



Silver Tox Experts (TE) call

Ag reprotox and study Ag effects on the biome

Draft minutes, call 8 May 2018 (16:00 - 17:00 CET)

Participants

- Katrien ARIJS, Consultant for EPMF (Arche, Belgium)
- Arno BUTHE (Heraeus, Germany)
- Marie-Laure LEDRICH (Traxys, Luxembourg)
- Olga Lemke (BASF, Germany)
- Mark RAFFRAY, Consultant for EPMF (Raffray Biosciences Ltd, United-Kingdom)
- Nissanka RAJAPAKSE (Johnson Matthey, United-Kingdom)
- Steven VERBERCKMOES (Umicore, Belgium)

1 Approval of the minutes of the last meeting (11 Apr 2018)

The minutes of the 11 Apr meeting (PM) at LTAP were approved. Minutes of the TE meeting (AM) still to be circulated.

2 Updated proposal Prof. Lison gut biome study

The updated proposal from Louvain University is available in Annex 1 and broadly aligns with the design discussed at the 11 Apr meeting (extension study period from 4 to 10 weeks, additional analyses, etc.). Comments / questions to Prof. Lison from the TE are directly included in Annex 1 (**AP1**). Additions:

- **Diet make-up/analysis:** Ag can be reactive with food (e.g. sulfidation) so important to check stability. **AP2-3**
- **Gut inflammatory marker optional work (+30 k€?):** it was clarified with S. van den Brule that we do not have to decide on whether we want to include this now; this can be decided once we have the other study results (samples will be taken and frozen anyway).

3 Proposal AML for ICP-MS sample analysis

S Verberckmoes contacted AML to check the possibility to outsource the Ag, Cu and Se analyses to them: see Annex 2. Comments / additions from the TE:

- Ag should be measured in whole blood.
- Costs are a lot lower than at St-Luc. Moreover, the TE are of the opinion that AML is more experienced with ICP-MS analyses.
- At this moment, AML is not able to do the sample preparation of different matrices by microwave-acid digestion for Ag analysis in tissues. If someone else can do the sample preparation, AML is willing to perform the analyses at same price as analysis in plasma.
- Delivery time is not stated now but previous communication mentioned 3-4 months. **AP4**
- **The TE are in favour of doing the ICP-MS measurements at AML and the sample preparation at Louvain University. AP5**



4 Update on latest info from ESTF

A few weeks ago, PMC was contacted by ESTF regarding a request from Kemi to the ECHA ED Expert Group for their opinion on further testing for ED properties for SZZ and SSHZP, while Kemi previously stated there was no indication that ED was seen as a significant concern. It seems the shift in position from Kemi on ED is mainly related to the new ED requirements under the BPR and the fact that the available studies on SCAS are old and do not specifically investigate ED MoA. Therefore, their suggestion to test further (or to at least have the opinion of the ECHA ED Expert Group on the need for additional testing) is mainly related to a procedural data gap and does not seem to change their scientific opinion on silver and ED. However, Kemi did mention the EOGRTS as a possible study to address the data gap. ESTF wanted to have our opinion on ED knowledge for silver.

ESTF was updated on the status of our EOGRTS TP and the fact that we have updated it (referring to the dissemination website for the most recent version, as it is there), and we said we expect to have the DD soon. Even though their read-across approach is different (and mainly based on studies with SZZ and SSZHP), ESTF seemed to think the study could also be of value for them (also because it is not clear yet if their read-across approach will be acceptable).

The ECHA ED Expert Group met on 19 April and the meeting came to no overall conclusion on the ED potential for SZZ and SSHZP, although the consensus seemed to be in favour of accepting the existing data and no ED effects. Further written comments were requested from the experts by 27 April. ESTF has submitted comments (via CEFIC) supporting the use of existing data and the negative ED position.

ESTF has now requested a face-to-face PMC-ESTF meeting to discuss our respective positions and possibilities for common action. From ESTF side it would be Andrew Goodyear and Ian Watt (STF Chair) and perhaps some toxicology expert input depending on the level of detail needed. **AP6**

5 Any other business

- M. Raffray informs the TE of another metal association which proposes to do the most complex EOGRTS (all cohorts + F2 generation).
- It seems that LPT is increasing their capacity to accommodate the performance of EOGRTS. **AP7**
- S. Verberckmoes is taking a training on the EOGRTS on 6 June and will report back to the TE.
- BASF has a list of labs that have been approved for performance of the EOGRTS. **AP8**

Annexes

1. Proposal AgAc gut biome study, Louvain University, 23 April 2018
2. Proposal AML for ICP-MS measurements

Actions

Table 1. Actions agreed at the 8 May TE call

	What?	Who?	When?
1.	Follow-up additional questions in Annex 1 with prof. Lison	PMC Sec	Done



2.	Check with BASF analytics department if there is prior knowledge on stability AgAc in diet	O. Lemke	ASAP
3.	Check how stability of test substance in the diet was analysed in PGM dietary studies	PMC Sec	Done
4.	Check with AML: <ul style="list-style-type: none">• Timing for ICP-MS analyses;• If they can do Ag measurements in whole blood;• If spiked samples are included in the analysis.	S. Verberckmoes	ASAP
5.	Check if Louvain University is willing to do sample preparation for ICP-MS measurements and then send samples to AML for analysis	PMC Sec	Done
6.	Follow-up joint PMC-ESTF meeting	PMC Sec	Ongoing
7.	Check with LPT if they are able to perform EOGRTS	PMC Sec	May 2018
8.	Send list of BASF approved labs for the EOGRTS to PMC Sec	O. Lemke	May 2018