LANXESS
Energizing Chemistry

LANXESS comment on the proposed harmonized classification and labelling of silver nitrate

LANXESS and its affiliate Microbial Control (Switzerland) GmbH are of the opinion that a classification of **silver nitrate for mutagenicity is not supported by conclusive data**.

We support the conclusion that the in vivo micronucleus study by Boudreau et al (2016) with silver acetate is the most relevant in vivo study to represent silver nitrate as it is both robust and performed with a soluble salt. This viewpoint aligns with the RAC opinion for silver (CLH-O-0000007152-82-01/F, Page 54) which concludes that "Boudreau et al., 2016 presents valuable information with silver acetate, showing that the release of copious amounts of silver ion does not give rise to a positive in vivo genotoxic response".

It is not appropriate to rely on data obtained from silver nanoparticles due to significant differences in kinetics and deposition between silver nanoparticles and soluble silver salts. In addition, the data on silver nanoparticles is inconsistent and of questionable reliability. This inconsistency may stem from the varying characteristics of different silver nano particles (size, shape, surface coating) which lead to different responses. This is in line with the CLH decision for silver and the RAC opinion for silver (CLH-O-0000007152-82-01/F, Page 54) which states that "while the mutagenicity database for silver is extensive for several forms and compounds of silver, the data are inconclusive overall because of contradictory findings and in many cases a lack of sufficient information for each study report. Some concerns remain with respect to the in vivo findings for both chromosomal aberrations and DNA strand breaks but the negative results generally in this case outweigh the positive ones".

LANXESS and its affiliate Microbial Control (Switzerland) GmbH are of the opinion that the evidence does not convincingly support placing **silver nitrate in Category 1B for effects on sexual function and fertility and the effects on development. We believe that** the concerns linked to effects resulting from the silver ion are rather adequately addressed **by Category 2.**

The classification of silver nitrate in Repr. Category 1B would be based solely on read across from silver acetate. Moreover, the bioavailability of silver (ion) from silver acetate and silver nitrate is similar based on the evidence provided in the comparative toxicokinetic oral gavage study (Anonymous et al – 2021). However, direct acute or corrosive/irritation effects are by-passed by gavage application. Therefore, it is questionable whether the reproductive toxicity data developed using dietary administration of silver acetate are directly and equally applicable to silver nitrate. The mechanism of toxicity of silver nitrate likely involves exposure to silver ions, but there is a lack of experimental data regarding the influence of nitrate on general toxicity (acute effects and local corrosivity) and whether or not this would exacerbate the effects observed with silver acetate to the extent that it would lead to more pronounced general toxicity

that would preclude classification. Given the lack of evidence for the contribution of the nitrate anion to toxicity, this will remain a major uncertainty. Moreover, data on silver nanoparticles should be discounted due to significant differences in kinetics and deposition between silver nanoparticles and soluble silver salts.

In conclusion, the concerns related to the effects of the silver ion are adequately addressed **by Repr. Category 2**, which is consistent with the existing RAC opinions for metallic silver and silver zinc zeolite. These opinions are largely based on the same data supporting the current proposal.