Scientific Committee on Health, Environmental and Emerging Risks
SCHEER

Scientific Opinion on "Draft Environmental Quality Standards for Priority Substances under the Water Framework Directive"

Bisphenol-A

The SCHEER adopted this document
during the plenary meeting on 12 October 2022

ACKNOWLEDGMENTS

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This Opinion has been subject to a commenting period of four weeks after its initial publication (from 6 July to 6 August 2022). Comments received during this period were considered by the SCHEER. For this Opinion, the main changes were made in the following sections of the text: 7.1 and 7.2 (probabilistic approach), 7.7, 4. (question 2) and abstract.

Keywords:
Bisphenol-A, Water Framework Directive, environmental quality standards

Opinion to be cited as:
SCHEER (Scientific Committee on Health, Environmental and Emerging Risks), Final Opinion on Draft Environmental Quality Standards for Priority Substances under the Water Framework Directive - bisphenol-A, 12 October 2022

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PDF ISSN 2467-4559 ISBN 978-92-68-06282-1 doi:10.2875/763397 EW-CA-23-012-EN-N

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ABSTRACT

For the draft dossier on Environmental Quality Standards on Bisphenol-A, the SCHEER offers the following opinion:

A probabilistic approach was possible and this allowed an SSD-based freshwater MAC-$QS_{fw,eco}$ of 129 µg L^{-1} to be derived with a separate marine SSD able to generate a MAC-$QS_{sw,eco}$ of 31 µg L^{-1}, both using an AF of 10. The SCHEER supports this approach but recommends amending the acute dataset (see answer to question 2. from the Commission).

The SCHEER notes that whilst Bisphenol-A (BPA) has a relatively rich dataset concerning its ED properties, there is still some controversy over its ED potency across taxonomic groups. The SCHEER does not endorse basing the final AA-$QS_{fw,\ eco}$ on the deterministic data evaluation. Instead, the SCHEER recommends using the best-fitting model as the basis for the probabilistic derivation of the final AA-$QS_{fw,\ eco}$, using the amended chronic dataset (see answer to question 1. from the Commission).

The SCHEER supports the proposed **$QS_{fw\ sed}$ of 0.82 mg kg^{-1}** and **$QS_{sw\ sed}$ of 0.16 mg kg^{-1}** to protect benthic organisms.

To protect predators from secondary poisoning from BPA exposure through consumption of freshwater food, the SCHEER support the **$QS_{Biota,\ sec\ pois,\ fw}$ in fish** of **5.96 mg kg^{-1}_{ww} (rounded to 6.0)** and **1.73 mg kg^{-1}_{ww} for bivalves (rounded to 1.7)**, and the associated predicted **$QS_{fw\ biota}$ for fish of 89 µg L^{-1}** and **$QS_{fw\ biota}$ for bivalves of 12 µg L^{-1}**. For marine predator secondary poisoning protection, the SCHEER support the **$QS_{Biota,\ sec\ pois,\ sw}$ in fish** of **2.98 mg kg^{-1}_{ww}** and **0.17 mg kg^{-1}_{ww} for bivalves**, and the associated predicted **$QSs_{w\ biota}$ for fish of 44 µg L^{-1}** and **$QSs_{w\ biota}$ for bivalves of 1.2 µg L^{-1}.**

To protect human health, the **$QS_{biota\ hh\ food}$ of 0.005 µg kg^{-1}** and the **$QS_{water\ hh\ food}$ of 0.073 ng L^{-1} for fish and 0.034 ng L^{-1} for bivalves** are based on a provisional TDI of 0.04 ng BPA kg^{-1}_{bw} d^{-1} proposed by EFSA (2021) whose final Scientific Opinion is not yet published. An EU drinking water $QS_{dw,\ hh}$ of 2.5 µg L^{-1} already exists. Thus, the SCHEER confirms that the $QS_{dw\ hh}$ has been correctly evaluated but its endorsement by the SCHEER is dependent on the confirmation of the TDI of 0.04 ng BPA kg^{-1}_{bw} d^{-1} (EFSA, 2021). Thus, the SCHEER identifies the AA-$QS_{water\ hh,\ food}$ of 0.034 ng L^{-1} as provisional critical value, pending confirmation of the TDI.

TABLE OF CONTENTS

1. BACKGROUND

Article 16 of the Water Framework Directive (WFD, 2000/60/EC) requires the Commission to identify Priority Substances among those presenting significant risk to or via the aquatic environment, and to set EU Environmental Quality Standards (EQS) for those substances in water, sediment and/or biota. In 2001, a first list of 33 Priority Substances was adopted (Decision 2455/2001) and in 2008, the EQS for those substances were established (Directive 2008/105/EC or EQS Directive, EQSD). WFD Article 16 requires the Commission to periodically review the list. The first review led to a Commission proposal in 2011, resulting in the adoption of a revised list in 2013 containing an additional 12 Priority Substances. Technical work to support a second review has been underway for some time, and several substances have been identified as possible candidate Priority Substances. The Commission will be drafting a legislative proposal, with the aim of presenting it to the Council and the Parliament sometime around mid-2022.

The technical work has been supported by the Working Group (WG) Chemicals under the Common Implementation Strategy for the WFD. The WG is chaired by DG Environment and consists of experts from Member States, EFTA countries, candidate countries and several European umbrella organisations representing a wide range of interests (industry, agriculture, water, environment, etc.).

Experts nominated by WG Members (operating as individual substance Expert Groups and through the Sub-Group on Review of Priority Substances, SG-R) have been deriving EQS for the possible candidate substances and have produced draft EQS for most of them. In some cases, a consensus has been reached, but in others there is disagreement about one or other component of the draft dossier. The EQS for a number of existing priority substances are currently also being revised.

The EQS derivation has been carried out in accordance with the Technical Guidance Document on Deriving EQS (TGD-EQS) reviewed by the SCHEER[1].

2. TERMS OF REFERENCE

DG Environment now seeks the opinion of the SCHEER on the draft EQS for the proposed Priority Substances and the revised EQS for a number of existing Priority Substances. The SCHEER is asked to provide an Opinion for each substance. We ask that the SCHEER focus on:

Generic questions to the SCHEER

- Have the EQS been correctly and appropriately derived, in the light of the available information and the TGD-EQS?
- Has the most critical EQS (in terms of impact on environment/health) been correctly identified?

Additional questions to the SCHEER

Additional questions to the SCHEER can be found in the file Questions to SCHEER Committee Draft dossier on Bisphenol A in their full extent, otherwise they are listed below:

[1] https://circabc.europa.eu/ui/group/9ab5926d-bed4-4322-9aa7-9964bbe8312d/library/ba6810cd-e611-4f72-9902-f0d8867a2a6b/details

1. Is it correct to include reproduction endpoints as acute data or survival/growth as chronic data?

2. Is the validity of the following ecotoxicity studies included in the draft dossier correct?

3. Is the MAC-$QS_{sw,eco}$ derived correctly using the deterministic approach?

4. Is the MAC-$QS_{sw,eco}$ derived correctly using the probabilistic approach?

5. Is the Assessment Factor (AF) applied correctly to the AA-QS_{fw} using the deterministic approach?

The SCHEER responds to these questions at the end of the Opinion.

3. OPINION

It should be noted that in a separate synthesis Opinion, the SCHEER provides an analysis of weaknesses and unresolved issues common to all dossiers. This includes a discussion of the risk assessment method and of SCHEER's concern regarding the completeness of the data used for the estimation of the different QS values.

Bisphenol-A (BPA) has some estrogen-agonist properties, however, there continues to be considerable disagreement within the scientific community over the levels at which endocrine disrupting effects might occur (Hengstler et al., 2011; Myers et al., 2009; Vandenberg et al., 2009), and indeed the taxonomic groups that might be vulnerable (Fodor *et al*., 2020). This complicates the derivation of an AA_QS if the apparent effect is suggested to be an estrogen related endocrine disrupting effect.

Specific comments on the different sections of the dossier are listed below.

Section 7. Effects and quality standards

Section 7.1. Acute aquatic ecotoxicity

Deterministic approach

Acute ecotoxicity data are available for 9 taxonomic groups and 23 different species including algae, cyanobacteria, cnidarian, mollusc, crustacean, insect, platyhelminthes, fish and amphibian freshwater species

For freshwater, it was observed that the most sensitive value was an EC50 of 1.5 mg L^{-1} for the crustacean *Gammarus pulex*. Given the comprehensive dataset (with a log-transformed standard deviation <0.5), an AF of 10 was suggested, which would give a potential MAC-$QS_{fw,eco}$ of 150 µg L^{-1}.

For saltwater, it was observed that the most sensitive value was an EC50 of 0.23 mg L^{-1} for the echinoderm *Strongylocentrotus purpuratus*. Given the smaller dataset (with a log-transformed standard deviation >0.5) than for freshwaters, an AF of 100 was suggested, which would give a potential MAC-$QS_{sw,eco}$ of 2.3 µg L^{-1}.

Probabilistic approach

The freshwater dataset met the criteria for construction of a Species Sensitivity Distribution (SSD) as listed in the EQS Technical Guidance (EC, 2018) - the database contains data

points of >8 different taxonomic groups and contains more than 15 species. Since the data had a normal distribution and goodness of fit to an SSD, this could be carried out with some confidence. An HC_5 of 1.29 mg L^{-1} was obtained and when the AF of 10 is applied this gave a **MAC-$QS_{fw,eco}$ of 129 µg L^{-1}** (rounded to **130 µg L^{-1}**), which the SCHEER endorses under the assumption that the initial data collection is complete.

The saltwater dataset met the criteria for construction of a Species Sensitivity Distribution (SSD) as listed in the EQS Technical Guidance (EC, 2018) - the database contains data points of >8 different taxonomic groups and contains more than 10 species. Since the data had a normal distribution and goodness of fit to an SSD, this could be carried out with some confidence. An HC_5 of 0.31 mg L^{-1} was obtained and when the standard AF for an SSD based on marine species of 10 was applied, this gave a MAC-$QS_{sw,eco}$ of 31 µg L^{-1}. However, in its answer to the Commission's additional question 2, the SCHEER recommends reclassifying the embryo larval study from Roepke *et al.* (2005) from acute to chronic data. Moreover, a further analysis of the Roepke *et al.* (2005) study, finds its failure to measure exposure concentrations means it would also be unsuitable to include in the chronic dataset and should not be used in preparing a chronic aquatic SSD. Therefore, the SSD should be recalculated without this point before the MAC-$QS_{sw,eco}$ is finalised.

The SCHEER supports the preference of the probabilistic method to derive the QS, in this case MAC-QS, in favour of the deterministic method.

Section 7.2. Chronic aquatic ecotoxicity

Deterministic approach

Whilst the study of (Oehlmann *et al*., 2006) using *Marisa cornuarietis* would normally be identified as revealing the most sensitive organism from which a deterministic AA-QS might be derived, the dossier does not see this study as suitable for this purpose. Some controversy still surrounds this work, and the SCHEER supports the decision not to use it as the basis for the derivation of a deterministic AA-QS.

The dossier discusses the study of (Lahnsteiner et al., 2005) on brown trout with a NOEC of 2.4 µg L-1 as suitable for providing the lowest critical value despite concentrations of BPA being unmeasured in the study. Instead, the study of (Chen et al., 2017) on zebrafish is deemed potentially most suitable, in particular regarding the effect on egg production. Only three effect concentrations are used and the results might have been more convincing if a wider range had been used in the study by Chen *et al*. (2017). The spawning experiment, which is the relevant part of the study for the dossier, (6 females plus 6 males in three replicates) has a small effect on malformation at the lowest but not highest concentrations, lower hatching success at the lower and intermediate concentrations but not at the highest. There is evidence of lower egg production at the immediate concentration 2.28 µg L^{-1}, and slightly less so at 22.8 µg L^{-1}. The key value is the significant egg reduction at 0.228 µg L^{-1}, which is used in the dossier as the anchor point for the final calculation. Based on that calculation, a final NOEC of 0.174 µg L^{-1} is proposed in the JRC dossier. The SCHEER could not identify the arguments in the dossier on how this final value was estimated from the experimental value of 0.228 µg L^{-1}. Given the abundant data available, an AF of 10 is proposed, giving a AA-$QS_{fw,eco}$ of 0.0174 µg L^{-1}.

Although a reasonable amount of literature was available for 11 marine species and 7 taxonomic groups, none of the effect concentrations were found at the level of the freshwater results. Therefore, it was proposed to carry across the same key data from (Chen *et al*., 2017) with the zebrafish NOEC of 0.174 µg L^{-1} with the same AF of 10 for a potential AA-$QS_{sw,eco}$ of 0.0174 µg L^{-1}.

In summary, the absence of a clear dose-response curve for several of the reproduction end-points and the lower variation in egg production compared to what might be expected (Skinner and Watt, 2007) invited caution in the reliance on the Chen *et al*. (2017) study. The SCHEER does not endorse the EQS based on this deterministic approach.

Probabilistic approach

An SSD was assembled from 23 data points (from 10 taxonomic groups) on chronic toxicity to freshwater species together with 11 data (from 8 taxonomic groups) on chronic toxicity to marine species (table 7.3.3.1).

The SCHEER supports the decision to refrain from establishing a mode-of-action specific SSD, in view of the complexity and context-dependency of BPA's mode of action.

Various models were applied to the data, of which the dossier considered the log-normal distribution giving a sufficiently accurate fit (Kolgomorov-Smirnov, accepted at the P=0.05 level). This SSD results in an HC5 of 1.7 µg L^{-1} which, with an AF of 5, would give an AA-$QS_{fw,eco}$ of 0.34 µg L^{-1}.

Whilst the SCHEER supports the probabilistic method with the SSD wherever possible, a case could be made to re-evaluate the SSD because there may be a need to reconsider the choice of data for recalculating the SSD (see answers to specific questions1 and 2, further below).

Currently, the final conclusion of the BPA EQS dossier reads with respect to the AA-$QS_{fw, eco}$: "*Therefore, the AA-$QS_{fw,}$ based on the deterministic approach, and relying on the lowest acute toxicity value for the fish Danio rerio (zebrafish), is currently retained as the key AA-AQ value for Bisphenol-A*". The SCHEER does not endorse this conclusion as the SCHEER supports preferentially using the probabilistic method with the SSD wherever possible. However, the SCHEER requests an SSD be re-evaluated but excluding the data in references Roepke et al (2005), Lahnsteiner et al (2005) and Chen et al (2017) which it considers unreliable as discussed above and in response to additional Question 1 regarding their use in the deterministic approach.

The SCHEER appreciates the detailed comparative evaluation of different SSD models and suggests using the best-fitting model as a basis for the probabilistic derivation of the AA-$QS_{fw, eco}$.

Section 7.4. Sediment ecotoxicology

Data on four benthic species were available, two freshwater and two marine, where studies had been made of their response to BPA in sediment. All data was seen as being potentially relevant to setting freshwater and marine standards. The end-points included emergence, biomass, growth, survival and reproduction after 10 to 28 d exposure. From these, the lowest NOEC gave a **$QS_{fw\ sed}$ of 0.82 mg kg^{-1}** following the application of an AF of 10. The SCHEER supports this value. For the marine water, from the same starting point, an AF of 50 was applied according to the TGD, which resulted in a **$QS_{sw\ sed}$ of 0.16 mg kg^{-1},** the SCHEER also supports this value.

Section 7.5. Species sensitivity distribution according to EU risk assessment 2008 and 2010

The SCHEER has no comment on this section which does not seem to relate to the EQS derivation.

Section 7.6. Secondary Poisoning

The potential for bioaccumulation for BPA was indicated by a Log K_{ow} > 3.0 and by a BCF-value >100. Therefore, the criteria triggering an assessment for secondary poisoning are met. The dossier selects a NOAEL value of 50 mg $kg^{-1}_{bw}d^{-1}$ as the concentration in a study on mice where endocrine disruption outcomes were observed at concentrations up to 600 mg kg^{-1}. Here the mouse study NOAEL value of 50 mg $kg^{-1}_{bw}d^{-1}$ could be converted to 11 µg BPA kJ^{-1} of food. But food consumption is related to both the daily energy expenditure of a predator (here given as 87 kJ d^{-1}) and the energy content of the food. If a fish contains 5523 kJ kg^{-1}_{fw} of food energy and a bivalve 1602 kJ kg^{-1}_{fw}, then for those who predate these animals, a level of 59.6 mg BPA kg^{-1}_{ww} of fish could be consumed as the level not to be exceeded and 17.3 mg BPA kg^{-1}_{ww} for bivalves. But given the uncertainties on the representativeness of relying on a mouse value for toxicity from diet, an AF of 10 was applied to give a **$QS_{Biota,\ sec\ pois,\ fw}$ in fish** of **5.96 mg kg^{-1}_{ww} (rounded to 6.0)** and **$QS_{Biota,\ sec\ pois,\ fw}$ of 1.73 mg kg^{-1}_{ww} for bivalves (rounded to 1.7)** which the SCHEER can support.

The next step to consider is what concentration in the freshwater would lead to these concentrations in fish and bivalves given a certain BAF value. Here no BAF value is known, so instead it may be calculated by BCF x BMF. However, no experimental BMF value exists either. Here the TGD indicates that where the BCF is <2000 then the BMF may be set at 1. The BCF reported in Table 5.1 was experimentally derived and used here to give a **$QS_{fw\ biota}$ for fish as 89 µg L^{-1}** and **$QS_{fw\ biota}$ for bivalves as 12 µg L^{-1},** which the SCHEER can support.

To protect against secondary poisoning in the marine environment, the same starting point and AF of 10 was used but lower protective thresholds for the consumer were necessary due to their being further higher tiers of consumers, thus a **$QS_{Biota,\ sec\ pois,\ sw}$ in fish** of **2.98 mg kg^{-1}_{ww} (rounded to 3.0)** was derived (half that of freshwater fish) and **$QS_{Biota,\ sec\ pois,\ fw}$ of 0.17 mg kg^{-1}_{ww} for bivalves** (10^{th} of that of freshwater bivalves). This was related to lipid normalisation. When this is back calculated to the equivalent water concentration as above, we are given a **$QS_{sw\ biota}$ for fish as 44 µg L^{-1}** and **$QS_{sw\ biota}$ for bivalves as 1.2 µg L^{-1}**, which the SCHEER can support.

Section 7.7. Human health

Bisphenol-A has the potential to bioaccumulate (Log Kow 3.4, see Table 5.1) and has some endocrine-disrupting and reprotoxic properties, therefore it is necessary to derive a QS to safeguard the risk against human exposure. The starting point was the TDI of 0.04 ng BPA kg^{-1}_{bw} d^{-1} provided by EFSA (2021). Assuming that fish is the contaminated food source, that diet consist of 20% fish and that each individual consumes 0.00163 $kg^{-1}_{fish}kg^{-1}_{bw}$ d^{-1} results in a **$QS_{biota\ hh}$ of 0.005 µg kg^{-1}_{biota}**. Thus, for humans eating fish or bivalves, the associated water in which these food sources live would need to not exceed a **$QS_{water\ hh\ food}$ of 0.073 ng L^{-1} for fish and 0.034 ng L^{-1} for bivalves**.

Based on the provisional TDI of 0.04 ng BPA kg^{-1}_{bw} d^{-1} provided by EFSA (2021) and considering that 20% of the TDI are allowed to originate from the consumption of drinking water, a body weight of 70 kg and a daily intake of 2 L of tap water, the **$QS_{dw\ hh}$** would be **2.8 ng L^{-1}**. The SCHEER endorses this proposed $QS_{dw\ hh}$ assuming that the TDI of 0.04 ng BPA kg^{-1}_{bw} d^{-1} is confirmed. The SCHEER notes however that, there is a current EU standard for BPA in drinking water of 2.5 µg L^{-1}.

4. CRITICAL EQS

The SCHEER identifies that the AA-$QS_{water\ hh,\ food}$ of 0.034 ng L^{-1} is the critical value for setting the EQS, based on the EFSA (2021) provisional TDI value. Should this TDI not be confirmed, the critical EQS would require to be re-evaluated.

5. SCHEER RESPONSES TO ADDITIONAL QUESTIONS PUT BY COMMISSION

1. *Is it correct to include reproduction endpoints as acute data? Is it correct to include survival/growth endpoints as chronic data?*

The guidance document (Ref) defines a chronic study as *"a study in which:*
(i) the species is exposed to the toxicant for at least one complete life cycle, or

(ii) the species is exposed to the toxicant during one or more sensitive life stages.

On this basis, SCHEER considers data related to hatching success and embryo and larval development as chronic data (data from the studies by Chan & Chan, 2012; Duan *et al*., 2008; Zhou *et al*., 2011; Liu, 2011 and Roepke *et al*., 2005). The EC_{50} value provided by Özlem *et al* (2008) can be deleted from the assessment, given that the NOEC from the same study is already included in the chronic dataset.

In principle, SCHEER considers survival to be one of the classical endpoints for acute toxicity, widely employed, for example, in studies on the acute toxicity to daphnids. However, survival after an exposure that covers at least a substantial fraction of a lifecycle should be considered chronic (see above quote from the TGD). The SCHEER is therefore of the opinion that the data on survival of *Gammarus pulex* after 14days exposure (Johnson et al., 2005) and *Poecilia reticulata* after 30 days of exposure (Kinnberg and Toft, 2003) should remain classified as chronic.

Growth is a typical endpoint for chronic toxicity, in particular if the exposure covers a substantial fraction of the life cycle of an organism. The SCHEER is therefore of the opinion that the data on growth of *Cyprinus carpio* after 49 days of exposure should remain classified as chronic (Bowmer & Gimeno, 2001).

2. *Is the validity of 24 ecotoxicity references in an accompanying table correct?*

The SCHEER had some concerns regarding the reliability of Chen *et al*. (2017) and Lahnsteiner *et al*. (2005) studies. The SCHEER also concluded that the study of Oehlmann *et al*. (2006) should not be used as the basis for deterministic calculations; but that it may be used for the probabilistic approach.

However, a minority view was expressed that the Oehlmann *et al.* reference was not sufficiently reliable to be kept in the chronic aquatic ecotoxicity dataset and should not be used in drawing an SSD as part of deriving a probabilistic AA_QS.

3. *Was the MAC-$QS_{sw,eco}$ derived correctly using the deterministic approach?*

No, see answer to question 1. The SCHEER recommends including the EC_{50} of 0.23 mg L^{-1} for the echinoderm *Strongylocentrotus purpuratus* as a chronic data point.

4. *Is the MAC-$QS_{sw,eco}$ derived correctly using the probabilistic approach?*

Regarding questions 1 and 2, in the derivation of the MAC-$QS_{sw,eco}$, probabilistic approach, as mentioned above, the SCHEER suggests considering some ecotoxicity data not as acute toxicity data, but instead using them for the derivation of AA-QS. Consequently, the SSD analysis needs to be updated.

5. *Is the Assessment Factor (AF) applied correctly to the AA-QS_{fw} using the deterministic approach?*

The SCHEER supports using an AF of 10, given the abundant literature that is available, covering all major species' groups.

The SCHEER however recommends the use of the probabilistic approach for the determination of the AA-QS_{fw}.

6. LIST OF ABBREVIATIONS

AA-QS	Annual Average Quality Standard
ADI	Acceptable Daily Intake
AF	Application Factor
AMR	Anti-Microbial Resistance
BAF	Bioaccumulation Factor
BCF	Bioconcentration Factor
BMF	Biomagnification Factor
BPA	Bisphenol-A
EC50	Effective Concentration 50%
ED	Endocrine Disruption
EQS	Environmental Quality Standards
HC5	Hazardous Concentration 5%
MAC-QS	Maximum Acceptable Concentration Quality Standard
MIC	Minimum Inhibitory Concentration
NOAEL	No Observed Adverse Effect Level
SSD	Species Sensitivity Distribution
TDI	Tolerable Daily Intake

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