19 November 2013, 10:30 – 16:30
Metals Conference Centre – Aluminium Room
Rue du Duc 100 – 1150 Brussels (BELGIUM)

MINUTES

AP refer to Action Points listed at the end of this document

1. Welcome & Introduction

1.1. Reminder on Confidentiality and Competition Law. Participants were reminded on their obligation to comply with confidentiality and Competition Law provisions.

1.2. Tour de table and apologies. The list of participants is available in Annex 1.

1.3. Approval of the agenda. The Agenda (Annex 1) was approved. The slides presented during the meeting are available in Annex 2.

1.4. Status of actions agreed at and approval of the minutes of the last meeting (4 Sep 2013).

Slides 5 and 6 of Annex 2 provide an overview of the status of the various actions agreed at the previous meeting; most were finalized or to be addressed during the meeting.

P. Simpson clarified that as regards action 5, a note on RIVM's ERL will be prepared in due course, after the Ag (compounds) Dossiers are updated in Q1 2014.

P. Simpson also informed the Ag WG that the on-going ASRIT test at Laus could not be finalized because of interference with the test item, and can hence not be finalized unless another guideline is used (ISO). WCA will circulate a proposal for approval accordingly (**AP1**).

On-going actions which remain unfinished today, as well as actions on hold/in time, were added to the list of actions agreed at this meeting (Table 1 below, **AP14**, **15**, and **16**).

2. Effects assessment – Status of Ag IUCLID 5 file sections 4 to 8

2.1. Environmental effects.

A number of documents were circulated before the meeting, in order to inform and/or collect comments from the Ag WG:

- **Literature searches:** many papers have been published on nanoAg in the recent months. WCA's screening and selection was based on the relevance of the study for REACH, as well as on the quality of the study (using Kimish ranking + PMC quality criteria related to minimum characterisation work for studies involving nanoforms).

- **Endpoint study summaries:** an extract of the IUCLID 5 file on all the ecotox and environmental fate sections, which support the effects assessment of all forms of Ag covered in the Dossier. The enlargement of the scope to include nanoforms of Ag resulted in an increased robustness of the overall assessment and read-across approach, since the dataset has become larger and the evidence supporting the driving effect of Ag ion stronger.

- **PNEC summary document: PNEC summary document:** a description of the derivation and resulting value of each PNEC, including the latest SSD and eco-region approach to derive robust and relevant PNECs for soil. As regards the PNECfreshwater, although additional information has become available, it was decided not to include this in the PNEC derivation

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and not to update the SSD. The reason for this was that the SSD has been approved by regulators (UK), and because the additional information would not have significantly changed the PNEC. If information would continue to grow significantly for this environmental compartment, PMC would review its PNEC accordingly. The Ag WG had no objections to this approach.

- **CSR:** Members were invited to review and comment on the read-across justification contained in the CSR (page 24), which will be shifted towards the beginning of the CSR in a future version.

Comments on the above documents and IUCLID 5 sections on ecotox effects and environmental fate (**AP5** and **6**) will be addressed at a dedicated conference call on 2 Dec 2013 at 2:30 pm.

2.1.1 Freshwater: from BLM, to pre-BLM speciation, to no PMC work – exploring partnership.

The link between the speciation, bio-availability, and chronic toxicity of Ag ion in freshwater remains unclear to date and prevents an opportunity for further refinement of the Ag PNECfreshwater, which is the lowest aquatic PNEC of all metals.

Though PMC was originally interested in elucidating these links with specific tiered research (speciation, BLM, etc.), another customer from WCA with pre-regulatory product stewardship interests in Asia (Unilever) has recently decided to proceed with this work on its own funds, in order to share the output of the research with PMC in exchange of PMC's soil related work.

This possible 'partnership' between Unilever and PMC will be further explored and documented in a dedicated Memorandum of Understanding, which will probably not be ready before end Q1 2014, after Unilever has obtained funding from the Canadian government, selected its MSc student, and launched its pre-BLM speciation research with WCA.

The Ag WG emphasized the importance of proceeding with this work (which does not only benefit REACH but and water related assessment) which has been very helpful for other metals and could significantly improve the Ag case as well.

2.1.2 Marine water: GLP audit of Nautilus, feed-back from Zn, and agreement on way forward (including change of test house for marine SSD testing work).

The Ag WG agreed to proceed with Nautilus for the comparative oyster embryo test under the condition that Environmental Standards audits their work, as well as the characterisation work done by Nanocomposix (**AP2**). Under these conditions (not GLP accredited but GLP compliant) the study could be assigned a Klimish rank of 1 or 2 and be useable in the REACH Dossier. The result of this test may be available before the commencement of the Evaluation in March 2014.

As regards the SSD marine, PMC will have to place most of its additional marine tests with another test house than Brixham Environmental Laboratories (BEL), which is closing down. It was suggested to follow BEL's experts and assess Nautilus' work in selecting a new candidate laboratory for these marine tests. WCA will look back at the original tenders which had been received and revert with an updated recommendation accordingly (knowing that the number of contract laboratories performing marine ecotox work in the EU besides academia is very limited) (**AP3**).

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2.1.3 Soil: CSIRO report, SSD soil, eco-region approach, resulting PNECsoil, and additional research needs.

Following the soil ecotoxicity work done on non-aged soils at AECOM, CSIRO performed a much broader and state-of-the arte study on aged/leached soils representing a broad range of soils, and six taxa. Some of the soils were sourced from Australia, where CSIRO is based, however it was important to select a broad range of soil properties that would allow to derive a bioavailability correction. The soils are therefore considered representative for the whole world, including the EU (as per GEMAS work co-sponsored by various metals associations in 2010). Furthermore, the overall testing method was approved by ECHA as part of its discussion and decision on PMC's formal Testing Proposal.

The two years programme was finalised over summer 2013 and a draft report was circulated on 30 Oct 2013. WCA used the results of the CSIRO bio-availability and aging correction work to derive PNECs for five typical EU soils on the basis of a normalised terrestrial toxicity database, using both the SSD and eco-regions approaches, which is explained in WCA's PNEC summary document. The availability of additional soil data, together with the CSIRO data, allowed to derive species sensitivity distributions for soils now (not included in previous dossiers).

CSIRO's work demonstrated the influence of ageing (which allows natural soil processes such as adsorption, leaching, etc. to occur in presence of the tested metal, i.e. Ag) on the amount that is actually bio-available and can cause an effect.

The generic PNECsoil derived on the basis of this refined work (using 10th percentile of each soil property) using an assessment factor of 3 is 1,24 mg/kg wet weight, when the original PNECsoil calculated on the basis of equilibrium partitioning and an assessment factor of 10 was 0,79 mg/kg wet weight (almost half of new PNEC).

Though PMC now has evidence to demonstrate that Ag forms non-bio-available complexes with S in soil, it cannot explain why effects on terrestrial organisms can still be measured. Additional research is proposed by CSIRO to address this gap: a two years programme with a cost of around 500.000 Australian dollars. Since this work will not be finalised in time for Evaluation by The NL, it was agreed to discuss its content and timing at the next Ag WG meeting (**AP13**).

2.1.4 Overall feed-back from Mgmt Cttee on Ag project research.

In preparing the 2014 budget for discussion and pre-approval by the Management Committee it appeared that PMC's Ag project was entering into a new phase of work aimed at refining and strengthening the risk assessment done under REACH (somewhat going beyond strict REACH information requirements) either pro-actively and/or in response to the Evaluating Member State's decision (i.e. The NL's decision and information requirements after Evaluation).

Considering the amounts involved in these longer-term research items and the possible co-sponsorship opportunities (because the nature of the work is not limited to REACH compliance), the Management Committee requested the Ag WG to prepare more complete research proposals/business cases before including any Ag research budget in PMC budgets.

In the event additional work needs sponsoring in the areas of freshwater (speciation, BLM, etc. with Unilever) or soil (fate of (nano)Ag in soil by CSIRO), these need to be properly justified in a dedicated proposal/business case so they can be considered by the Management Committee for possible inclusion in a PMC budget (**AP12**).

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2.2. Human health effects: Status of NTP study, impact of results from NTP study on DNEL (if any)

As for the environmental sections above, many papers have been published on nanoAg in the recent months. All IUCLID 5 human health sections contain all relevant information identified during the most recent literature search and result in no change of the classification of Ag.

US NTP/FDA/NCRT have conducted a highly relevant 90-day oral toxicity study with nanosilver (three sizes) and silver acetate in direct comparison. Final results/report are not yet available. Only preliminary findings have been published at a conference. An endpoint study record with the available findings is included in the dossier and the study is mentioned in the discussion on repeated dose toxicity. It is anticipated that this study will significantly complete and strengthen the database and confirm a number of results which have already been published by other authors.

A few comments among the following ones were shared during the meeting:

- Klimisch scoring of some of the studies identified during the recent literature search
- Need to more fully describe the studies in the study summaries, to make sure all aspects are properly addressed/countered when e.g. their relevance for REACH is questionable, the results equivocal, or the dose selection requires further justification
- Consider developing guidance and principles around assessing the human health effects and toxicokinetics of (nano)materials under REACH

The Ag WG agreed to leave the waivers for the carcinogenicity endpoint unchanged. The waiver on the two generation reproductive toxicity study has been slightly reworded by EBRC, and now considers a recently published 28-day combined repeated dose with reproductive /developmental screening study. On developmental toxicity/teratogenicity, the published study by NTP on silver acetate (Price, 2002) is the key study. Since this study was negative, a developmental study in a second species could be required. A waiver has been added on this second species study, discussing the low toxicological profile of silver in this regard.
Comments from the Ag WG on the justification provided for these waivers are naturally welcome. It was nevertheless suggested to consider adding a place-holder for a possible two generation reproductive toxicity in a future Ag budget, in case the Evaluating Member State requests so as part of the Substance Evaluation decision (**AP17**).
The comments on the human health sections of the IUCLID 5 file (**AP5** and **6**) will be discussed at a dedicated conference call to be organised on 10 Dec 2013 at 2:30 pm.

As regards the DNEL, it was agreed to include the following DNEL values in the updated registration dossier:

- DNEL inhalation for workers remains at 0,1 mg/m³; unchanged from previous version of the dossier (based on SCOEL OEL, inhalable fraction, based on human epidemiological data on argyria). This DNEL is used in the exposure scenarios / risk characterisation for all workplaces, including nanoAg.
- In parallel, a DNEL is formally calculated on the basis of Sung *et al.*'s study on rats. This DNEL, rounded to 0,01 mg/m³ is applicable to particles in the size of ca. 20 nm, i.e. the material tested in the rat study. Based on the consideration of particles sizes actually expected in workplaces air (where nanoparticles are assumed to aggregate) it is argued in the dossier, that the original DNEL of 0,1 mg/m³ for the inhalable fraction is protective for all workplaces, including those where nanoAg is handled.

The 0,01 mg/m³ DNEL was calculated on the basis of the Human Equivalent Concentration (HEC) approach which is an alternative manner to derive DNELs. Indeed, rather than applying an assessment factor (AF) and rough re-calculations of an animal study result for allometric scaling

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to human, the HEC approach (typically used by German authorities and experts) allows to:

1) Convert the animal study result in a human equivalent result or HEC where the allometric scaling (i.e. the conversion from animal physiology / morphology / breathing patterns, etc. to humans) is re-calculated more precisely and without using unnecessarily conservative AF; and
2) Convert the tested material's particle size data to real material's particle size data, which provides an additional margin of safety (for cold processes) by demonstrating the relative low alveolar deposition of the tested material versus the material that should be found on the workplace.

It is important to note that the above approach does have the weakness that 1) there is no information on particle size distribution of dusts at actual workplaces in the silver industry and that 2) the arguments are currently based on laboratory dustiness data, which is available only for one uncoated nanoAg powder (and two µm sizes powders). As regards next steps, see section 3.2. below.

2.3. Feed-back from reviewers on the effects dataset

Confidentiality Agreements have been signed with Dr Violaine Verougstraete and Hugo Waeterschoot, who have received draft documents for review/comment.
Since the information was still in draft form, the reviewers have been invited to await final deliverables before commencing their review. The Ag WG will be informed on their feed-back as soon as possible.

3. Exposure assessment – Status of exposure scenario work

3.1. Environmental exposure: site-specific assessments after inclusion of nanoAg and new PNECsoil

WCA ran an exposure assessment using the most up to date spERCs, and Ag PNEC values (revised PNECsoil), and using the Msafe approach, which determines the highest annual tonnage of Ag manufacture which leads to demonstration of safe use (RCR < 1). The Msafe calculation assumes an RCR of 1 and then calculates back which tonnages can be used. If the PNECs change, the RCR remain largely unchanged, but the tonnages allowed change.

The Msafe tonnage of the GES for manufacturing is significantly increased from 40 to 200 t/a. This tonnage is only exceeded by a single manufacturing site that used SpERCs, rather than site-specific data, for its environmental assessment. A new site-specific assessment was performed for this site, which demonstrates safe use (this will be sent to the company involved in due course). Other manufacturing sites with tonnage > 200 t/a already assess site-specific environmental risks based on measured data. These sites continue to demonstrate safe use with the refined PNECsoil.

Overall RCR in the revised ES for downstream uses of Ag and Ag compounds are smaller (further below 1) than compared to the 2010 assessment. Since the Msafe tonnage is derived on the basis that RCR will = 1 for at least one compartment at the Maximum safe tonnage (i.e 200 t/a in this case), and the freshwater compartment is the most sensitive for silver, the RCR for the freshwater compartment exceeds 1 at a tonnage of 200 t/a before any of the others. Hence, a value of 1.01 is expected in the generic ES for the freshwater compartment.

An updated environmental ES package will be circulated w/c 25 Nov which will include the above results as well as any nanoAg-specific sections and statements.

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As regards the site-specific Tier 3 assessment (demonstrating safe use per site, especially for those not fitting with the Msafe generic ES, and using measured data rather than modelled data), it was agreed to generate an anonymised Tier 3 report to be attached to the joint registration dossier (**AP11**).

3.2. Occupational exposure: feed-back from PMC Members, resulting scope of existing ES, nanoAg specific assessments, and recommended way forward (dustiness, exposure monitoring programme, etc.)

An updated ES paper was circulated prior to the meeting, which only contained updated occupational exposure scenarios in order to address nanoAg. The ES involving spraying needs to be further refined once clarification on the process and process conditions has been received (EBRC is in contact with the relevant sites).

In order to confirm/refine the currently recommended nanoAg risk management measures, and to further support the DNEL of 0,1 mg/m³ (inhalable fraction) also for nanoAg workplaces (see section 2.2), dustiness data of various nanoAg samples (with and without coating), and inhalation monitoring data would need to be generated.

As regards dustiness, it was agreed for the PMC Secretariat to send a mail to the nanoAg related PMC Members inviting them to send their sample(s) to a dedicated test house by 15 Jan 2014, in order to participate in a dustiness testing programme (**AP7**).

As regards the generation of nanoAg inhalation monitoring data, a firm strategy can only be proposed by EBRC after having visited the concerned/interested sites to better capture the possible specificities of a nanoAg manufacturing/using workplace. And even so, considering the very small quantities of nanoAg which are manufactured annually by the concerned PMC Members, and the associated frequency of production (and associated frequency of nanoAg release/exposure) a meaningful inhalation monitoring programme would be difficult to implement in a short timeframe (i.e. before Substance Evaluation commences).

3.3. Consumer exposure: feed-back from RIVM, status of exchanges with NIA, nanoAg companies, and Ag Task Force, and options to proceed

Though it is clear that one of The Netherlands' REACH Competent Authority (RIVM)'s main concern relates to consumer uses of nanoAg (i.e. nanoAg used in consumer products), in the absence of any information on these uses among PMC Members and their DU, it was suggested to not include any consumer ES for nanoAg in the Ag Registration Dossier update to be reviewed by The Netherlands (unless any Member disagrees and provides the relevant information (**AP8**)).

The PMC Secretariat indicated that a number of contacts had been established with the Nanotechnologies Industries Association (NIA) and some of its Members, and that none of the feed-back received indicated any interest in supporting PMC in producing such a consumer ES for nanoAg. Moreover, it appears that most uses of nanoAg by NIA members are subject to the Biocide Directive and not to REACH. PMC will organise a meeting with representatives from the Silver Task Force in charge of the Biocides dossier preparation, in order to agree on a common interpretation of Biocidal and REACH uses of (nano)Ag, among other items (e.g. comparing PNECs) (**AP4**).

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4. Next steps

4.1. Common IUCLID 5 sections, including scope of dossier and classification profiles

Slides 44 to 46 of Annex 2 summarise the work that needs to be done by the Ag WG, the PMC Secretariat, and the individual Members of the Ag joint registration, in order to finalise the Ag Registration Dossier update.

PMC Secretariat emphasized the need for individual registrants to generate/complete the relevant analytical information section of IUCLID 5, as well as to duly complete sections 3.2 and 3.4 to distinguish generic Ag and nanoAg specific information (to prevent future stigmatisation or listing/prioritisation on unfounded grounds). It was agreed to leave section 3.7 of IUCLID 5 unchanged as this section is resource-intensive to complete and will not become mandatory soon.

4.2. Overview of Ag project priorities

All priorities as approved at the previous meeting have been followed up appropriately; the focus being on ensuring a successful Ag updated Registration Dossier submission before March 2014.

4.3. Timing for finalisation and submission to ECHA

In light of the above progress and pending items, it was agreed to cancel the originally anticipated Ag updated Registration Dossier submission in Dec 2013 and to have a single Dossier update in Feb 2014.

5. AOB, next meetings and closing remarks

No other business was raised during the meeting.

The next Ag WG exchanges will be organized as follows:
- 2 Dec 2013, 2:30 pm CET: Conf Call with WCA to review ecotox and environmental fate sections of IUCLID 5 file
- 10 Dec 2013, 2:30 pm CET: Conf Call with EBRC to review tox and toxicokinetics sections of IUCLID 5 file
- Jan 2014 (date and time to be confirmed (**AP9** and **10**)): Conf Call with WCA and EBRC to review exposure assessment and exposure scenarios

Table 1. Actions agreed at 19 Nov Ag WG meeting

	What?	Who?	When?
1.	Circulate proposal of new testing protocol for ASRIT on nanoAg	WCA	Dec 2013
2.	Sign proposal from Nautilus and Environmental Services to launch oyster embryo testing and associated audits	CB	20 Sep 2013
3.	Identify test houses able to conduct marine ecotox testing for SSD marine work (including Nautilus) and revert with recommendations	WCA	Q1 2014
4.	Meet with Silver Task Force in charge of Silver Biocides dossier to: • Agree on Silver uses covered by REACH and Biocides	CB	Dec 2013

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	What?	Who?	When?
	• Compare PNECs		
5.	Access and provide comments on Ag IUCLID 5 file available on Hosting System	Ag WG	ENV: 2 Dec conf call + 31 Dec 2013 HH: 10 Dec conf call + 31 Dec 2013
6.	Read and provide comments on draft CSR and its annexes (except Exposure Scenario annex)	Ag WG	Idem above
7.	Prepare sample(s) of nanoAg that should be included in extended dustiness test programme (in support of nanoAg exposure assessment) – cf. *ad hoc* communication with all relevant details	NanoAg manufacturing companies	15 Jan 2014
8.	Confirm how/no consumer use scenario for nanoAg should be included in the updated joint registration dossier	Ag WG RIVM?	31 Dec 2013
9.	Read and provide comments on updated Exposure scenarios (Annex 3 of CSR)	Ag WG	15 Jan 2014
10.	Organise Ag Exposure Assessment conference call(s) with WCA and EBRC	CB	Jan 2014
11.	Prepare anonymised site-specific Tier 3 environmental exposure assessment to be attached to the updated joint registration dossier before submission	WCA	Jan 2014
12.	Follow-up preparation of Memorandum of Understanding between PMC and Unilever (on speciation and BLM work) in order to formulate a business case for approval by the Ag WG and Mgmt Cttee	WCA	Q1 2014
13.	Present summary of CSIRO's recent research proposal to Ag WG for discussion and consideration; and if relevant formulate a business case for approval by the Mgmt Cttee	KR	2014
14.	a. Derive classifications for impure profiles of Ag, AgCl and AgNO3 b. Include classifications in respective ID Cards c. Upload classifications into respective IUCLID 5 files d. Derive transport classifications for all Ag substances and intermediates' profiles e. Post latest (transport) classifications onto PMC inventories	ARCHE KA EBRC ARCHE AR	Sep 2013 Q1 2014 Q1 2014 Q1 2014 Q1 2014
15.	Include clear dossier scope in Ag and Ag compounds dossiers prior to dossier update submission	EBRC+WCA	Feb 2014
16.	Decide upon use of Chesar and subsequently on: - Need to push for derivation of standard phrases for metals industry with Eurométaux - Need to translate short ES of Ag and other PMC substances	Ag WG	2014
17.	Anticipate possible need for two-generation reproductive toxicity (on a second species) for Ag in Ag-specific costs of the PMC 2015 (?) budget	CB	2014

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