



Silver Work Group

Expert meeting Reprotoxicity

Agenda, Brussels, 23 November 2017 (09:00-16:30 CET)

1. Welcome and Introduction (*K. Arijs*) (09:00 - 09:15)
 - Reminder on Confidentiality and Competition Law
 - Tour de table and apologies
 - Approval of the agenda

2. Silver reproductive toxicity - current status (*M. Raffray*) (09:15 - 09:45)
 - Status current knowledge silver reproductive toxicity
 - Picture from 2-generation studies on silver containing active substances (SCAS)
 - Impact of latest publications from Sprando et al./Babu et al.
 - PMC updated strategy as of Nov 2017

3. Process / timeline EOGRTS Testing proposal (TP) (*K. Arijs*) (09:45 - 10:00)
 - Dossier evaluation process - where do we have opportunities to provide input?

4. RAC mindset on reprotox classifications (10:00 - 10:45)
 - Brief summary of examples: silver zinc zeolite (SZZ), borates, 2-benzyl-2-dimethylamino-4'-morpholinobutyrophenone, cobalt (*K. Arijs, O. Lemke, S. Verberckmoes*)
 - Assessment of impact on situation for silver (*M. Holsapple*)

5. Stress-testing examples (*All / round table discussion*) (10:45 - 11:15)
 - Expected arguments and possible rebuttal positions (What are the most problematic reprotox findings relevant to silver? Where is the sector position currently weak? What can be done to address these weaknesses? To what extent should findings on nanosilver be taken into account?)

6. Defence of EOGRTS TP (*M. Holsapple*) (11:15 - 12:00)
 - Arguments for why TP should be maintained in context of recent reprotox / DIT data
 - After adaptation, how will TP address key weaknesses in other studies & data gaps

12:00 - 13:00 Lunch



7. Adjustments to EOGRTS TP (*M. Holsapple*) (13:00 - 14:00)
 - Technical adjustments to make TP more viable/defensible (accounting for latest triggers)
 - Key test parameters for inclusion (standard & adapted to silver situation)
 - Dose setting for EOGRTS

8. Mechanism of action (MoA) insights (*M. Raffray*) (14:00 - 15:00)
 - Key MoA studies
 - Relevance of Ag-Cu axis effect
 - Silver impacts on gut microbiome
 - Need for MoA external expert input?

9. Enabling work (*M. Holsapple*) (15:00 - 16:00)
 - Key uncertainties and data gaps where enabling studies could inform (ideally short-term work and/or desktop efforts). Cost-benefit and timeline prediction
 - Linkage to EOGRTS design - e.g. dose-level setting, MoA, DIT aspects etc.
 - Confirm which studies should be progressed as enabling efforts versus integration of sub-studies/parameters in new EOGRTS

10. Re-visit stress-test / Confirm technical defence plan (*All*) (16:00 - 16:30)

Annex 1: Participants

Katrien ARIJS, Consultant for EPMF (Arche, Belgium)

Arno BUTHE (Heraeus, Germany)

Michael HOLSAPPLE, Invited expert developmental immunotoxicity (Consultant, US)

Marie-Laure LEDRICH (Traxys, Luxembourg)

Olga LEMKE (BASF, Germany)

Mark RAFFRAY, Consultant for EPMF (Raffray Biosciences Ltd, UK)

Nissanka RAJAPAKSE (Johnson Matthey, UK)

Steven VERBERCKMOES (Umicore, Belgium)