, the studies were not considered valid for deriving a PNEC based on the experimental design, the lack of measured exposure concentrations, and the statistical approaches used in evaluating the results.

In the work of Kloas et al. (1999), juvenile frogs were exposed to two different levels of BPA under static renewal conditions. The fact that exposure concentrations were not measured in such systems is problematic, given the ready biodegradability of BPA (West et al. 2001). Further, no documentation was provided of the test conditions (temperature, water quality), which may also have an impact on the sex ratio. The study used one replicate test vessel per treatment and therefore it is impossible to determine whether the potential effect is a sampling or statistical artifact.

The statistical analyses used by the authors appear to be inappropriate. Kloas et al. (1999) analyzed the statistical significance of the data using the Kruskal-Wallis test combined with the Mann-Whitney test. Independent analysis of the data using the Kruskal-Wallis test failed to show significant differences between treatments. Normally the Mann-Whitney test is used to determine which treated group is statistically different from the control after the Kruskal-Wallis test indicates significant differences between treatments. Because the latter did not reveal such differences, it is unclear how the Mann-Whitney test was applied given that there was only one replicate test vessel. Lastly, the authors compared the sex ratios to a solvent control. However, the more appropriate comparison is to the expected sex ratio (50:50) as long as the controls do not significantly vary from the expected.

Levy et al. (2004) attempted to further refine the experimental approaches to assessing changes in sex ratio with *X. laevis*, but the work suffers from many of
the same deficiencies of experimental design (although test concentrations were measured) and application of statistical methodologies. Levy et al. (2004) did use two replicate test vessels per test concentration; however, the authors then effectively reduced this to a single replicate by pooling the data for the two replicates. In so doing the authors removed any potential for estimation of the experimental error associated with the sex ratio endpoint. The findings of a second experiment described by Levy et al. (2004) using three BPA concentrations further highlights the uncertainty in the validity of the results. The effects on sex ratio were only noted at the intermediate dose, indicating a lack of dose response. Furthermore, a histological examination of the gonads failed to indicate intersex conditions at any of the test concentrations, which would be expected if there were significant shifts in sex ratio occurring. Thus, due to methodological deficiencies, the X. laevis results reported by Klop et al. (1999) and Levy et al. (2004) were not used to calculate SSD-based PNEC values.

Subsequent work by Pickford et al. (2000, 2003) with X. laevis was conducted in accordance with GLP guidelines. BPA concentrations were carefully maintained using a flow-through system and were analytically verified. At the end of the 90-day test, no skewing of sex ratios was found even at 500 μg/L, the highest BPA concentration tested, and a 50/50 sex ratio was reported for the controls and all test concentrations. The findings of Pickford et al. (2000, 2003) were considered valid for use in the PNEC calculations.

**Invertebrates**

Several chronic aquatic toxicity studies with invertebrates have been recently sponsored by the Polycarbonate/BPA Global Group. Each study was conducted according to standard guidelines in accordance with GLP. Carafella (2006) reports the results of a 42-day study conducted with the amphipod, *Hyalella azteca*. The study reports NOEC for survival and growth endpoints of 1000 μg/L and a NOEC for reproduction of 490 μg/L. Sayers (2006) reports the results of a life cycle test with the rotifer, *Brachionus calyciflorus*. A NOEC of 1800 μg/L was reported, based on the measurement of the intrinsic rate of population increase.

Several other authors have published findings of the effects of BPA on invertebrate species. Pascoe et al. (2002) reports the effects of BPA on the survival, growth, and development of the Hydra, *Hydra vulgaris* Cnidarian. The lowest NOEC was 42 μg/L based on survival. In contrast, the work reported by Fukuhori et al. (2005) reports inconsistent growth with both enhanced and reduced growth parameters noted during their 35-day test with the *Hydra oligactis* and was not used in the PNEC derivation. Hill et al. (2002) reports the results of 9-day growth experiments on poriferan sponges *Heteromyenia* sp. The authors report a NOEC of 1600 μg/L based on growth. Watts et al. (2003) examined the effects of BPA on larval molting and mouthpart structure in life-cycle renewal test using the insect *C. riparius*. Time to first molt and mean wet weights of first instar larvae were only affected at 1000 μg/L, but not 100 μg/L. The studies of Pascoe et al. (2002), Hill et al. (2002), and Watts et al. (2003) were scored as valid and will be used for the PNEC calculations.
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**Aquatic plants**

An additional study sponsored by the Polycarbonate/BPA Global Group examined the effects of BPA on the aquatic duckweed plant *Lemna gibba* and was reported by Putt (2003). Duckweed is not very sensitive to BPA with a NOEC of 7800 μg/L based on frond growth.

**Mollusks**

Recent publications by Oehlmann and colleagues have claimed that BPA strongly stimulates female egg production and increases mortality in the prosobranch snail *Marisa cortumarietis* (Oehlmann et al. 2000; Schulte-Oehlmann et al. 2001; Oehlmann et al. 2006). Closer examination of these publications has identified a number of significant deficiencies in the experimental design, statistical analysis, and interpretation of the results that render them invalid for the PNEC calculations.

Shortcomings in the studies conducted by Oehlmann and colleagues include lack of knowledge of the influence of husbandry conditions on the growth, development, and reproductive performance of *Marisa*, variability of life history traits under laboratory conditions, lack of replication in most of the experiments, and use of inappropriate statistical methods that invalidate the claims of statistical significance (Dietrich et al. 2006; Forbes et al. 2007 a,b). The influence of husbandry conditions and knowledge of life history traits in control populations of *Marisa* are critical to properly designing toxicity tests with sufficient statistical power to detect the effects of treatments of BPA.

Aufderheide et al. (2006), Selck et al. (2006), and Forbes et al. (2007a,b) reported the results of a series of studies with *Marisa* that were designed to understand the influence of variables such as water quality and food source, while maximizing the ability to discern differences in egg production between controls and treatments. Forbes et al. (2007b) used a nested statistical design that enabled the identification of individual snails, which allowed the estimation of inter-snail and inter-vessel variability. No statistically significant effects on survival or reproductive output of adult *Marisa* were observed during a 12-week test using a range of BPA concentrations from 0.1 to 640 μg/L. Likewise, hatching success and juvenile growth were not significantly affected by any BPA treatment.

Statistical analysis showed that reproductive output was the most variable trait (mean within-replicate coefficient of variation was 45%), followed by juvenile growth (CV 28%), percent hatch (CV 18%), and time to egg hatching (CV 6 to 9%). The authors concluded that toxicity tests having sufficient power to detect differences in egg production should, therefore, have sufficient power to detect effects on other endpoints. Power analyses showed that a relatively high degree of replication is needed to detect effects on reproduction of *Marisa*. The authors calculated that an experiment using four treatments of BPA and a control that is capable of detecting a 26% treatment effect on egg production with 80% power would require 6 replicates per treatment and 12 replicates per control. This robust design, therefore, requires 36 tanks and 360 snails.

Warbritton (2007a) conducted a definitive study with *Marisa* that was designed based on the recommendations of Forbes et al. (2007b). BPA treatments ranged from 0.1 to 640 μg/L BPA. No treatment related effects on survival, egg production, or
hatching were found. Juvenile growth was marginally, but significantly reduced in females at 640, but not at 25 μg/L. Warbritton (2007b) also conducted a 3-month experiment with one treatment (25 μg/L) at 22°C (all other experiments were conducted at 25°C). This experiment was conducted to ascertain possible differences in fecundity at a lower temperature. No statistically significant effects on egg production related to BPA exposure were reported at 22°C.

Overall, the Forbes et al. (2007b) and Warbritton (2007a) studies used experimental designs of sufficient robustness to discern possible reproductive effects caused by exposure to BPA and used appropriate statistical analyses to properly interpret the data. A *Marina* species NOEC of 25 μg/L was used in the development of SSD-based PNECs.

**Summary of the Chronic Aquatic Database for BPA**

The U.S. Environmental Protection Agency (USEPA's) approach to developing water quality criteria (USEPA 1985) requires that the toxicity database include, at a minimum, eight unique families of aquatic organisms. The required taxa include two different families of fishes, a non-fish chordate family, planktonic and benthic crustaceans, insects, and other non-chordate or arthropod taxa. In addition, green algae and aquatic plants may be included. The EU technical guidance document (TGD) has tentatively adopted this requirement for diversity of taxa to calculate an SSD-based PNEC (EC 2003).

For BPA, 19 valid chronic aquatic toxicity studies covering 14 different species of organisms were identified in this study (see Table 1). Representing the animal kingdom are four species of fish, one amphibian, two crustaceans, one insect, one mollusk, as well as rotifers, hydra, and sponges. Plants are represented by green algae and an aquatic macrophyte. Overall the dataset covers ten distinct families of aquatic organisms, which meets the requirements of both the USEPA and EU TGD guidance (USEPA 1985; EC 2003).

Each study reports one or more endpoints related to survival, growth and development, and/or reproduction. The lowest NOEC for any endpoint that was determined within each study was identified. If two or more studies for the same species are available, the longest duration study was used to represent the species. This was true for the medaka and fathead minnow species for which partial and full life-cycle studies exist. The observed toxicity of BPA to aquatic organisms ranged from the lowest NOEC value of 16 μg/L from a multi-generation test with fathead minnows to the highest NOEC value of 7800 μg/L for the aquatic macrophyte, duckweed.

**DEVELOPMENT OF PNEC VALUES**

Four separate SSD methods were examined with BPA, along with the traditional deterministic AF approach. The SSD approaches used were:

1. ETx 2.0 was obtained from The Netherlands National Institute of Public Health and the Environment (RIVM) (RIVM 2004). This program is used to calculate a lower 5th percentile concentration from the distribution of chronic NOEC values.
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(i.e., an HC5 value). The SSD assumes a normal distribution of species sensitivity that is log transformed to perform the calculations. The assumption that the toxicity dataset fits a log-normal distribution is tested using the Anderson-Darling test for normality.

2. A Final Chronic Value (FCV) was calculated using the USEPA method for calculating National Ambient Water Quality Criteria (USEPA 1985, 1995). Using only the four most sensitive toxicity values, the FCV calculation assumes a log triangle distribution of species sensitivity. The FCV is the lower 5th percentile from the SSD.

3. Sigma Plot software (Systat 2000) was used to calculate 5th percentile values. SigmaPlot is a commercially available software package. A log-normal distribution of species sensitivity is assumed.

4. A distribution approach consistent with that used by Environment Canada in their conduct of chemical-specific risk assessments was used (CEPA 1997). All data were simply ranked and Microsoft Office Excel (2003) software was used to calculate the lower 5th percentile value, assuming a log-normal distribution.

RESULTS

Calculation of SSD-Derived PNEC Values

HC5 derived from ETx 2.0 (RIVM 2004)

An HC5 value was calculated for BPA that represents the lower-bound 5th percentile of NOEC values of the distribution of species-specific toxicity results (see Table 2 and Figure 1). The HC5 value calculated for BPA was 18 μg/L.

![Graph](image)

**Figure 1.** PNEC for bisphenol A calculated using the RIVM ETx software. PNEC = 18 μg/L.
Table 2. PNEC values for BPA derived using either SSD or traditional assessment factor approaches.

<table>
<thead>
<tr>
<th>Method</th>
<th>ETx</th>
<th>USEPA</th>
<th>SigmaPlot lower 5th percentile</th>
<th>Distributional lower 5th percentile</th>
<th>Range of SSD-based PNEC values</th>
<th>Traditional AF approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNEC (µg/L)</td>
<td>11</td>
<td>71</td>
<td>22</td>
<td>11</td>
<td>11 to 71</td>
<td>1.6</td>
</tr>
</tbody>
</table>

**FCV calculated using USEPA procedures (USEPA 1985)**

A Final Chronic Value (FCV) was calculated for BPA using the four most sensitive toxicity results (see Table 2 and Figure 2). FCVs are calculated using the geometric mean of the NOEC and LOEC for each study result yielding maximum-allowed toxicant concentrations (MATCs). The rationale for use of MATCs is that the MATC gives a more likely estimate of the true NOEC, since treatment concentrations are rather arbitrarily chosen (USEPA 1985). In addition, many compounds exhibit threshold levels of toxicity and the MATC may be viewed as the lowest concentration of a chemical that might produce a harmful effect on an organism. If multiple tests of similar duration are available for a species, a species MATC may be calculated. For BPA, an FCV of 71 µg/L was obtained.

![Figure 2](image-url)  
**Figure 2.** PNEC for bisphenol A calculated using the USEPA Final Chronic Value (FCV) approach (only the lowest four toxicity values are used). MATC values are the geometric means of the measured NOECs and LOECs. PNEC = 71 µg/L.
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Intercept = -2.675
Slope = 1.005
r² = 0.9622

90th centile = 24 μg/L
95th centile = 11 μg/L

Figure 3. PNEC for bisphenol A calculated using the SigmaPlot (SYSTAT 2000) HC5 approach. PNEC = 11 μg/L.

Lower-bound 5th percentile value from SigmaPlot (SYSTAT 2000)

SigmaPlot yields lower bound 5th percentile toxicity values (see Table 2 and Figure 3). The SSD derived using SigmaPlot uses species-specific NOEC values, although either LOEC values alone or the MATC values could also be used. For BPA, a lower-bound 5th percentile of 11 μg/L was calculated.

Lower-bound 5th percentile value from a distribution plot

Using the distributional approach of Environment Canada (CEPA 1997), the lower-bound 5th percentile concentration was calculated. Species NOEC values were used for the SSD plot (see Table 2 and Figure 4). For BPA, a lower-bound 5th percentile concentration of 22 μg/L was determined.

PNEC calculated using the AF approach

The SSD-derived PNEC values can be compared to a PNEC calculated using the traditional AF approach. The species-specific NOEC values were ranked and plotted from low to high concentration (see Table 2 and Figure 5). The lowest NOEC is 16 μg/L from the fathead minnow multigeneration test and this NOEC was divided by an AF of 10. Because three or more NOEC values for different taxa are available (Table 1), the lowest AF of 10 is justified (USEPA 1984; CEPA 1997; EC 2003). The resulting traditionally derived PNEC based on the use of AF of 10 for BPA was 1.6 μg/L.
Figure 4. PNEC for bisphenol A calculated using the distributional approach. PNEC = 22 μg/L.

Figure 5. PNEC for bisphenol A calculated using the traditional assessment factor approach (most sensitive species and endpoint divided by an AF = 10). PNEC = 1.6 μg/L.
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Measured BPA Concentrations in U.S. and European Surface Waters

Concentrations of BPA in surface waters of North America and Europe have been compiled from the scientific literature and government reports (Clark et al., manuscript in preparation). Relevant studies were obtained after identification by comprehensive literature searching. All studies were critically reviewed for validity using the methods presented in Klecka et al. (2007). The reviews emphasized the adequacy of sampling strategy and methods, quality assurance data, and analytical methodologies. The number of samples from representative and unique surface water locations that were analyzed for BPA totaled 1068 and 848, for North America and Europe, respectively.

The median and 95th percentile measured BPA concentrations in North American and European surface waters are presented in Table 3. In North America, 80% of the sampling locations had no detectable BPA, whereas in Europe, 49% had no detectable BPA. The difference in percent detections is attributed to the use in the studies conducted by the U.S. Geological Survey of analytical methods developed for the simultaneous analysis of dozens of analytes; a consequence of which often yields less sensitivity (Kolpin et al. 2002).

In North America, concentrations of BPA in surface waters have a median of 0.081 \( \mu g/L \) and a 95th percentile of 0.47 \( \mu g/L \). Most of the U.S. surface water data has been recently collected by the U.S. Geological Survey and has largely focused on areas that are susceptible to contamination (see for example Kolpin et al. 2002). In European surface waters, BPA concentrations have a median of 0.010 \( \mu g/L \) and a 95th percentile of 0.35 \( \mu g/L \).

Comparison of Measured BPA Concentrations to PNEC Values

Using the range of SSD-based PNECs (11 to 71 \( \mu g/L \)) and the concentrations of BPA in North American and European waters, ranges of hazard quotients (HQ) are calculated according to the USEPA (1998) and are presented in Table 3. HQs are the ratio of exposure to effect concentrations. BPA concentrations are most usefully

Table 3. Hazard quotients* and surface water concentrations of BPA in the United States and Europe.

<table>
<thead>
<tr>
<th></th>
<th>North America</th>
<th>Europe</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of samples*</td>
<td>( n = 1068 )</td>
<td>( n = 848 )</td>
</tr>
<tr>
<td>No. of detects**</td>
<td>( n = 216 (20%) )</td>
<td>( n = 433 (51%) )</td>
</tr>
<tr>
<td>BPA concentrations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hazard quotients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (50th percentile)</td>
<td>0.081 ( \mu g/L )</td>
<td>0.010 ( \mu g/L )</td>
</tr>
<tr>
<td>95th percentile</td>
<td>0.47 ( \mu g/L )</td>
<td>0.35 ( \mu g/L )</td>
</tr>
<tr>
<td>ranges</td>
<td>0.0011 to 0.0074</td>
<td>0.0004 to 0.0091</td>
</tr>
<tr>
<td>0.0066 to 0.043</td>
<td>0.0049 to 0.052</td>
<td></td>
</tr>
</tbody>
</table>

*Hazard quotients calculated as the ratio of the surface water concentration divided by the range of SSD-based PNEC values (11 to 71 \( \mu g/L \)). **Represents only the number of unique sampling locations, eliminating duplicate samples and multiple sampling events at any given location. ***Varying detection limits.

summarised by median or 50th and 95th percentile values as the distributions are skewed by a small number of values at the high end of the concentration range. In North American surface waters, HQ values for BPA range from 0.0011 to 0.0074 using the median concentration of 0.081 μg/L and from 0.0066 to 0.045 using the 95th percentile concentration of 0.47 μg/L. In European surface waters, HQ values range from 0.00014 to 0.00091 using the median concentration and from 0.0049 to 0.032 using the 95th percentile concentration. Based on the lack of overlap in the measured surface water concentrations and the range of calculated PNEC values in this assessment, communities of aquatic organisms in North American and European surface waters are not expected to be adversely impacted by exposure to BPA.

DISCUSSION

PNECs Derived for BPA

The PNEC values that were calculated using four SSD methods are compared to the traditional PNEC calculated using the AF approach as shown in Table 2. The PNECs that were calculated using SSD methods ranged from 11 to 71 μg/L, a range that covers a factor of about seven between the high and low values. Three of the SSD-derived PNECs (calculated using the RIVM HC5, SigmaPlot 5th percentile, and Distributional 5th percentile methods) range from 11 to 22 μg/L, about a factor of two apart. The differences in these PNECs (ranging from 11 to 22 μg/L) are due to slightly differing calculation methodologies. The choice of a specific method would be dependent on the specific regulatory needs of a specific country employing the procedures.

The fourth PNEC of 71 μg/L was calculated using the USEPA FCV method. This latter PNEC is different from the other three primarily due to the use of the species geometric mean of the NOEC and LOEC (i.e., the MATC), instead of strictly using the NOEC values. The rationale for use of MATCs in FCV derivation is that the MATC gives a more likely estimate of the true chronic threshold effect concentration (USEPA 1985). This is due to the fact that many chemical substances exhibit threshold levels, i.e., the lowest concentration of a compound that might produce a harmful effect on an organism. For any threshold material, a continuous exposure or series of exposures below the aquatic threshold concentration should not cause an unacceptable effect on aquatic organisms. As defined by the USEPA, an FCV derived from MATCs is intended to be an estimate of "a threshold of unacceptable effect" to a sensitive aquatic species. In addition, the USEPA has detailed the application of the threshold effect in FCV derivation, noting the following, "if maintained continuously, any concentration above the criterion is expected to cause an unacceptable effect. On the other hand, the concentration of a pollutant can be above the criterion without causing an unacceptable effect if (a) the magnitude and duration of the excursions are appropriately limited and (b) there are compensating periods of time during which the concentration is below the criterion" (USEPA 1985).

In most of the studies identified in Table 1, multiple endpoints were measured. The endpoints may be grouped into the categories of mortality, growth and development, and reproduction. Although the lowest NOEC for any endpoint measured
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Figure 6. Bisphenol A: NOEC values for mortality, growth, and development and reproduction endpoints. Data from Table 1.

in a study was used as the overall study NOEC to calculate PNEC values regardless of what category it represented, it is useful to compare the NOEC for each category of endpoint. The NOEC for the three types of observed endpoints were ranked from low to high and plotted by concentration (Figure 6). The endpoints at a given rank are not necessarily from the same study. There appear to be few obvious differences between the NOEC for the three general endpoints across studies in the distributions shown in Figure 6. In other words, the distribution of reproduction NOECs do not appear to be more or less sensitive than distributions of growth and development NOECs or mortality NOECs.

To further test this observation, the RIVM ETx 2.0 program was used to calculate individual HC5 values for the distribution of NOECs based on endpoints. The HC5 values for mortality and growth and development NOECs are 62 and 44 µg/L, respectively, as compared to the HC5 of 31 µg/L for reproduction NOECs. The reproduction-based HC5 value is within a factor of 1.7 of the HC5 of 18 µg/L calculated using all data. The HC5 of 31 µg/L based only on reproduction data and the HC5 value of 18 µg/L based on all data are lower than the HC5 values based on either mortality or growth because of the single lowest NOEC of 16 µg/L, which is based on F2 generation hatchability. Absent this value, the HC5 value based on reproduction data is 118 µg/L and the HC5 value based on all data is 30 µg/L. The reason for the changes in the HC5 values is due to the influence on the shape of the species sensitivity distribution from the one NOEC. This type of influence on the HC5 value or any of the PNECs calculated using the other methods is independent of the type of endpoint. Any substantially different NOEC (either high or low) will
change the tails of the distributions and affect the PNEC that is calculated (e.g., the HC5).

Key Assumptions about Using the SSD Approach to Calculate PNEC Values

In the SSD approach to determining PNEC values, a concentration at any percentile (here, 5%) is calculated from a distribution of toxicity values. A number of assumptions are inherent in this approach: (1) the SSD is well modeled by the selected distribution; (2) the sensitivity of the species in the laboratory approximates the sensitivity of species in the field; (3) the sample of species is random, or at least representative of a community; and (4) protection of the prescribed percent of species confers an appropriate level of protection on a community.

The assumption that the actual distribution of species sensitivity follows the lognormal distribution (the most common distribution assumed) can be tested with the RIVM ETx 2.0 program. This program uses the Anderson-Darling test for normality of the distribution of effect concentrations. For the BPA dataset, the calculated Anderson-Darling statistic of 0.345 (for n = 14) is well below the critical value of 0.752 at the $p = .05$ level of significance. Thus, the assumption of a normal distribution (log transformed) was confirmed for the BPA dataset. Had this assumption not been supported, other more sophisticated methods of calculating toxicity thresholds are available and may have been needed. For instance, Newman et al. (2000) examined toxicity datasets for 30 compounds and found that half did not meet the assumption of normality. The authors proposed the use of bootstrap methods to overcome this problem with good success. Grist et al. (2002) extended this type of analysis further proposing a hybrid bootstrap regression method.

When developing a toxicity dataset for a chemical, a standard group of aquatic species (fish, invertebrates, algae) are tested for which validated protocols exist. This base dataset is often supplemented by other less standard species. The combined dataset then may be used to conduct risk assessment. The inherent assumption is that the toxicity dataset with multiple species is representative of a community of species that is to be protected. Buckler et al. (2005) stated that although minimum datasets consisting of toxicity values for rainbow trout, bluegill, daphnids, and mysid shrimp provide satisfactory prediction of larger datasets of toxicity values, it is obviously desirable to have high quality data for as many species as possible. In fact, both the USEPA and the European Chemicals Bureau have general requirements (see Table 1) for minimum datasets for deriving a PNEC using SSD approaches, consisting of at least eight major taxa, including fish, non-fish vertebrates, insects, mollusks, crustaceans, annelids, plankton, and algae (USEPA 1985; EC 2003).

It is difficult to assess whether the laboratory-derived toxicity tests are a random sample of species in the field or at least representative of the species in the field. In general, species selected to become standard test organisms are thought to be relatively sensitive, at least to some toxicants. As noted by Versteeg et al. (1999), Daphnia, fathead minnows, and rainbow trout are often tested and are typically among the most sensitive species in a toxicity dataset. This is partly true for BPA, as the most sensitive species is the fathead minnow. The fact that the most sensitive life stages of these species are exposed in chronic tests further contributes to the conservatism built into a set of laboratory toxicity tests.
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Possibly the most important assumption for the use of SSDs to calculate PNEC values is that they confer an appropriate level of protection to a community of species. It is this final point that has garnered the majority of criticisms concerning the SSD approach and extrapolation to protection at the ecosystem level. In examination of this latter assumption, Versteeg et al. (1999) compared the application of single-species chronic toxicity data from the open literature (via the SSD approach) with published, high quality chronic model ecosystem data (e.g., microcosms, model ecosystems, and field situations) on the same chemical. If single-species data are indeed useful for extrapolating to the ecosystem level via the SSD approach, there should be substantial overlap in the distribution of single-species and model ecosystem data. Conversely, if single-species/SSD data are of limited use for extrapolating to an ecosystem, there should be limited or no overlap in the distributions. Versteeg et al. (1999) compared the SSD output from laboratory studies to ecosystem NOEC values for a variety of substances (n = 11), including organic compounds, metals, pesticides, and surfactants. The authors noted that observed field ecosystem NOEC values corresponded to concentrations expected to exceed the SSD-derived PNEC at the 5th percentile and that the lower 5th percentile values are good predictors of the lower 95% confidence interval on the mean ecosystem NOEC value. Their analysis indicated that a sufficiently large data set of laboratory-generated chronic test data (defined as n > 5 species) may be used to successfully determine concentrations for a compound that are protective of the system that the authors studied.

Additional supporting evidence is available from Van den Brink et al. (2006), who analyzed laboratory toxicity data for nine herbicides and compared respective SSD regressions against response data from field mesocosms. These authors noted that the lower confidence limit of the acute 5th percentile (i.e., acute HC5 value) and the median value of the chronic HC5 were protective of adverse effects in aquatic micro/mesocosms even under a long-term exposure regime. In studies using endosulfan, Hose and Van den Brink (2004) examined the utility of non-native laboratory species-based SSDs to be protective of local mesocosm responses and determined that the sensitivities of native organisms were not significantly different from those of non-native species. The authors also found that field mesocosm response to endosulfan was less sensitive than corresponding laboratory species and the laboratory-based acute 5th percentile SSD value was protective of field and mesocosm populations. Finally, Selck et al. (2002) compared PNEC values from both deterministic and probabilistic approaches with tributyltin and linear alkylbenzene sulfonate and found both methods yielded PNEC values that were protective of marine mesocosm responses.

The SSD approach represents a technique to reduce uncertainties in our understanding of ecological dynamics following chemical exposure. Evidence from numerous researchers with a wide variety of metal and organic chemicals indicates that low percentile SSD-derived effect concentrations are protective of field systems (Versteeg et al. 1999; Selck et al. 2002; Hose and Van den Brink 2004; Van den Brink et al. 2006).

Risk Management Decisions

At least two risk management decisions accompany the use and application of PNEC values derived using SSDs. The first is the selection of the protection level (e.g.,
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5th percentile). The lower-bound 5th percentile value has been used throughout this study as it is commonly employed. Other levels of protection could be used as well.

The second risk management issue to be decided is whether the SSD-derived PNEC at the chosen level of protection nevertheless warrants an additional AF to achieve an even greater level of protection. The available data suggest that no additional AF is needed if the PNEC calculated using SSD methods is based on chronic data. Using acute data for a series of pesticides, Brock et al. (2006) found that AFs of 2 to 10 may be warranted for acute HC5 values. Similarly, Maltby et al. (2005) suggests an AF of 5 be applied to HC5 values that are calculated using only acute studies. However, based on longer term studies, Van den Brink et al. (2006) and Versteeg et al. (1999) reported that chronic HC5 values with no AF used were protective of long-term exposure in mesocosms. As Forbes and Calow (2002) noted, studies that examine individual-level responses often provide protective estimates of population-level effects, and changes in species composition rather than on ecosystem processes is unlikely to grossly underestimate effects on ecosystems (Forbes and Calow 2002). Therefore, it does not appear that applying an additional AF to an SSD-derived PNEC based on chronic NOEC values is warranted for BPA.

SSD-Derived PNEC in Other Environmental Compartments

For the purposes of this article, PNECs were calculated for use in risk assessment of BPA in surface waters. Besides aquatic risk assessment, SSDs for any compound may be used to calculate PNECs for use in setting cleanup standards for surface waters, to support discharge permits, or in support of ecological risk assessments for potentially affected sites. With adequate data, PNECs based on SSDs for terrestrial species can also be calculated.

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REFERENCES

Bayer AG. 1999. Fish, Juvenile Growth Test (Oncorhynchus mykiss) of Bisphenol-A. Study Number: 707 A/38FF. Bayer AG, Leverkusen, Germany
SSD-Derived Predicted No Effect Concentrations for Bisphenol A


Caunter JE. 2006. Bisphenol A: 42-Day Exposure to Mature Adult Fathead Minnows (Pimephales promelas)—Phase 2 of the Study “Effects of BPA on Fathead Minnow Gonadal Histology.” Brixham Environmental Laboratory, Zeneca, Ltd., Brixham, Devon, UK


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Hose GC and Van den Brink PJ. 2004. Confirming the species-sensitivity distribution concept for endosulfan using laboratory, mesocosm, and field data. Arch Environ Contam Toxicol 47:11–20


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