Chairman: *Dave Boyd* (Johnson Matthey)

10 January 2011, 12:30 – 18:00
Metals Conference Centre
Rue du Duc 100, B-1150 Brussels

Minutes

1. Welcome and introduction

1.1. Tour de table. The list of participants is available in Annex 1.

1.2. Approval of the Agenda. The Agenda (Annex 1) was approved.

1.3. Objective of the meeting. To set-up a PMC PGM experts group including representatives from WCA and BIBRA in charge of developing an integrated testing strategy for the PGM project, and to exchange views on key elements of ITS design adapted to these substance series.

1.4. Organisational.

- The following representatives agreed to contribute to the PGM Expert Group (PGM EG): D. Boyd, R. Brasch, P. Copestake, E. Logan, M. Raffray, K. Rothenbacher, R. Thiele, S. Verberckmoes, P. Watts, P. Whitehead and R. Winde.
- The PGM EG will exchange/communicate as follows **AP1**:
  - REACHSuite will be used as repository of reference documents
  - PGM EG will hold monthly conference calls **AP1**
  - *Ad hoc* calls/meetings with specific companies will be organised where needed
  - *Ad hoc* face-to-face meetings will be organised to discuss key questions and deliverables
- Proposals will be prepared by WCA and BIBRA and subject to iterative commenting rounds in the following order/hierarchy:
  - PMC PGM Expert Group (PGM EG), chaired by D. Boyd with involvement of K. Rothenbacher
  - PMC PGM Work Group (PGM WG), chaired by D. Boyd – discussion and approval of proposals for consideration by next levels*
  - PMC Technical Advisory Panel (TAP), chaired by M. Raffray – technical validity and consistency with other PMC projects*
  - PMC Management Committee (MC) and Assembly, chaired by G. Ethier – key milestones and budgets

  * Envisaged to occur in parallel

2. Presentation of PGM project scope and deliverables:

A summary of the work done under each Phase of the PGM project over 2008-2010 is available below:

Phase	Work performed	Deliverable(s)
I	Literature search	Phase I reports for all PGM
II	Literature review Preliminary data gap analysis Preliminary category building Preliminary testing recommendations	Draft Phase II reports for all PGM (**AP6**, **AP10**)
II CLP	CLP testing recommendations	Testing recommendations matrix
III CLP	CLP testing programme	CLP reports including IUCLID 5 extracts (Jan 2011) Status reports from Harlan GLP reports from Harlan (expected) Sample trail from Harlan
V	IUCLID 5 files set-up and completion in light of REACH Registrations	IUCLID 5 files set-up and ongoing completion
V CLP	IUCLID 5 files set-up and completion in light of CLP notifications	CLP notifications finalised

It was agreed:
- To leave the Draft Phase II reports as draft reports and generate separate fully evolved ITS reports
- That the draft Phase II reports, which are based on literature searches dated 2008, are seen as a sufficient basis to prepare the ITS report and no need for a full literature update was identified. Some targeted actions on literature re-evaluation were agreed (see below).
- To summarise the content of the Draft Phase II reports and the CLP reports in appendices of the ITS reports

3. ITS

3.1. Overview of remaining data gaps: AP11

3.2. Model ITS prepared for Re: The PGM EG agrees to follow the same basic approach/format used for the Rhenium project ITS report. The PGM project ITS reports should in addition:
- Include full sections on physico-chemical and environmental endpoints;
- Consider available test data on out-of-scope substances with read-across potential;
- Be designed as living/working documents that will be continuously updated as the different tiers of the testing programme progress

3.3. Discussion on key principles

Timeline: Unless otherwise decided by PMC depending on ITS and business needs, PMC aims to complete all PGM registrations by 2013, although the actual deadline for most substances is 2018. This means a first ITS proposal must be finalised in Q2 so as to launch the necessary enabling and first tier tests in Q3 2011 at the latest.

Preliminary/enabling information: a robust/final ITS proposal can not be developed unless the information below is provided/generated (**AP2**, **AP4**, **AP5**, **AP8**, **AP9**, **AP10**):
1. Confirmation of PGM project scope - especially status (SCC, on-site, transported) and tonnage of intermediate compounds
2. Clarification on (true) hydrates and anhydrous solids – which are:
    - Only manufactured/imported as anhydrous
    - Only manufactured/imported as hydrates
    - Manufactured/imported as anhydrous and hydrate (specify relative proportion) but both are expected to display different properties
    - Manufactured/imported as anhydrous and hydrates (specify relative proportion) and both are expected to display similar properties
3. Confirmation on wide/dispersive use for those substances potentially benefiting from Annex III exemption
4. Eco-toxicology: solubility and T/D data
5. Toxicology/Exposure assessment: solubility and pH data, bio-accessibility, dustiness
6. Toxicokinetics and dosimetry: particularly absorption characteristics, e.g. dermal bio-availability, and respiratory tract deposition behaviour

ITS: The ITS shall be designed in a way that maximises the use of read-across, tiered testing approaches (e.g. mammalian toxicity starting with *in vitro* tests) and other alternatives to testing (e.g.: (Q)SAR such as for some organoligand complexes and other models) in order to minimise vertebrate animal testing.

Preliminary tests:
In line with the above list of information needs, it was agreed to gather/generate data on:
- **Solubility:** Solubility data remains outstanding for some of the PGM compounds. Umicore was

requested to provide in-house solubility data generated for the purpose of CLP preparation. Remaining solubility data will be generated at JMTC once samples are identified and requested.
- **pH:** This test is an important enabling test for skin/eye irritancy/corrosion prediction. It is recommend testing as many substances as possible, since some insoluble substances are said to have extreme pH. Umicore provided a reference for consideration by WCA; missing pH data can be generated in-house by PMC Members using the Young *et al*. study as reference
- **Enabling tests:** In addition to solubility and pH additional information on particle size, dustiness and bio-accessibility may be required to inform the ITS and determine read-across possibilities and REACH testing needs. These will be addressed again at the next PGM EG call/meeting.
- **Skin/eye irritation/corrosion:** It was proposed to prioritise these *in vitro* tests as soon as solubility and pH data has been collected.

Route of exposure:
- One way of minimising vertebrate animal testing is to carefully select the relevant route of exposure and to explore and duly apply route-to-route extrapolations. Additional consultant support and input from other Non-Ferrous Metals groups will be required to develop a strong and robust strategy that is consistent with the approach followed under other PMC projects (e.g.: silver).
- As a start, the following shall be considered:
    - Where possible and relevant, oral route preferred – ideally model from oral route results; possible in principle, subject to certain inclusion parameters, but needs further investigation
    - If inhalation needs to be considered, several conditions should be met
    - The dermal route needs to be considered if exposure circumstances dictate, but there are approaches which permit use of data from other routes in the case of systemic toxicity. Dermal absorption/bio-availability data is typically a pre-requisite for such determination.

Read-across:
- The categories proposed in the Draft Phase II reports should be considered as preliminary only (read-across may not be feasible within these categories). These will not be revised as such. Separate ITS reports will be produced instead, including separate ITS proposals for each new cross-cutting category if necessary.
- Oxidation state will be kept as a basal default read-across basis, but is unlikely to be used in isolation.
- Different read-across categories may be required for toxicology and eco-toxicology endpoints.
- Each read-across will be duly justified in each ITS report.

Samples:
- Sample availability should be considered in the design of the ITS as some compounds are not readily available (e.g.: not manufactured on a regular basis) or available in the quantities necessary for testing.
- In case of doubt, WCA+BIBRA are recommended to develop an ITS for the hydrated form as the default option, and request PMC Members to object if the anhydrous forms should also be tested (in which case both forms would be tested).

Testing programme:
- Once the ITS is developed, WCA+BIBRA will propose options that will take account of PMC preferences/priorities as well as the test houses' experience in metals, scientific credibility, capacity, cost, etc. and the likely risk and vulnerability associated with each option (e.g.: if tests are spread across several test houses instead of a one or a few).
- The possibility of launching the test programme in a sequential manner and per endpoint rather than per metal family was proposed for some cases (e.g.: skin+eye irritation/corrosion).
- The test programme will also be launched in a more targeted/*ad hoc* approach in other cases

(e.g. for mutagenicity and sensitisation endpoints). It will also take into account test houses capacity, and preferred registration timing or other PMC priorities, etc.).

Study monitoring:

- Study monitor: preliminary proposal from WCA+BIBRA is Martin Richards, known to BIBRA for > 20 years. He has recent directly relevant REACH experience, is familiar with the main CRO test houses, and would be hired by WCA and liaise with BIBRA to oversee testing programme. His charge rates need to be negotiated - proposal to be developed by WCA (to be considered by PMC upon receipt). Given the duplicative nature of the work blocks involved, a simplistic percentage of total study costs for monitoring (e.g. 5-10%) may not be appropriate in this instance – benchmarking and options are required (**AP3**).

IUCLID 5 set-up

- Information provided by PMC Members need to be properly documented for insertion in IUCLID 5 (even if not resulting from a test)
- Justification for read-across needs to be added (in each robust study summary endpoint and/or as a standalone justification/full final ITS report in section 13)
- Literature search need to be added: matrix with all used data (including Klimisch rank) + list of all references that were identified

3.4. Roadmap towards building an ITS for PGMs: Cf. Table 1 below

4. AOB, next meeting and closing remarks

4.1. Agreed actions/timeline. Cf. Table 1 below

4.2. Next conference calls/meetings:

- *Ad hoc* conference call: Early Feb 2011
- PGM EG ftf meeting: Brussels, 10 or 11 April 2011

Table 1. Priority 1 actions agreed at 10 Jan 2011 PGM Experts Group meeting

	Action	Who?	When?
1.	Create a PGM Experts Group mailing list including: D. Boyd, R. Brasch, P. Copestake, E. Logan, M. Raffray, K. Rothenbacher, R. Thiele, S. Verberckmoes, P. Watts, P. Whitehead and R. Winde Circulate invitation for monthly conference calls starting mid February till mid June 2011	PMC (AR)	ASAP
2.	Finalise PGM project scope – Revert with feed-back on invitation to confirm intermediate status, scc as per Dec 2010 ECHA Guidance, tonnage as on-site, tonnage as transported (including two 100-1000 t/a Pt and Pd intermediates)	PMC (CB)	End Jan 2011
3.	Formulate study monitor proposal including several options	WCA	End Jan 2011
4.	Generate list of existing and missing pH data	WCA	End Jan 2011
5.	Perform draft Annex III assessment and revert with list of candidate substances	WCA	End Jan 2011
6.	Generate list of received proprietary data including name of compound, CAS n°, test n° and test result	WCA	End Jan 2011
7.	*Ad hoc* conference call to discuss progress of above action points	PGM EG	Early Feb 2011

	Action	Who?	When?
8.	Gather data from PMC Members: ☞ newly generated (test) data ☞ wide/dispersive use for Annex III substances ☞ existing/estimated solubility data for all substances ☞ existing + generated pH data for all substances	PMC (KR)	End Feb 2011
9.	Launch remaining solubility tests	PMC (KR) + JMTC (DB)	End Feb 2011
10.	Expand original Phase I and II reports to make sure: - Proprietary data on out of scope compounds is reviewed, Klimisch ranked and considered, and - Toxicokinetics associated to dermal exposure-based waiving has been fully considered/explored	WCA BIBRA	End Mar 2011
11.	Finalise Annex III assessment and reasonable worst case data gap matrices including: - Revisited traffic light code to distinguish between definitive data gaps and situations where data is available/gap can be filled without (additional) testing (distinguish between data available, read-across, and adaptations) - LD50, classification, etc. provided/triggered by the available data	WCA	End Mar 2011
12.	Circulate above deliverables to PGM EG	PMC (KR)	End Mar 2011
13.	PGM EG meeting to discuss progress of above action points and address following actions: - Formulate an enabling testing programme proposal (bio-accessibility, dustiness) to support likely read-across proposals - Formulate an initial test proposal (including CRO+Study Monitor options) to start with eye+skin irritation/corrosion test programme on potential reference substances - as a starting package for early gap filling; relatively inexpensive, in line with avoidance of animal testing, could inform the next steps of ITS - Address skin sensitisation on a more targeted fashion, using D. Basketter's expertise as needed - Further develop which conditions should be met for inhalation tests to be considered - in addition to whether or not there is potential for inhalation exposure (to be confirmed via dustiness test and respiratory tract deposition modelling (MPPD)), it is possible to generate a stable test atmosphere, there were signs of toxicity in the oral acute test, among others. - Address mutagenicity on a more targeted fashion (e.g.: Rh 3+ programme to be designed differently from other groups) - Generate decision tree to select most relevant route of exposure	PGM EG	10/11 Apr 2011