Chairman: *Dave Boyd* (Johnson Matthey)

8th May 2012, 10:00 – 11:00 CET

List of participants

Bodo Berkner	Ferro	Germany
Dave Boyd	Johnson Matthey	United Kingdom
Roland Brasch	Heraeus	Germany
Edwin Broekaert	Umicore	Belgium
Manfred Probst	C. Hafner	Germany
Mark Raffray	Johnson Matthey	United Kingdom
Klaus Rothenbacher	EPMF	Belgium
Mike Shepherd	Vale	United Kingdom
Rüdiger Thiele	Heraeus	Germany
Steven Verberckmoes	Umicore	Belgium
Carol Wilson	Vale	United Kingdom
Roland Winde	Umicore	Germany

Draft Agenda

1. Welcome and introduction

The agenda and the minutes of the last meeting were approved. It was agreed to take agenda point 2.3 forward and discuss before agenda point 2.1.

The participants were reminded on their obligation to comply with confidentiality and Competition Law.

US TSCA 8(e) reporting requirements: since new test results will be presented during the call, participants were reminded that they may have obligations in the US under the EPA TSCA 8(e) rule to report and/or notify EPA if new information has become available that their substance poses a substantial risk to health or the environment. Such notices must be submitted within 30 calendar days. More information can be obtained from US EPA at http://www.epa.gov/oppt/tsca8e/

2. Testing Programme

2.1. Enabling- /phys.-chem. Tests – progress update:

2.1.1. Oxidising properties:

The oxidising tests are completed. One additional test had to be carried out for confirmation (hexahydroxy platinic acid). A draft report has been received by PMC at the day of the conference call and will be circulated shortly. Initial data indicate that there will be no need to classify this substance.

2.1.2 Water solubility testing:

a) Standard tests: all tests are completed, except for one (diammonium hexachlororuthenate) which is currently being tested by an external laboratory. Results are expected in June.

b) Non-standard tests: tests on 2 substances are still outstanding. One substance was only received on 3rd May and will be tested now. The other substance (Karstedt concentrate) had been put on hold until discussions with the Reconsile consortium have been completed. Since these discussions take

longer to complete than anticipated, the PGM WG decided to go ahead and test the Karstedt concentrate as well.

c) Transformation/dissolution tests: all tests have been completed and draft reports have been received by PMC. Final reports are in preparation and are expected in the coming weeks.

2.1.3. Bio-elution testing:

Bio-elution testing has started at CIMM. We have been informed that the laboratory will be closed as from this summer and that all tests need to be completed by then. This imposed strict deadlines and lead to the fact that one substance could not be included in the scope (see below).

The final scope is summarized on slide 9. All substances will be tested in gastric fluid and dermal; four substances have been selected for testing in lung fluids as well (the 4 metal blacks). This decision was made based on data from dustiness testing and lung deposition modelling; only substances that will reach the lungs to an appreciable extent need to be tested for bio-elution in lung fluids.

Unfortunately, no supplier for PdO could be found in time for the test start, so this substance had to be omitted from the scope.

2.1.4. Dustiness testing:

All tests have been completed by DMT and test reports are available on request.

Lung deposition modelling has been carried out by WCA on the basis of these data. A draft report by WCA has been received shortly before the call and will be circulated in the coming days.

The MPPD model allows to select several breathing modes, which differ in intensity and thus lung deposition (oro-nasal augmenter, oro-nasal mouth, mouth). For our purposes, a mode is needed which represents a 'reasonable worst-case' mode. It was agreed to use 'oro-nasal augmenter' mode for the calculations, similar to what had been done in earlier work for silver.

Selection of substances for bio-elution testing in lung fluids: this test is obviously only needed if the substance has the potential to reach the lung in an appreciable extent. Based on the draft MPPD data and dustiness data, PMC made the recommendation to test lung fluids bio-elution only for substances with a modelled lung deposition > 1% (trachea bronchial plus pulmonary deposition) and significant dustiness. This led to the conclusion that the Pt-, Pd-, Rh-, and Ru-black should be tested. An initial look at their particle size distributions (as far as available) indicated that these substances have appropriate PSD for the bio-elution testing and do not need further refining prior to the tests.

2.1.5. *In-vitro irritation testing:*

EPISKIN tests and ICE tests have been completed at CiToxLAB. The in-vivo tests and the BCOP test for Tetraammineplatinum dinitrate at Harlan are still pending (the material has not arrived at the lab yet). The as of yet available results are summarized in slide 13.

2.2. Fast-track testing: diamminedichloropalladium – progress update:

2.2.1. Ecotox testing:

The status of the ecotox testing programme is summarized in slide 15. The programme is proceeding well, no unexpected developments were noted. Due to lack of time, no in-depth discussion on this agenda point took place.

2.2.2. *Mammalian tox testing*:

The status of the mammalian tox testing programme is summarized in slides 16-17. The programme is proceeding well, no unexpected developments were noted. Due to lack of time, no in-depth discussion on this agenda point took place.

Appropriate route of exposure for acute toxicity testing:
We are currently testing the oral route in the testing programme, based on feedback from the PGM WG. However, Reach requires testing second route of exposure, if appropriate, and feedback from the PGM WG is needed in order to decide whether or not either the inhalation or the dermal routes are relevant for DDP.
Enabling test results indicate that the inhalation route is not appropriate due to low dustiness and less than 1% deposition to the lung. PMC thus recommends not to test the inhalation route.
Dermal exposure: no data is available to judge whether or not this route of exposure is relevant. Therefore feedback from PGM WG members was requested if the dermal route is relevant for DDP.
Action: Producers of DDP to confirm to PMC whether or not DDP has a potential for dermal exposure or if this can be ruled out. Deadline for responses: 22nd May 2012.

2.3. Next steps – discussion

2.3.1. Hydrated vs. anhydrous forms in further testing:
PMC informed the PGM WG that they have bilaterally discussed with the respective producers of palladium monoxide which form is relevant. The feedback obtained indicates that the hydrated form is not produced as such (it might be chemically identical to palladium dihydroxide) and that only the anhydrous form is relevant. It was agreed to take only the anhydrous form further in the Reach dossiers.

2.3.2. Sensitisation – CRO selection:
There were project management issues with Harlan in the sensitisation testing of DDP (LLNA assay). The PGM WG agreed with the recommendation to conduct future sensitisation testing at CiToxLAB. Some members confirmed that they have encountered similar issues with Harlan.

2.3.3. Genetic toxicity:
The genotoxicity results for Rh(III) substances are not straightforward to interpret: while the soluble tri-chloride, -acetate and –iodide compounds all have valid positive findings, the –nitrate has two valid negative tests (Ames and in vivo micronucleus). The question was discussed, whether or not the Rh(III) ion is the toxic agent and positive findings for Rh(III) should be read across to other Rh(III) substances.
PMC presented a slide (slide 25) to outline the hypothetical consequences if Rh(III) were considered mutagenic. (It should be noted that this slide only presents a "what if" scenario in order to facilitate the discussion. It does not represent any new data or recommendations for classification)
The PGW WG concluded that, although Rh(III) is probably the common mutagenic agent, a full basis for assignment of mutagenic potential to the various Rh(III) compounds is not yet established. Heraeus felt that there is no reason to reclassify the trinitrate since two valid negative tests are available for this substance.
The PGM WG consensus was that a better understanding is needed as to the reason why the trinitrate did not elicit a positive response, and hence whether there is one or more gating parameter(s) relevant to mutagenicity. The low solubility of the substance could be one of the reasons (precipitation was reported in the Ames assay). PMC was asked to take this issue up with Prof Kirkland and, if possible,

come up with a focused testing strategy to resolve this issue so that class effect aspects can be better defined, i.e. which Rh(III) compounds should be considered to be active for this endpoint.
Action: PMC to review the issue of Rh(III) genotoxicity and propose a way forward

For platinum dinitrate there is a need to proceed to in-vivo testing. The question was raised whether an in vivo micronucleus should be conduct or if a Comet assay would be more appropriate.
Action: PMC to set up a small task group to resolve this issue. Members who volunteered were Mark Raffray, Steven Verberckmoes, and Peter Grohnert (PG nominated by colleagues).

Tetraammineplatinum dinitrate: WCA recommend conducting a new Ames assay. The PGM WG suggests to read across from Tetraammineplatinum dichloride and –hydrogencarbonate should be attempted instead of conducting a new test.

Diammonium hexachloropalladate: An existing valid (neg.) Ames test is available, although with limitations. The PGM WG agreed to conduct a new confirmatory Ames test with 5 strains.

2.3.4. *CRO selection for full PGM testing programme*:

a) Genotoxicity testing: it was agreed to continue future testing with Covance. The experience so far is very good and if necessary support by D. Kirkland will be available
b) Ecotox testing: the ongoing testing programmes indicate good experience with both the Fraunhofer Institute Schmallenberg (DDP testing) and Brixham (Gold and PM-CN programme). Their cost is comparable and both labs offer competitive prices. It was agreed to conduct the full testing programme with both labs and split the tests evenly between Fraunhofer and Brixham.
c) Sensitisation: as discussed under agenda point 2.3.2 it was agreed to proceed with CiToxLAB for this endpoint.

2.3.5. *Exposure scenarios*:
PMC informed the PGM WG that work on ES will commence this summer. A coordination meeting between EBRC/WCA/PMC is planned for 31st May and a kick-off meeting with the full PGM WG will follow in June/July.
Action: PMC to check if the meeting can be combined other meetings in June to minimize travel requirements.

3. PGM project planning

3.1. Review of timeline

Project plans (Gantt charts) of the DDP programme and the full PMG programme were presented.

a) The DDP programme is proceeding as planned, with the repeated dose study (RDT) being the time-critical test.
b) The full testing programme will be started in summer after the enabling tests have been completed. This will mean that the testing programme will take until end 2013, followed by DNEL derivation and CSA/CSR preparation. A registration by the May 2013 deadline will thus unfortunately not be possible.

Due to time constraints, no further in-detail discussion took place.

4. AOB, next meeting and closing remarks

The time for the next meeting will be set once the meeting on exposure scenarios has taken place.

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