PRECIOUS METALS AND RHENIUM CONSORTIUM
Silver Work Group conference call:
Environmental Effects Assessment with WCA

Chairperson: R. Garrett (Ames Goldsmith)
Secretariat: C. Braibant & K. Rothenbacher (EPMF)

10 December 2013, 2:30 – 3:30 pm CET

PARTICIPANTS

1.	**Rodger Battersby**	EBRC	Germany
2.	**Bodo Berkner**	Ferro	Germany
3.	**Caroline Braibant**	EPMF	Belgium
4.	**Roland Brasch**	Heraeus	Germany
5.	**Edwin Broekaert**	Umicore	Belgium
6.	**Helena Byrdziak**	KGHM	Poland
7.	**Daniela Cholakova**	Aurubis	Belgium
8.	**Paul Dinning**	DuPont	United Kingdom
9.	**Maria Donner**	DuPont	United States
10.	**Bill Fasano**	DuPont	United States
11.	**Daniel Glowacki**	KGHM	Poland
12.	**Kevin Klipsch**	EBRC	Germany
13.	**Susan Munley**	DuPont	United States
14.	**Renaud Nicolay**	EPMF	Belgium
15.	**Manfred Probst**	C. Hafner	Germany
16.	**Nissanka Rajapakse**	Johnson Matthey	United Kingdom
17.	**Klaus Rothenbacher**	EPMF	Belgium
18.	**Mike Shepherd**	Vale	United Kingdom
19.	**Michael Thiel**	BASF	Germany
20.	**Ruediger Thiele**	Heraeus	Germany
21.	**Carole Wilson**	Vale	United Kingdom
22.	**Carolin Wippel**	BASF	Germany

CONCLUSIONS

1. CSR

Section 5.1 on Toxicokinetics: EBRC to ensure PMC batch 3 is included in all the report (e.g. the granulometry section, table 9).

No comments/ objections were received on sections 5.2 (Acute toxicity), 5.3 (Irritation), 5.4 (Corrosivity), and 5.5 (Sensitisation)

Section 5.6.3: "Summary of repeated dose toxicity", under inhalation exposure, studies on nanomaterials: EBRC to add additional text in the CSR and the IUCLID 5 file explaining in more details the HEC calculations and how this is used in the DNEL derivation (similar to the introduction made by R. Battersby to the HEC document discussed under item 2. HEC below).

Section 5.7 on Mutagenicity: Maria Donner (DuPont's genetic toxicologist)'s comments:

- Leaving out relevant information: Looking at CSR does not allow viewing all IUCLID 5 content but IUCLID 5 file contains the relevant information and needs to be looked at together with the CSR. Participants to look at the IUCLID 5 file and revert if information still appears to be missing.
- Dose selection: Explanations around dose selection are available in IUCLID 5 fields which are not imported to the CSR. For some studies there is no explanation on dose selection available in the original paper, and it is thus not possible to report more in the IUCLID/ CSR

- Results conclusions not properly captured:
    - E.g. on page 130 of the CSR, not all participants agree that the test study is equivocal (negative without metabolic activation versus positive without metabolic activation). The following was agreed: PMC Secretariat will circulate the Lloyd, M. (2010b) study report to the Ag Members, EBRC will verify the robustness of the weight of evidence approach (and ensuring the right information/conclusion is presented in the IUCLID 5 file and CSR), and Ag Members will then share their proposed interpretation of the Lloyd study and proposed wording for the IUCLID 5 file and CSR accordingly.
    - The positive Ames assay cannot be dismissed out of hand. EBRC will add more discussion, review the study in the context of other available data, and draw a conclusion based on the weight of evidence.
- Kim *et al.* (2012c)'s Klimisch score: currently scored as Klimisch rank of 4 though it should perhaps deserve 3. EBRC will address this.
- COMET Assay: The comet assay is generally regarded as powerful tool to detect even low numbers of DNA damage, and is discussed be scientist/regulators as a suitable test for nanomaterials. However, this assay is also prone to positive findings not caused by the test item but by e.g. inappropriate test design. Minimum quality criteria were used by EBRC to rate the available studies for their relevance in chemical safety assessment. The criteria as published by Tice et al. (2000) were used for this screening. In case a reference did not fulfil the criteria stated therein, it was considered of limited or no relevance for chemicals safety assessment. EBRC will amend the discussion in the CSR in this context.
- Summary and discussion of mutagenicity is outdated: EBRC will add some text on page 132 to ensure that the justification for discarding some recent studies is provided (as currently it could be interpreted as ignoring these more recent studies overall).

Section 5.8.3 on Carcinogenicity: The Ag Members agreed with the waiver.

Section 5.9 on Reprotoxicity:
Susan Munley (DuPont's reprotoxicity expert)'s comments:

- No classification on the basis of 'data lacking' (on page 22 of the CSR) was deemed acceptable

Waivers on pages 135 and 136 were agreed.

Section 5.11 on Derivation of DNELs: Pages 149 and 150, additional narrative should be added summarising the approach to deriving a DNEL inh, why the original DNEL based on the OEL is retained, and discussing the DNEL inh nano; the resulting DNEL inh nano value should be added to the tables 59 and 60 in order to document that we considered this seriously and did not dismiss information we did not like.

2. HEC

Regulatory acceptance: agreed to include HEC calculations in the dossier. It was agreed to include the HEC concept as an annex to the DNEL report knowing it has not yet been validated by regulators; it may hence trigger (hopefully constructive) discussions with the evaluating MS.
EBRC will review the document and explain in more details:
- how the MMADs were calculated and why there are two MMADs for two of the silver batches
- why Oller instead of Kalberlah's PSD corrected HEC values are referred to in the second last paragraph of page 7,

- explain in more details why a sufficient margin of safety is estimated for nano Ag based on the available PSD data from PMC materials. If appropriate, add a short calculation, and
- "Concluding remarks": EBRC to provide recommendations for further work in a direct mail to PMC rather than in the report itself

3. DNEL

- It was agreed to retain the current DNEL inh based on the existing OEL. Specifically for nanoAg, it was agreed to derive a separate DNEL inh nano. It is assumed that the current DNEL is also protective for nanoAg, however it is appreciated that this is based on rather limited data and therefore a separate DNEL inh nano should specifically be reported in the CSR.
- Statement that "The dermal absorption . . . is negligible (<1% of applied dose) . . .": EBRC to add more discussion and include references to corresponding CSR chapter.
- Section 4.1.2.3 "Application of Assessment Factors": It was agreed to retain and AF of 2.5 for "Remaining differences in TK". The explanation in the report states that they " . .. are not considered to be of particular relevance . . .; furthermore, such differences are largely accounted for in the calculation of a 'HEC' . . .. It has been nevertheless retained". The Ag WG agreed to retain the AF in order to be conservative.
- In some cases (4.1.2.4) it is not clear which specific DNEL is referred to; EBRC to clarify.
- Add DNEL inh nano in DNEL report to executive summary, as a separate column to tables reporting these values.