

Committee for Risk Assessment
RAC

Annex 3
Records

of the targeted consultation following the submission of a preliminary summary of an in-vivo comparative Toxicokinetic Study on four Silver (Ag) forms

Silver

EC Number: 231-131-3
CAS Number: 7440-22-4

CLH-O-0000007152-82-01/F

Adopted
2 June 2022

ANNEX 3 – RECORDS OF THE TARGETED CONSULTATION FOLLOWING THE SUBMISSION OF A PRELIMINARY SUMMARY OF AN IN-VIVO COMPARATIVE TOXICOKINETIC STUDY ON FOUR SILVER (AG) FORMS

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

The proposal for the harmonised classification and labelling (CLH) of silver (EC 231-131-3; CAS 7440-22-4) was submitted by the Sweden and was subject to a consultation, from 19/10/2020 to 18/12/2020. The comments received by that date are compiled in Annex 2 to the opinion.

The European Precious Metals Federation (EPMF) has provided a preliminary summary of a new, partly still ongoing in-vivo comparative Toxicokinetic Study on four Silver (Ag) forms; silver acetate (AgAc), and silver nitrate (AgNO₃), one Agsilver nanoparticles (AgNP) and a sub-micron size powder-form (AgMP) of bulk elemental silver. An ad hoc consultation was launched from 06/07/2021 to 20/07/2021 and the comments received are listed below.

Comments provided during consultation are made available in the table below as submitted through the web form. Any attachments received are referred to in this table and listed underneath, or have been copied directly into the table.

All comments and attachments including confidential information received during the consultation have been provided in full to the dossier submitter (Member State Competent Authority), the Committees and to the European Commission. Non-confidential attachments that have not been copied into the table directly are published after the consultation and are also published together with the opinion (after adoption) on ECHA’s website. Dossier submitters who are manufacturers, importers or downstream users, will only receive the comments and non-confidential attachments, and not the confidential information received from other parties. Journal articles are not confidential; however they are not published on the website due to Intellectual Property Rights.

ECHA accepts no responsibility or liability for the content of this table.

Substance name: silver
EC number: 231-131-3
CAS number: 7440-22-4
Dossier submitter: Sweden

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
20.07.2021	Poland	Nano-tech Polska	Company-Manufacturer	1
Comment received				
<p>We consult report European Precious Metal Federation with our friend - <confidential>, Ph. D hab. of microbiology. In attachment 1 you will find her opinion, and in attachment 2 all report. On page 4 and 7 you will find important conclusion (market yellow). Please give us opinion about it.</p> <p>I would like to show you Proposal for Harmonised Classification and Labelling (attachment_3)this report should give information about Silver, but most information is about silver compound, which are completely different substances than silver, usually silver compounds are dissolve in water and silver is not, what as you know is the most important properties of each xenobiotics in toxicology.</p> <p>If you will read please concentrate on information about possible classification. On page 58 you will read that silver - pure silver is not irritant, page 59 (10.5.3) the same. page 63 - no skin sens effect.</p> <p>Nano silver not give geno effect too.</p>				

ANNEX 3 – RECORDS OF THE TARGETED CONSULTATION FOLLOWING THE SUBMISSION OF A PRELIMINARY SUMMARY OF AN IN-VIVO COMPARATIVE TOXICOKINETIC STUDY ON FOUR SILVER (AG) FORMS

ECHA note – An attachment was submitted with the comment above. Refer to public attachment attachment_with comments.zip
RAC's response
Thank you, noted.

TOXICITY TO REPRODUCTION

Date	Country	Organisation	Type of Organisation	Comment number
20.07.2021	Poland	Nano-tech Polska	Company-Manufacturer	2
Comment received				
<p>Classification is not about pur silver or nano silver, but about silver compoud or silver coat. Very important for assessment of xenobiotic is its possibility to dissolve in water. Silver is not soluble in water and is not ion. this substances can't be compared.</p> <p>ECHA note – An attachment was submitted with the comment above. Refer to public attachment attachment_with comments.zip</p>				
RAC's response				
<p>Thank you for the comment. Classification is for the substance that is identified in the CLH proposal and proposed CLP Annex VI entry. Impurities, additives and minor components are normally not mentioned in Annex VI unless they contribute significantly to the classification of the substance. The test substance may be different to the substance for which an Annex VI entry is proposed (e.g. when read-across is applied) and the test substance need not be a pure substance for a classification for the substance to be included in Annex VI to CLP. Toxicokinetics and bioavailability of test substances and silver is taken into consideration by RAC and the applicability of data from other silver compounds is assessed in the RAC opinion.</p> <p>It is noted that mutagenicity and reproductive toxicity are separate hazard classes and each have their specific classification criteria in CLP Regulation. However, the known induction of genetically based inheritable effects in the offspring is addressed in Germ Cell Mutagenicity (Section 3.5), since in the present classification system it is considered more appropriate to address such effects under the separate hazard class of germ cell mutagenicity.</p>				

Date	Country	Organisation	Type of Organisation	Comment number
08.07.2021	Sweden		MemberState	3
Comment received				
<p>As discussed in several sections of the CLH report the different silver containing active substances and forms of silver are expected to differ in the release of silver ions depending on chemical composition, physical properties and exposure conditions etc. The results from the TK study with silver in massive form, different salts and the nanofom thus confirms what was assumed and considered in the CLH report although the new data now available provides quantitative information to more accurately establish bioavailability.</p> <p>However, bioavailability shall, as stated in Art. 12 of CLP only be considered for classification purposes when conclusive scientific experimental data show that the substance is not biologically available and those data have been ascertained to be adequate and reliable. The new TK study shows that silver is bioavailable from all forms to some extent and distributes to the tissues examined.</p> <p>It is noted that the amounts (ng/g tissue) found in gonads (ovary, uterus, testis) is higher</p>				

ANNEX 3 – RECORDS OF THE TARGETED CONSULTATION FOLLOWING THE SUBMISSION OF A PRELIMINARY SUMMARY OF AN IN-VIVO COMPARATIVE TOXICOKINETIC STUDY ON FOUR SILVER (AG) FORMS

than in bone marrow for almost all forms. This should be considered in the assessment of the genotoxic potential of silver and any non-threshold effects.

Overall, the results from the study are in line with the considerations in the CLH report regarding differences in release of silver ions from different silver containing active substances and the assumption that only 5% of the silver ions released could be absorbed in the gastrointestinal tract.

Nevertheless, in the absence of accompanying substance-specific toxicological data for each endpoint and each form of silver releasing silver ions, we consider that silver should be classified in accordance with its intrinsic properties (hazard) and not on the basis of considerations of risk.

RAC's response

Thank you, please see the assessment of the bioavailability and toxicokinetics of silver and silver compounds in the RAC opinion.

PUBLIC ATTACHMENTS

1. attachment_with comments.zip [Please refer to comment No. 1, 2]