The European Precious Metals Federation (EPMF) position on the RAC opinion related to the classification of silver metal

22 March 2023

The EPMF takes note of the RAC opinion on the classification of silver metal (EINECS: 231-131-3; CAS: 7440-22-4) and the related proposal by the European Commission to include the following entries into the next ATP to the CLP:

Index No	Chemical Name (EC / CAS)	Classification		Labelling	
		Hazard class & category	Hazard statement + M-factors	Pictogram, Signal word	Hazard statement + Suppl. Hazard statement
047-004-00-9	silver massive: [particle diameter ≥1 mm] (231-131-3 / 7440-22-4)	Repr. 2 STOT RE 2	H361f H373 (nervous system)	GHS08 Wng	H361f H373 (nervous system)
047-005-00-4	silver powder: [particle diameter >100 nm <1 mm] (231-131-3 / 7440-22-4)	Repr. 2 STOT RE 2 Aquatic Acute 1 Aquatic Chronic 1	H361f H373 (nervous system) H400 (M=10) H410 (M=10)	GHS08 GHS09 Wng	H361f H373 (nervous system) H410
047-006-00-X	silver nano: [particle diameter >1 nm ≤100 nm] (231-131-3 / 7440-22-4)	Repr. 2 STOT RE 2 Aquatic Acute 1 Aquatic Chronic 1	H361f H373 (nervous system) H400 (M=1000) H410 (M=1000	GHS08 GHS09 Wng	H361f H373 (nervous system) H410

The EPMF would like to thank sincerely the RAC for having postponed its discussion and opinion to ensure inclusion of the most recent scientific data generated by EPMF in the discussions. More specifically, the *in vivo* comparative toxicokinetics study[1] and Extended One Generation Reproductive Toxicity Study[2] have been finalized in 2021 and 2022, respectively, and included in the RAC evaluation.

The EPMF appreciates that RAC acknowledges the *in vivo* toxicokinetics data in the grouping and read-across approach. Indeed, the RAC opinion includes that "*a read-across from positive studies on silver compounds to classify silver is not supported by RAC*"[3].

However, the EPMF does not support the statement "*RAC places emphasis only on the data from silver metal and its physical forms where available (mostly on silver nanoparticles, only a few data on massive silver)*"[4]. This position is in contradiction with the results of the *in vivo* toxicokinetics study performed by the EPMF. This study demonstrates that a very fine silver powder with a median diameter of 350 nm (i.e. a conservative model for silver in powder and – especially - massive forms) has a distinct profile of Ag levels in blood and Ag levels in tissues (Figure 1), when compared to silver in nanoform.

[1] Anon., *et al*., (2021) Silver Acetate, Silver Nitrate, Micron-sized Silver and Nanoparticulate Silver: A Comparative Toxicokinetic Study in Rats by Single and Repeat Administration. Labcorp Study Number: CC71MP

[2] Renaut R et al. (2022) Silver Acetate: Extended One Generation Reproductive Toxicity Study in the Sprague Dawley Rat by Dietary Administration. Labcorp Early Development Laboratories Ltd. Labcorp Study Number 8437234

[3] RAC opinion on silver metal, CLH-O-0000007152-82-01/F, p. 15.

[4] RAC opinion on silver metal, CLH-O-0000007152-82-01/F, p. 15.

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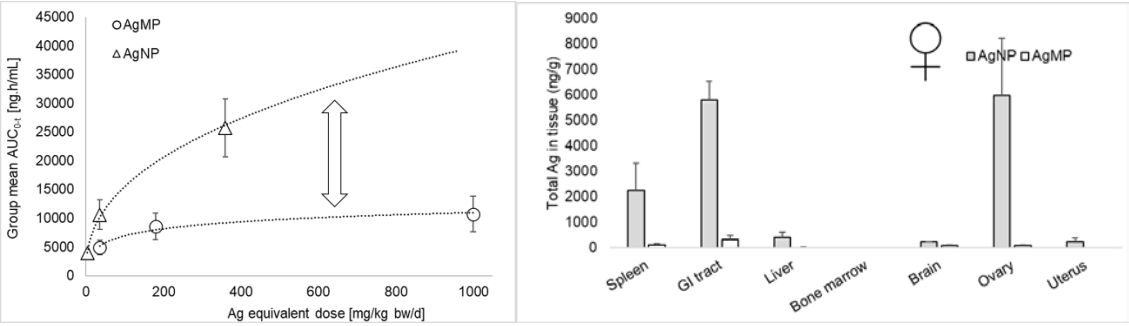

Figure 1: Bioavailability data for nanosilver (AgNP) and a conservatively fine silver powder (AgMP) following 28 days repeated dosing via oral gavage. Left: Achieved systemic exposure (‚Ag in blood') with the difference in systemic exposure illustrated by the dotted lines. Right: Ag in tissue at equivalent treatment level (36 mg Ag/kg bw/d). Similar conclusions are made for male tissues (incl. testis) and higher dosing levels.

These findings of a distinct bioavailability profile between nanosilver and silver in powder and massive forms are further strengthened by

1. the stability of serum Cu-levels (as hypothesised Mode of Action for reproductive toxicity effects) when test animals are sub-chronically exposed to a conservatively fine silver powder at limit dose (1000 mg/kg/d) and
2. studies demonstrating a negligible solubility of silver in powder (µm-size) or massive forms (mm-size and larger) in aquatic or acidic media compared to nanosilver.

Taken together, the available data do not support a grouping of silver in nanoform with silver in powder and – especially – massive forms for read-across approaches.

The proposed ATP entries allow to have different classification entries for silver metal in massive form, silver metal in powder form and nanosilver. The EPMF would like to ask the Commission and the CARACAL to:

1. re-consider the distinct bioavailability and dissolution profiles of nanosilver versus silver in massive and powder forms, and
2. not group and read-across data from nanosilver to silver in massive and powder forms (with special focus on silver in massive form).

This will lead to a scientifically justifiable non-classification of silver in massive form for mammalian and environmental endpoints, and a non-classification of silver in powder form for mammalian endpoints.

ABOUT THE EPMF

Since 2007, the European Precious Metals Federation has supported European companies working with gold, silver, rhenium, and the six metals referred to as the Platinum Group including platinum, palladium, osmium, rhodium, ruthenium, and iridium.

Our 35 Member Companies and 3 national associations include world leaders in extraction, refining, and recycling of precious metals. They also include a highly diverse range of companies involved in consumer and industrial applications that touch the lives of European citizens from jewellery to financial investments to the mobile phones in their pockets to the catalytic converters in their vehicles to the solar panels and rapid chargers at their homes.

The EPMF facilitates the interface between policy makers, regulatory authorities, and the precious metals industry on a wide range of issues.

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