



EPMF, Eurometaux, European Commission meeting on silver classification

Draft minutes

13th March 2019, D1

Participants: Katrien Arijs (EPMF), Peter Baricic (DG GROW), Sylvain Bintein (DG ENV), France Capon (EPMF), Ludovic Chatelin (DG Santé), Andrej Kobe (DG ENV), Katrin Schutte (DG ENV), Violaine Verougstraete (Eurometaux).

The Commission welcomed the participants. France Capon thanked the Commission for their availability to discuss the industry concerns on ongoing processes in the REACH/CLP and BPR areas and the overlap between a classification proposal submitted by Sweden and a testing proposal evaluated under REACH.

A set of slides (attached as Annex 1) was distributed. Katrien Arijs started by explaining the outline of the slides, starting with a very short introduction of EPMF up to summary of the EPMF's position.

She explained that EPMF (website: www.epmf.be) is an association, coordinating the actions of a number of members on REACH, CLP, EHS, Sustainability, Trade and Tax aspects. They cover a series of metals (metals and their compounds) displayed on slides 4 and 5, used in a variety of sectors. All the substances have been registered under REACH (about 100) as above the registration tonnage band.

With regard to silver and its compounds, it is important to note that EPMF has registered 8 substances including silver, silver nitrate and silver chloride. But under the BPR, it is the silver taskforce (ESTF) that has submitted and is following the single core active substance dossier that is supporting 10 substances (silver containing active substances or SCAS), also including silver, silver nitrate and silver chloride.

	Ag REACH	Ag BPR
Scope	EPMF Ag project includes 8 substances/Dossiers: 1. Silver (incl. nano) 2. Disilver oxide 3. Silver nitrate 4. Disilver sulphate 5. Disilver carbonate 6. Silver chloride 7. Silver bromide 8. Silver iodide	ESTF single core active substance dossier supporting 10 substances ('SCAS'): 1. Silver 2. Silver (reaction mass with SiO ₂) (nano) 3. Silver chloride 4. Silver chloride (reaction mass with TiO ₂) 5. Silver nitrate * 6. Silver sodium hydrogen zirconium phosphate * 7. Silver phosphate glass 8. Silver zeolite * 9. Silver zinc zeolite * 10. Silver copper zeolite *
Under review by	ECHA (Dossier Evaluation)	Keml, Swedish CA
CLH	Not a requirement	Requirement (* = CLH proposal submitted; * = CLH opinion adopted)



As there was a question on the relationship between the two industry groups, it was explained that the two groups -that are completely separate entities- have regular meetings and try to align as much as possible. There are some divergent datasets. It should also be acknowledged that the ESTF is a group of different producers who may be competitors. The group is coordinated by Fieldfisher, who provides more legal support than scientific one. They were informed but not invited by EPMF to join the meeting of today, as EPMF followed ECHA's advice to first meet bilaterally. The ESTF will be informed on the outcomes.

ECHA is reviewing some of the silver dossiers (Evaluation for an EOGRTS testing proposal on silver acetate in the silver metal dossier). A number of CLH processes have taken place or are ongoing: more specifically, Kemi (Sweden) has submitted CLH proposals on silver, silver sodium hydrogen zirconium phosphate, silver zeolite and silver copper zeolite (for which the public consultation is still awaited). A CLH opinion was already adopted on silver zinc zeolite.

Because of the common elements between the two groups but also because of the use of read-across, regulatory decisions have shared relevance for both groups, i.e. EPMF and ESTF.

What is the background for the Extended One Generation Reproductive Toxicity Study?

EPMF identified a data gap on reprotoxicity and submitted in 2015 a Testing Proposal (TP) for an EOGRTS (OECD TG 443). They proposed to use silver acetate as test substance and that the outcome of the study would be applicable to all silver compounds, as effects are assumed to be associated with the silver ion. In 2016-2017 further research was published on reproductive toxicity potential of ionic silver. EPMF examined this new data but concluded that there were still several weaknesses and that the data gap still remains. They did an update of the TP design in 2018 to e.g. include the DIT cohort and fully reflect the latest scientific information available

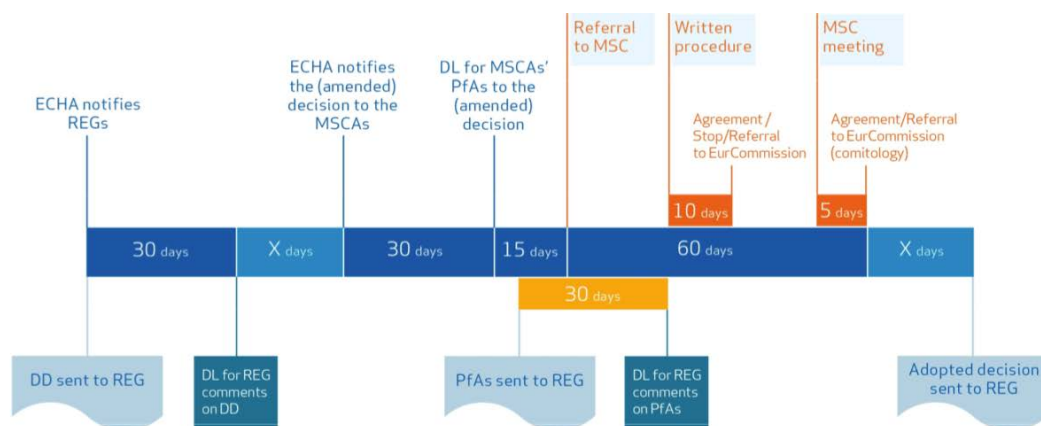
It was questioned why silver acetate is proposed whilst silver nitrate is the most (water) soluble substance. There are two main reasons: silver nitrate is actually corrosive and silver acetate is the most bioavailable. Currently, there is no registration dossier for silver acetate as it did not exceed the 1 ton but the volume could increase soon due to a change in the market, so this starts to be under discussion.

It was asked whether the aim is to read-across to all other silver compounds. This is indeed the aim; EPMF was keen to generate more information on the ion. ECHA stated in the draft decision that the read-across as described in the TP is considered plausible for the purpose of the TP evaluation seems acceptable to them (to be confirmed with outcomes of the testing).

It was also clarified that it is industry who proposed to include the DIT cohort, but not the DNT.

ECHA's draft decision on the TP was received in December. So far, ECHA accepted the test design/test substance but the TP is now going through the next steps of the process (see timeline below). There is no certainty whether the amended decision was notified already to the MSCAs.

But even in this case, test results can be only be made available the earliest by mid-2021.



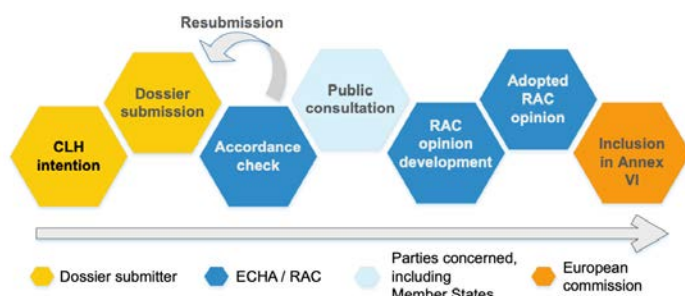
NB: A decision can be adopted directly if no PfAs are received.

More details were asked about the timing and the lag time between 2015 and 2017. France Capon explained that the TP has been “pending” in ECHA for some time and picked up again as a priority when the question was raised in the context of the Metals and Inorganics Sectorial Approach (MISA). ECHA explained that it is a complex dossier as they need to look at parallel information from the biocides to prepare the draft decision. The teams in ECHA involved in CLH and TP have been discussing together the case. Industry had also a meeting with ECHA (CLH unit, MISA coordinator early February).

More details were provided on the CLH processes, in slide 9:

- 2015: CLH silver zinc zeolite (SZZ): a Repro cat. 1B was proposed by Kemi but a cat 2 was agreed by RAC also because the effects observed in the study are partly due to other moieties than Ag (Zn, zeolites)
- 2017: CLH proposals were submitted by Kemi for:
 - Silver zeolite (SZ) and silver copper zeolite (SCZ): Repro cat. 2 proposed, read-across from the silver zinc zeolite
 - Silver sodium hydrogen zirconium phosphate (SSZHP): no Repro classification proposed, based on substance-specific data and less bioavailability of the Ag ion
 - Public consultation not yet started
- Dec 2018: a CLH proposal was submitted for silver nitrate, proposing a Repro cat. 1B. This proposal is still in the accordance check phase.
- The ESTF reported that Kemi had mentioned that they would submit proposals for elemental silver and silver chloride in a short future (Repro cat. 1B?)

In line with the scheme presented below, the RAC opinion for silver nitrate may be available before the outcome of the EOGRTS.



Commission confirmed that following the CLH timing, we may strive to the inclusion of silver in an ATP in 2022, meaning that the test results should become available before this.

Katrien Arijs concluded by presenting the EPMF position:

- There are data gaps regarding the reproductive toxicity of Ag^+ and the current data is insufficient to classify AgNO_3 / Ag^+ as Repro 1B
- Further significant data is expected from REACH studies (TP). The EOGRTS would provide superior end result to hazard assessment and will ensure regulatory efficiency
- A conference call with Kemi is scheduled on 21 March to discuss the proposal and the process. The request for a meeting (transformed into a call) was sent to both the BPR and CLP experts in Kemi but the CLP experts were not in (visible) copy of Kemi's reply.

It was commented that the C&L inventory contains a repro cat 2 entry for silver nitrate. **Do we know the basis for this entry?**

General Section						
EC / List no.	Name	CAS Number	Additional Notified Information			
231-853-9	Silver nitrate	7761-88-8				

Classification		Labelling		Specific Concentration limits, M-Factors	Notes	Classification affected by Impurities / Additives
Hazard Class and Category Code(s)	Hazard Statement Code(s)	Hazard Statement Code(s)	Supplementary Hazard Statement Code(s)			
		H272				
		H314				
Repr. 2	H361					
Aquatic Acute 1	H400	H400				
		H410				

DG Santé commented that they have not seen the Swedish dossier. There is however a common agreement in the BPR field to first have the RAC opinion before proceeding to the BPC. The calendar of the BPR is actually missing in the slides. DG Santé confirmed that Sweden waits for the RAC opinion to be able to go to BPC and is doing its job properly and correct when they say they are under pressure of Commission. He commented that arguments, like testing data to come, can be raised during the Public Consultation on the CLH proposal so that RAC considers the data.

It was clarified that RAC needs to formulate an opinion on the data that is available. In this context, test data can be considered only if made available during the 18 months RAC has from the start of the Public Consultation onwards (and announced during the Consultation). It was asked what would happen in the BPC if the test results confirm/infirm the classification proposed by RAC. DG Santé indicated that in this case, Sweden would have to revise its dossier.



It was asked which arguments were used by RAC to classify silver zinc zeolite as cat 2 rather than cat 1B and whether those can be raised again for silver nitrate. Some of the elements can be used but there was some additional complexity due to zinc and zeolite.

It was asked whether industry has insights on the reasons/arguments Kemi is basing its repro 1B on.

It was asked to industry to clarify what would be the added value of the EOGRTS vs. existing data used by Kemi. Industry explained that they have screened the available evidence (there are several studies available for silver acetate, nanosilver, etc.) and some studies suggest pre- and post-natal developmental effects. But most of these studies are presenting deficiencies (non-GLP, use of single dose levels, individual animal data not reported, presence of maternal toxicity, relevance to ionic silver unclear...) and typically do not assess all parameters of relevance (compared to the EOGRTS). The EOGRTS would address the missing parameters for ionic silver and look at longer exposure period.

Sweden proposes a classification for both developmental effects and fertility but what is the evidence for fertility? Industry explained that available evidence for anti-fertility effects is weak: several studies with nanos and SCAS showed no clear effects on fertility. There is one study with silver acetate claiming effects but it is unclear whether the observed antifertility effect is due to effects on parent animals and detailed investigations comparable to those in an EOGRTS were not conducted. **Will the EOGRTS provide some information on fertility?** Commission stressed that the TP does not include an extension to F2. This is actually supported by ECHA (as reported in the draft decision) as the 10 weeks pre-mating exposure/observation should cover fertility and the EOGRTS should thus allow a more comprehensive and robust assessment of fertility endpoints than the current available studies.

DG ENV indicated that a possible option would be to inform RAC that there is an ongoing EOGRTS and take this in their opinion. RAC cannot delay its opinion as the 18 months period starts with the Public Consultation but could include in their conclusions an opinion whether the classification may be changed or not by the EOGRTS outcome. This could be triggered by a specific question from Commission but feasibility of this needs to be checked with ECHA and RAC.

DG ENV mentioned that MSC could also decide that the test is not needed, considering the ongoing classification proposal. Industry agreed but stressed the 'chicken and egg' timing issue. The TP has now been 'hanging' for 4 years, with as result that Sweden is now pushing for a classification. Can DG Santé not alleviate the pressure on Sweden to wait for the (better) outcomes. DG Santé replied that they cannot delay further the process. The substance is on the market and included in their review programme. The dossier is pending since 2007 and the process foresees that first RAC's scientific opinion should be gathered before the dossier is processed under BPC. Sweden has not yet resubmitted their Annex XV dossier but DG Santé knows they are working on it. He mentioned that from his perspective there is an issue of efficiency between the BPR and CLP. The Annex XV formatting requested by CLP is very demanding as not aligned with the BPR templates.

DG ENV explained that they do not want to create a precedent by postponing a process due to the need to generate new data. RAC is the best way forward as this is the committee in charge of classifications. It will not help to have MSC involved in this overlap discussion as MSC does not feel empowered to consider the different processes. They may question whether the test really is needed considering animal welfare. They may also add some requirements (e.g. a DNT) making the timing aspects even more challenging. Therefore, pushing for the TP before a discussion at RAC level is not the recommended option.



Having a question posed by Commission would provide RAC with a hint that there will be new data, but this requires to have a clear view on the added value of the EOGRTS (how much weight can it have in a weight-of-evidence approach used in RAC for the reprotox classification?) and check with RAC/ECHA if this is feasible. **It was agreed that industry would prepare a table comparing the data available to Kemi and supporting their cat 1 B and the information that would be added by the EOGRTS.**

DG ENV came back to the cooperation within industry. The ESTF should be keen to support a delay in the process as the 1B will have significant consequences (exclusion). It is indeed what is expected but so far no significant scientific input has been provided by ESTF which is relying on EPMF for the scientific argumentation.

It was asked whether it could create a legal issue that the test is carried out on another substance (silver acetate). DG SANTE confirmed that this is not an issue, as read-across is used as well in BPR.

Commission kindly proposed to check whether the amended draft decision was already distributed to the MSC members (*post-meeting note: it was confirmed that the draft decision was not distributed yet but Commission kindly proposed to inform EPMF as soon as it will be*). Based on the best estimation, the discussion could come to MSC in June or October. It was stressed that if there are no comments from MS, the DD could go via a written procedure. This gives time to Sweden to submit Annex XV.

A couple of additional questions were posed, e.g. with regard to nanos. What is the impact on nanosilver? Does the ESTF also cover silver nanos? Based on the current EPMF knowledge, the nanoform covered by ESTF is a reaction mass of silver and SiO₂ but not the nanoform of elemental silver. **It was recommended to check with them what their portfolio covers** as there seems to be also nanosilver not related to a reaction mass in the records of DG Santé.

It was also asked which classification is included in the registration dossier. Industry explained that at this stage, the dossier refers to no classification but with a data gap. France Capon explained that a cat 1B would have significant impacts as 60% of uses of silver is in the consumer area. Still if the EOGRTS data points towards such a classification, they will implement it. Commission asked whether some risk management measures are communicated through the supply chain, considering the potential repro effects. Industry agreed that this could be improved. Production of silver is often linked to production of copper and nickel, meaning that there is risk management in place but further down in the supply chain there is no interaction yet on the classification. EPMF is currently considering how to communicate the classification issue further down the supply chain'.

DG Envi. explained that they will further discuss with ECHA. DG Santé mentioned that they will see ECHA (BPR) in the coming days, as well as be in contact with Kemi. They will mention to Kemi that the CLP colleagues should be involved in the conference call organized with EPMF on 21st March 2019.

DG Santé also mentioned that the EOGRTS is not part of the information requirements under the BPR but that discussions are ongoing in the context of the EDs guidance development, with comparable diverging views as seen under REACH.

Industry thanked Commission and indicated that they will send some notes of the meeting with the table illustrating the added value of the EOGRTS in the classification discussion of silver as a reprotox cat 1B.



Agreed actions:

- ***Check inventory as existing cat 2 for silver nitrate (Industry)***
- ***Check with ESTF the silver nano entries/coverage (Industry)***
- ***Prepare a table comparing the data available for Kemi's proposal and the data that would be generated by the EOGRTS (Industry)***
- ***Think about more formal communication on classification of silver/data gap/RMM in the supply chain (Industry)***