27 October 2011, 3:00pm CET

Chairperson: A. Alderman (Johnson Matthey)
Secretariat: C. Braibant (EPMF)

MINUTES

1. **Welcome and Introduction**

   1.1. **Confidentiality and Competition Law.** The participants were reminded on their obligation to comply with confidentiality rules and Competition Law.

   1.2. **Confirmed participants and apologies.** *Cf. slide 2 of Annex 2.*

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

   1.4. **Actions of the last meeting.** *Cf. slide 6 of Annex 2*; all actions have been completed with the exception of one which is on-going and will be completed by the next Re WG meeting in Dec 2011 (preparation of a Licence to Use for entities wishing to use data from the Registration Dossier and/or CLP notification).

   1.5. **Approval of the minutes of the last meeting.** The minutes were approved.

2. **Scope adjustments/confirmation.** Slide 8 of Annex 2 reflects the latest version of the Re project inventory. This contains three substances (one in the 10-100 t/a) and three intermediates (one as non-SCC).

3. **Progress of testing programme.** *Cf. Slides 10-11 of Annex 2.* The testing programme is progressing very well, with most of the tests being finalised and none revealing any hazard so far.
   The remaining tests are:

   - ***In vivo* eye irritation (Harlan, UK):** required in follow-up of the negative results obtained in the *in vitro* study performed at LAB, Hungary. In some cases *in vitro* tests are acceptable for classification (e.g.: skin irritation) whereas in other cases they are not. Indeed, whereas for the mutagenicity studies the *in vitro* tests have regulatory acceptability and are valid to derive a no-classification, in the case of eye irritation studies the *in vitro* tests are used to assess the potential for severe irritation/corrosion. If the *in vitro* eye irritation shows no effects, it is not sufficient to justify a no-classification but it indicates an *in vivo* test can be performed to assess mild to moderate irritation potential. If the *in vivo* study is also negative, then the substance can be non-classified.

   - **Combined repeated dose toxicity study with the Reproductive/developmental toxicity screening study (Charles River, UK):** This study combines several steps which can run more or less sequentially. **AP1**
     It has been difficult to obtain a homogenous suspension of APR in water and corn oil (a homogeneous suspension must be prepared in order to be administered to the test animals) and tests are currently on-going with a 40% PEG400/water suspension to check suitability. The fact that this emulsion may increase the bioavailability of APR and its potential accumulation in the tissues of the animal were questioned. **AP2**

Once the preparation of the suspension is achieved, a 7 days range-finding study can commence in order to determine the doses which need to be administered to the animals for the main study in order to determine the maximum tolerated dose and a dose-response curve. Histopathological examination may be performed as part of the 7-day range-finding study, if necropsy and other parameters suggested severe adverse effects. This would take for up to 7 weeks.
Although the current schedule indicated that draft results of the 7 days range-finding study would be available by the next Re WG meeting in Dec, the discussion on the vehicle to be used to produce a homogeneous suspension may affect this schedule. **AP3**
The discussion around proper vehicles and suspension preparation raised some doubts on the overall reliability of the existing acute oral toxicity study performed in the 70's and originally Klimisch-ranked 2. Since this study used vegetable oil to prepare the suspension which was administered to the test animals and PMC trials did not succeed with corn oil (APR formed a deposit in the bottom), there are reasons to believe the study may not be valid anymore and should be ranked with 3. The need to repeat the acute oral toxicity study (performed on vertebrate animals and hence not recommended from an animal welfare perspective) will depend on the outcome of the repeated dose study, which results can be used as a weight of evidence (in combination with the existing acute oral toxicity dataset) to fill the information requirement in a scientifically robust manner. **AP4**

- **Bio-elution study (CIMM, Chile):** A Bio-elution study allows determining the bio-accessibility of a given substance in an artificial body fluid, which mimics the conditions to which the given substance could be exposed after dermal contact and ingestion, among others. Performing a bio-elution test on rhenium metal would allow determining what happens with the material when in contact with artificial sweat or gastric acid and the dataset available for Ammonium perrhenate can be read-across to rhenium for these two exposure pathways (dermal and oral). The test is run in parallel with other bio-elution tests on Au, PGM and PGM compounds at CIMM, with which PMC has already a satisfactory relationship and which the best test house to perform these tests from a cost-quality viewpoint. The test involves a sample preparation phase (to obtain required particle sizes; d90 < 100 µm) to be performed in a specialised test house (probably the Fraunhofer Institute in Germany) before the samples can be sent to CIMM. Draft results are expected one month after commencement.

- **Toxicokinetic assessment:** Paper-based exercise for the likely toxicokinetic behaviour of APR is required to fulfil REACH requirement (8.8 in Column 1 in Annex VIII), to the extent that can be derived from the relevant available information.

- **Particle size distribution (Harlan, UK or DMT, Germany):** According to the Dec 2010 ECHA guidance on intermediates potassium perrhenate should be regarded as a non-SCC intermediate requiring a full 1-10 t/a Registration Dossier. One of the items which are required under REACH is particle size, which can be determined by a variety of methods, depending on how the particle size information will be used or applied. **AP5**

The Re project testing programme was the first full testing programme launched by the Consortium; it shows the communication, administrative and technical workload and steps involved in such a programme,

especially when tests are conducted at different test houses (due to their differences in expertise). The learning lessons of the Ag and Re project should allow a better preparation for other PMC projects.

4. **Next steps and likely need for CSR.** *Cf. Slides 13-14 of Annex 2.* So far no hazard has been identified and APR remains not classified. The need for a CSR will depend on the outcome of the combined repeat Dose and Reprotox study results expected in Q2 2012 according to the current schedule (cf. item 3 above, second bullet point, 4th §).

5. **ID cards and IUCLID 5 filling.** *Cf. Slides 16-17 of Annex 2.* One ID Card is prepared for each substance and intermediate in scope of the Re project. The aim of these ID Cards is to act as references for substance identification and sameness under REACH. It was clarified that the composition given in each ID Card was inspired from the Ag model and may hence list constituents or impurities which are not present in a Re material. **AP6** It was noted that the typical purity was obtained from MMTA standards; the classification derived by PMC in Dec 2010 applies to pure Re materials where none of the impurities (if present in concentrations higher than 0,1 %) influence the classification. If specific impurities are known to be present in a Re material they should be listed. Where their presence induces a different classification, the classification should be updated or complemented with (an) additional classification profile(s).
   WCA has already prepared one IUCLID 5 file for each Re material and is completing each file with the existing data and the data which is being generated in the testing programme. Based on the documented read-across strategy, all information on APR is added to the other files in order to make them as complete as possible and pre-empt any future information requirements under REACH. For some parts of section 1 content of the ID Card will be used. Members will also be required to generate data on the identification, composition and form/size of their substances and intermediates. For section 3.5 addressing the uses of each substance and intermediate, the Re WG members are required to complete an excel sheet (Annex 3) with all their and their customers' identified uses for each substance and intermediate. **AP7**

6. **Overall project progress, timeline and budget.** *Cf. Slides 19-23 of Annex 2.* The project is progressing as per the agreed schedule, which may be slightly adjusted on the basis of the outcome of the discussions on the selection of vehicle. **AP2**
   The number of test houses and steps involved in the monitoring of the testing programme is more significant than expected (not an exhaustive list):
   - contacting, comparing, visiting and selecting test houses
   - obtaining, reviewing, and commenting study proposals, contracts and protocols
   - ensuring sample provision
   - monitoring the test and discussing draft results
   - reviewing and commenting the draft, interim and final test reports
   - ensuring sample storage, archiving or return

   In light of the above WCA has foreseen a budget increase of ~ 11 000 £, which was supported by the Re WG. Testing costs have been slightly increased to cover for additional work required in determining the appropriate vehicle (~ 2400 £).
   Based on the current schedule (cf. item 3 above, second bullet point, 4th §), final IUCLID 5 files would be ready for review by the (Lead) Registrant(s) in Oct 2012; followed by submission before the end of that year.

7. AOB, next meetings and closing remarks

No other business was raised.

The next meeting will take place in Brussels on the 6th of December 2011 as from 4:30 pm CET as an evening meeting (**AP8**) to allow WCA and PMC secretariat's participation in the 7 Dec 2011 EM workshop on bio-elution and minimise travel costs/changes for Re WG participants.

Further meetings or conference calls will be scheduled in Feb and Jun 2012 (to be confirmed in due course).

Sincere thanks were expressed to WCA for following this project so closely and so professionally.

Experts were invited to meet as soon as possible to resolve the vehicle issue referred to in the second bullet of item 3 above in order to avoid any significant delays in the schedule.

Annexes:

1. Agenda
2. Slides
3. Use questionnaire

Table 1. Actions agreed at the 27 Oct 2011 Re WG conference call

	What?	Who?	When?
1.	Schematise the steps and work phases involved in the Repeat Dose/Reprotoxicity test package	WCA	ASAP
2.	Discuss the likelihood for PEG400 to enhance the hydrophilicity, bio-availability and/or bio-accumulation of APR at an *ad hoc* conference call	WCA and PMC experts	2 Nov pm or 4 Nov am (2011)
3.	Inform PMC on confirmed schedule	WCA	ASAP
4.	Consider the need to perform an acute oral toxicity study	WCA	After finalisation of range-finding study and/or repeated dose study
5.	Determine which method should be used to determine the particle size of potassium perrhenate	WCA + PMC	ASAP
6.	Check ID Cards (especially composition) and revert with comments, corrections or comments to rondepierre@epmf.be	Re WG	End Nov 2011
7.	Read the front page instructions and complete the questionnaire, circulate the use survey to downstream users and collect responses to it, and submit all completed questionnaires to minako.tallen@wca-environment.com	Re WG	End Nov 2011
8.	Prepare Agenda 6 Dec 2011 Re WG meeting and include: - Overall progress of testing programme - Outcome of discussion on vehicle selection - Present steps and phases of Repeat Dose/Reprotox study - Confirm schedule of testing programme - Review compositions and agree on ID Cards - Review uses reported to WCA	CB	End Nov 2011