Scientific Committee on Health, Environmental and Emerging Risks
SCHEER

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

Silver and its compounds

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ABSTRACT

The dossier on Environmental Quality Standards for "Silver and its compounds" was reviewed by the SCHEER according to the general mandate on EQS dossiers.

The SCHEER endorses the **MAC-$QS_{fw,eco}$ = 0.022 µg L^{-1}**, derived with a deterministic procedure. The SCHEER agrees with the decision of not performing the probabilistic approach due to the incompleteness of the dataset.

The SCHEER also endorses the deterministic **AA-$QS_{eco,fw}$ = 0.01 µg L^{-1}** and agrees with the probabilistic values obtained with different SSD curves (0.012 and 0.016 µg L^{-1} respectively). As a final **AA-$QS_{eco,fw}$**, the rounded value of **0.01 µg.L^{-1}** obtained combining the deterministic one and the two probabilistic values, is endorsed by the SCHEER

As indicated by the Technical Guidance for Deriving Environmental Quality Standards, freshwater and saltwater data cannot be pooled for metals.

For saltwater, the SCHEER agrees that there are no sufficient data available for the deterministic and probabilistic derivation of the MAC-$QS_{sw,eco}$ and for the probabilistic derivation of the AA-$QS_{sw,eco}$.

The SCHEER endorses the AA-$QS_{sw\ eco}$ **=0.17 µg.L^{-1}** obtained with the deterministic procedure for the salinity of 30‰. On the contrary, it is the opinion of the SCHEER that the AA-$QS_{sw\ eco}$ for the salinity of 10‰ is not properly derived and cannot be endorsed.

For sediment ecotoxicity, the SCHEER endorses the **AA-$QS_{freshwater,\ sed}$ =4.78 µg.kg^{-1}_{dw}** obtained with the Equilibrium Partitioning method. The SCHEER agrees with the impossibility to derive an AA-$QS_{marine\ water,\ sed}$ due to the lack of a marine K_{dsed}.

For secondary poisoning, the NOAEL value used to derive the QS_{biota} refers to silver acetate. Therefore, the tentative QS_{biota} must be modified by transforming the NOAEL in ionic silver. The same correction must be made for the derivation of the $QS_{biota,hh\ food}$.

Finally, the SCHEER appreciate that antimicrobial resistance is dealt with in the dossier. However, this assessment is not used for the derivation of EQS. The SCHEER recommends that a section on how to deal with antimicrobial resistance should be included in the Technical Guidelines.

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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. EQS for a number of existing priority substances are also currently 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:
1. whether the EQS have been correctly and appropriately derived, in the light of the available information and the TGD-EQS;
2. whether the most critical EQS (in terms of impact on environment/health) have been correctly identified.
Where there is disagreement between experts in the working group on Chemicals or when there are other unresolved issues, we ask that the SCHEER consider additional points, identified in the cover note(s).
For each substance, a comprehensive EQS dossier is or will be available. DG Environment is providing three EQS dossiers ahead of the 3-4 March SCHEER Plenary and expects to provide most of the remaining dossiers over the next three months. The dossiers contain much more information than simply the draft EQS; the SCHEER is asked to focus on the latter.

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

In some cases, especially where additional points are raised, additional documents may be provided. Some of the studies referred to in the dossiers are not publicly available. If the SCHEER needs to see these studies, it is invited to please contact DG Environment.

3. OPINION

Silver is a naturally occurring element. Therefore, the assessment of Environmental Quality Standards (EQS) must be performed using specific approaches that must be different from those used for organic contaminants (particularly for xenobiotics) and must account for its natural occurrence and for the natural background levels that may be extremely different in different geographic areas with different geochemical characteristics.

In its opinions on several Risk Assessment Reports (RARs) on metals, the SCHER highlighted these particularities and developed a series of recommendations (see for example, SCHER, 2009).

The peculiarity of metals is also described in the Technical Guidance for Deriving Environmental Quality Standards in the Common Implementation Strategy for the Water Framework Directive (EC, 2018).

The dossier on "Silver and its compounds" considers in an appropriate manner these peculiarities and, in general, it is correctly developed. However, several issues (formal and substantial) need to be revised.

The title of the dossier is "Silver and its compounds". However, in most parts of the dossier, the focus is only on ionic silver, without any mention of the most common compounds that may be present in the environment (see for example the comments on section 5.2). It must also be considered that silver is the basis for important nanomaterials. Should Ag-based nanomaterials be considered as silver compounds or should nanomaterials, of any origin, be considered as particular compounds to be assessed separately? The health and environmental effects of nanosilver, including the role in antimicrobial resistance, were evaluated in two SCENIHR (2014) and SCCS (2018) opinions. It is the opinion of the SCHEER that this is a relevant issue that should be at least mentioned in the dossier.

Moreover, the dossier is incomplete in some parts (e.g., section 6.2.2 on monitoring data collection). It is the opinion of the SCHEER that it is important to provide monitoring data (from EU countries) on silver and its compounds to fill this gap. In particular, data from relatively pristine areas (at least in relation with Ag pollution) would provide information on the natural background concentrations that may be relevant to evaluate the reliability of the calculated EQSs.

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

Section 3 Proposed Quality Standards (QS)

There are no values provided in the tables in section 3 (sub-sections 3.1 and 3.2). We recommend that the proposed EQSs be summarised in this section.

Section 4 Uses and quantities

Minor comment on Line 5: the word "tons" is missing (at ≥ 10 000 to < 100 000 tons per annum).

Section 5 Water solubility

Metallic, elemental silver is practically insoluble, as indicated in the dossier. However, the dossier refers to "Silver and its compounds". In other EQS dossiers for metals (see for example the dossier on Lead and its compounds, EC, 2005), the solubility of some of the

most relevant compounds (inorganic salts and some organic compounds) is reported. It would be relevant for Ag too, also including nanosilver compounds.

Section 6 Measured concentrations from EU monitoring data collection

The section is currently in progress. The information (particularly if data on pristine areas will be available) may be relevant for hypotheses on background values.

Section 7 Acute and chronic aquatic ecotoxicity

The dependence of silver toxicity on environmental parameters (DOC, hardness, etc.) is discussed. However, no mention is made on pH, which is a fundamental parameter affecting the solubility and bioavailability of most metals. If there is some evidence of a negligible role of pH on silver toxicity, it should be mentioned. Otherwise, pH must be considered as a factor affecting toxicity.

The effect of chloride is mentioned, but with contradictory statements in different lines of the same paragraph (third paragraph of the section):

"*in fact toxicity of silver was higher at increased chloride levels (Dethloff et al., 2007).* "

And a few lines below:

"*In marine waters silver exists predominantly in less bioavailable chloride complexes, resulting in reduced toxicity with increasing salinity in at least some fish species (Wood et al., 2010).*"

It is possible that chorine plays a different role in freshwater (Cl concentration in the range of a few mg/L) and in marine water (Cl concentration around 35-39 g/L). However, the role of chlorine must be further clarified.

Although a biotic ligand model (BLM) for Ag exists, it has not been considered because it is developed only for acute toxicity. It is the opinion of the SCHEER that the existing BLM (probably also including pH effects) should be considered, at least to evaluate the reliability of acute data.

Section 7.1.1. Data consideration and evaluation of reliability

The available studies on silver acute and chronic toxicity on freshwater organisms have been evaluated for their reliability using the Klimisch and CRED approach. It is the opinion of the SCHEER that the selection of reliable studies is appropriate.

Section 7.2.1. Deterministic derivation of MAC-QS$_{fw\ eco}$

It is the opinion of the SCHEER that the acute toxicity data are properly selected and the application of an AF of 10 is appropriate, considering that the hypothesis of a similar mode of action is acceptable. Therefore, the proposed MAC-QS $_{fw\ eco}$ of 0.022 $\mu g.L^{-1}$ is endorsed by the SCHEER.

However, a sentence in this section is unclear:

"*In addition, reliable effect values for cyanobacteria was available, which is believed to belong to the most sensitive species (European Communities, 2018).* "

Indeed, a reliable value for cyanobacteria is reported in the complete table of ecotoxicity data. However, it is not clear why it is believed to belong to the most sensitive species.

For the probabilistic derivation of a MAC-QS $_{fw\ eco}$ the dataset is incomplete.

Section 7.3.1. Deterministic Derivation of AA-QS$_{fw\ eco}$

It is the opinion of the SCHEER that the chronic toxicity data are properly selected and the application of an AF of 10 is appropriate, considering that reliable chronic data are available for three species representing three trophic levels. Therefore, the proposed AA-QS $_{fw\ eco}$ of 0.01 $\mu g.L^{-1}$ is endorsed by the SCHEER.

The dossier explicitly asks the SCHEER Committee to advise on the reliability of the three sub-lethal toxicity studies performed on *Hyalella azteca*, *Corbicula fluminea*, and *Isonychia bicolor* (Diamond et al., 1990), and therefore on their suitability for QS derivation. It is the opinion of the SCHEER that the three studies may be considered reliable (although with minor restrictions). Therefore, they may be used for QS derivation.

Section 7.3.2. Probabilistic Derivation of AA-QS$_{fw\ eco}$

The probabilistic evaluation is based on an SSD curve derived with 12 species representing 10 taxonomic groups. Moreover, another SSD curve is derived using three additional species (*Hyalella azteca*, *Corbicula fluminea*, and *Isonychia bicolor,* taken from the article by Diamond et al., 1990).

Considering the characteristics of both SSD curves, the dossier proposes that an AF lower than 5 is not justified. The SCHEER agrees with this proposal.

Therefore, the following probabilistic AA-QS$_{fw}$ are proposed:

- SSD curve on 12 species: **AA-QS$_{fw}$ = 0.012 $\mu g.L^{-1}$**
- SSD curve on 15 species: **AA-QS$_{fw}$ = 0.016 $\mu g.L^{-1}$**

The two values are similar, and both are consistent with the deterministic AA-QS$_{fw}$ **.**

A rounded value of **AA-QS $_{fw\ eco}$ = 0.01 $\mu g.L^{-1}$** obtained combining the deterministic one and the two probabilistic values, is endorsed by the SCHEER.

Although a freshwater microcosm study was selected, it was considered as not reliable for the derivation of an AA-QS$_{fw}$. No reliable mesocosms or field studies are available.

Sections 7.4 and 7.5. Acute and chronic marine ecotoxicity

As indicated by the Technical Guidance for Deriving Environmental Quality Standards, freshwater and saltwater data cannot be pooled for metals. This is particularly important for silver because toxicity is strongly influenced by salinity. Therefore, the reliable data available for the derivation of EQS are relatively scarce.

For the deterministic derivation of a MAC-QS$_{sw\ eco}$, as well as for the probabilistic derivation of a MAC-QS$_{sw\ eco}$, and a AA-QS$_{sw\ eco}$, no sufficient data are available.

For the Deterministic Derivation of AA-QS$_{sw\ eco,}$ in table 7.9, reliable data are reported for crustaceans, fish and echinoderms for the salinity of 30‰, while only crustaceans and fish are reported for the salinity of 10‰. For both salinities, an AF of 50 is applied.

In the Technical Guidance for Deriving Environmental Quality Standards, the AFs for the marine environment are more conservative (usually by a factor of 10) in comparison to those used for freshwater. The rationale for that is not a higher sensitivity of marine organisms in comparison to freshwater organisms, which is not supported by any scientific evidence. It derives from the higher biodiversity existing in the marine environment. Indeed, the number of taxonomic groups in the marine environment is much higher, many of them with high ecological relevance (e.g., sponges, coelenterates, echinoderms, etc.). This is an additional factor of uncertainty for the deterministic derivation of EQSs.

It is the opinion of the SCHEER that, according to table 4 of the Technical Guidance for Deriving Environmental Quality Standards, an AF of 50 is appropriate only for the salinity of 30‰ (two long-term results from saltwater species representing two trophic levels (algae and/or crustaceans and/or fish), plus one long-term result from an additional marine taxonomic group (e.g., echinoderms, molluscs)).

It is the opinion of the SCHEER that the AA-$QS_{sw\ eco}$ **=0.17 µg.L^{-1}** for the salinity of 30‰ is properly derived.

For the salinity of 10‰, long-term results from species representing only two trophic levels are available. According to table 4 of the Technical Guidance, an AF of 500 should be applied. This AF may be lowered to 100 or 50 if some conditions (described in note C of table 4) are fulfilled. However, it is the opinion of the SCHEER that these conditions are not fulfilled. Therefore, it is the opinion of the SCHEER that the AA-$QS_{sw\ eco}$ for the salinity of 10‰ is not properly derived and cannot be endorsed.

In the last paragraph of section 7.5.1, a different procedure followed by RIVM for the derivation of AA-$QS_{sw\ eco}$ is described. However, the values proposed by RIVM for the AA-$QS_{sw\ eco}$ are not reported.

The results of two studies on marine mesocosms are described (section 7.5.2) but not used for the derivation of EQS. It is the opinion of the SCHEER that these studies do not provide ecologically relevant information and it agrees that they should not be used for the derivation of EQS.

Section 7.6. Sediment ecotoxicity

An AA-$QS_{freshwater,\ sed}$ was derived using the equilibrium partitioning method while it was impossible to derive an AA-$QS_{marine\ water,\ sed}$ due to the lack of a marine K_{dsed}. It is the opinion of the SCHEER that the **AA-$QS_{freshwater,\ sed}$ =4.78 µg.kg$^{-1}_{dw}$** is properly calculated.

Section 7.7. Summary of derived QS to protect water quality

In conclusion, the SCHEER endorses all the QS values reported in the summary table of section 7.7, with the only exception of the AA-$QS_{marine\ water,\ eco}$ for the salinity of 10‰.

Section 7.8. Identification of issues relating to uncertainty in relation to the QSs derived

It is the opinion of the SCHEER that the listed reasons for uncertainty are reasonable. However, there are no reasons for modifying the EQS.

Section 7.9. Secondary poisoning

From the available information, the conclusion of the dossier is that silver may be bioaccumulated, but the process is species-specific, controlled by physiological processes and not by physical partitioning (e.g., BCF). It is the opinion of the SCHEER that this hypothesis is reasonable, and that the procedure adopted to derive a tentative **QS_{biota}** is correct. However, the NOAEL value used to derive the **QS_{biota}** (0.4 mg/kg bw/day) refers to silver acetate. If transformed into ionic silver, the value is 0.26 mg/kg bw/day. Therefore, the tentative **QS_{biota}** must be modified.

Section 7.10. Human health

SCHEER considers that in order to optimally compare silver exposure concentrations used in the different studies, the no observed adverse effect levels in mg silver containing compounds (SCC)/kg bw/d should be converted into estimated doses of silver ion

equivalents based on silver content and release ($NOAEL_{SCC}$ x silver content (%) x silver ion release (%)). However, data on silver ion release is seldom available.

Therefore, SCHEER agrees with the selection of the lowest NOAEL value of 0.4 mg silver acetate/kg bw/day (0.26 mg ionic silver/kg bw/day), from FDA, 2012, to derive the $QS_{biota,hh}$.. However, a correction needs to be made in the TL_{hh} calculation: it should be 0.26 mg ionic silver/kg bw/day, giving a tentative $QS_{biota,hh}$ value of 0.32 mg/kg bw/day, (instead of 0.49 mg/kg bw/day).

As to the provisional CLH proposal of Repr. 1B; H361d for silver (CAS Nº 7440-20) based on fertility and sexual function, it would be beneficial to have access to the latest information on the CLH process and also to make reference to other silver compounds, as it may be relevant for the assessment of the human health effects (and environmental effects) based on a WoE approach.

SCHEER also agrees that the $QS_{biota,\ sec\ pois,fw,}$ being more conservative, could be used to establish the EQS_{biota} instead of the $QS_{biota,hh}$. However, the derivation of the $QS_{water,\ biota}$ for silver of 0.012 µg/L is associated with uncertainties related to using BCF and BAF to assess silver bioaccumulation through the food chain.

Most of the silver is not truly dissolved but remains in the form of complexes and/or colloids due to the presence of complexing ions and organic matter in the test system. It is therefore difficult to know the exact concentration of silver ions in the test solutions. On the other hand, through ingestion, metals bound to ingested colloids or particles that would not be available in the water phase can become available to metabolic processes of the organism.

Section 8 Contribution of Silver to the antimicrobial resistance

We appreciate the notion that AMR is dealt with in the dossier. However, this assessment is not used for the derivation of EQS. (Recommendation: A section on how to deal with AMR should be included in the Technical Guidelines.)

SCHEER supports the assessment presented in the document and considers that there is a theoretical risk of bacteria acquiring overall resistance against silver by several modes of action which may be acting simultaneously in the affected organism (interactions with nucleic acids (*Jung et al., 2008)*, generation of reactive oxygen species in the cell *(Matsumura et al., 2003)*, proton leakage through the membrane *(Dibrov et al., 2002)*, binding to key functional groups of fungal enzymes *(Russell, 2003)*. It is assumed that the mechanism depends on the concentration of the silver ions present, the sensitivity of the microbial species to silver and the environment in which the two interact; however, modes of action have been mostly studied separately with different bacterial species. There is concern about the development and spreading of plasmid- or genome-encoded co-resistance - to silver and antibiotics.

Possible occurrence of silver-resistant bacteria in the wider environment (i.e., outside industrial facilities, hospitals, dental care units or laboratories) cannot be excluded and horizontal transfer of genes is possible.

SCENIHR[2] points out in its Opinion that ubiquitous low levels of a biocide may maintain selective pressure: *……" Any application that encompasses the widespread regular use of biocides at sub-lethal concentrations maintains a continuous selective pressure and thus increases the risk of selecting resistant bacteria. This may occur in a number of uses including hospitals, food production and cosmetics manufacturing etc. Their level of*

[2] SCENIHR Effects of the Active Substances in Biocidal Products on Antibiotic Resistance Version of 4 November 2008

resistance can increase through selection, for example by repeated exposure to a low concentration of a biocide or to increasing concentrations of a biocide".

The wide-spread use of silver in sub-MIC concentrations might create a pool of co- and/or cross-resistant bacterial strains in humans and in the environment. However, information is lacking about how wide-spread silver resistance occurs in humans and in the environment. Antibiotic resistance is one of the main threats to human health today and, learning from past experience, it is necessary to carefully consider the risk of co- and cross-resistance of silver used as a disinfectant.

4. LIST OF ABBREVIATIONS

AA-QS	Annual Average Quality Standard
AF	Application Factor
AMR	Anti-Microbial Resistance
BCF	Bioconcentration Factor
CLH	Classification and Labelling Harmonised
CRED	Criteria for Reporting and Evaluating Ecotoxicity Data
EQS	Environmental Quality Standards
FDA	Food and Drug Administration
MAC-QS	Maximum Acceptable Concentration Quality Standard
RARs	Risk Assessment Reports
SCC	Silver Containing Compounds
SSD	Species Sensitivity Distribution

5. REFERENCES

Chiffoleau JF, Auger D, Roux N, Rozuel E, Santini A (2005). Distribution of silver in mussels and oysters along the French coasts: data from the national monitoring program. Mar Pollut Bull. 50(12), 1719-1723.

Dethloff GM, Naddy RB, Gorsuch JW (2007). Effects of sodium chloride on chronic silver toxicity to early life stages of rainbow trout. Environ Toxicol Chem. 26(8), 1717-1725.

Diamond JM, Mackler DG, Collins M, Gruber D (1990). Derivation of a freshwater silver criteria for the New River, Virginia, using representative species. Environ Toxicol Chem., 9(11), 1425-1434.

Dibrov P, Dzioba J, Gosink KK, Häse CC (2002). Chemiosmotic mechanism of antimicrobial activity of Ag(+) in Vibrio cholerae. Antimicrob Agents Chemother 46(8), 2668-70.

EC (European Commission), 2005. Common Implementation Strategy for the Water Framework Directive Environmental Quality Standards (EQS) Substance Data Sheet Priority Substance No. 20 Lead and its Compounds.

EC (European Commission), 2018. Technical Guidance for Deriving Environmental Quality Standards. Common Implementation Strategy for the Water Framework Directive. Guidance Document No. 27 Updated version 2018.

Jung J, Ahn Y-J, Kang L-W (2008). A novel approach to investigating protein/protein interactions and their functions by TAP-tagged yeast strains and its application to examine yeast transcription machinery. J Microbiol Biotechnol 18(4), 631-638.

Matsumura Y, Yoshikata K, Kunisaki S, Tsuchido T (2003). Mode of Bactericidal Action of Silver Zeolite and Its Comparison with that of Silver Nitrate. Applied and Environmental Microbiology, 69(7), 4278–4281.

Metian M, Bustamante P, Cosson RP, Hédouin L, Warnau M (2008). Investigation of Ag in the king scallop *Pecten maximus* using field and laboratory approaches. Journal of Experimental Marine Biology and Ecology, 367(1), 53-60.

Russell AD, Hugo WB (2003). Antimicrobial Activity and Action of Silver. Progress in Medicinal Chemistry – Vol 31, edited by G.P Ellis and D.K. Luscombe. Elsevier Press, p 351-370.

SCCS (Scientific Committee on Consumer Safety), 2018. Opinion on Colloidal Silver, adopted 24-25 October 2018, SCCS/1596/2018.

SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks), 2008. Assessment of the Antibiotic Resistance Effects of Biocides, adopted 19 January 2009 after public consultation.

SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks), 2014. Nanosilver: safety, health and environmental effects and role in antimicrobial resistance, adopted 10 -11 June 2014.

SCHER (Scientific Committee on Health and Environmental Risks), 2009. Scientific opinion on the voluntary risk assessment report on copper and its compounds, environmental part. Adopted 12 February 2009. European Commission, Health & Consumer Protection DG Directorate, Brussels.

Wood CM, Grosell M, McDonald DM, Playle RC, Walsh PJ (2010). Effects of waterborne silver in a marine teleost, the gulf toadfish (*Opsanus beta*): Effects of feeding and chronic exposure on bioaccumulation and physiological responses. Aquatic Toxicology 99, 138–148.