MINUTES

1. **Welcome and Introduction.** Participants were reminded on their obligation to comply with confidentiality and Competition Law rules. The Agenda (Annex 1), slides (Annex 2) and background documents (Annex 3) were circulated prior to the meeting and also made available via GoToMeeting.

2. **Au Project**
   - **2.1. Progress of collection of existing data on Au compounds.** In relation to the mammalian toxicity test programme, information requests have been sent to PMC Members, to substances providers such as Springer, Alfa Aesar and Sigma-Aldrich, as well as to Evonik by 24 Nov 2011. To date, all responses received indicate no proprietary information exists. **Post meeting note:** During a telephone call held on 13 Dec 2011 Evonik indicated they may have some relevant data to share (not before end Jan 2012). In addition, their registration intentions for Au (III) substances will be discussed with them when their existing data is considered (**AP1**). Some further attempts will be made to obtain information existing in the pharmaceutical industry (**AP2**) but it in parallel WCA will commence a literature search to identify all publicly available information on the compounds of interest (**AP3**).
   - **2.2. Discussion on disproportionation of Au, relevant form of Au.** The information available indicates gold is more likely to exist in the form of Au 3+ or Au0/colloidal gold rather than in the form of Au 1+ in the environment and in the body. The outcome of this discussion can be used as a justification when documenting the read-across strategy from TCA to other Au compounds in scope.
   - **2.3. Progress on agreed tests (physico-chemical, eco-toxicology, bio-elution).** All tests are on-going, with a major obstacle being the delayed sample provision. Although sample providers are regularly reminded on the importance of providing test articles in time or on informing PMC secretariat in the case the sample cannot be provided within the requested timeframe, continuous reminding is needed. Next steps will involve direct calls to the sample providers (as far as allowed by PMC resources) and involving management level in the sample request to increase commitment.
     For the ecotox testing programme WCA and K. Rothenbacher have exchanged views on the selection of the most appropriate test media; it was agreed to use a low-EDTA medium (ISO medium) for the algal tests and a no-EDTA medium for the Daphnia test.
     Potential pH-related issues in ecotox tests will be assessed on the basis of the results of the on-going dose-range finding studies (using 100 mg/l as maximum concentration), once these are available in early Jan 2012 (**AP4**).
     As regards the bio-elution programme, which includes PGM, Re and Au samples, it is expected to commence in March 2012 when the sample preparation has been agreed and finalised. Based on the size of the gold samples provided for the CLP testing programme in 2010 it is expected that the powder may be too coarse for the bio-elution and that sample preparation and refinement may be needed, unless the sample provider can manufacture the sample in the required size (**AP5**).
   - **2.4. Proposed TCA mammalian toxicity testing.** If potential effects of pH in mammalian toxicity tests can be avoided or resolved (shortly after the *ad hoc* meeting with Dr David Kirkland on 14 Dec 2011), the Mouse Lymphoma Assay (MLA) and Micronucleus tests can begin (early 2012, after testing houses have been recommended by WCA and selected by the Au+PM CN- WG).
     Further testing requirements will be considered based on the results of the literature search, the ecotox and bio-elution tests (**AP3 - 6**).
   - **2.5. ITS finalisation and timeline of the Au project.** Once the results of the on-going physico-chemical tests required to finalise the Annex III assessment of the Aurio and the Balsams compounds are available the ITS report will be updated with the information available at the time. Subsequent tiers in the testing strategy work will be documented as addenda to the

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final ITS report (expected end Feb 2012) (AP7). Unless testing cannot proceed as expected, and assuming exposure data collection and assessment for CSR preparation can be done in 2012, the files would be ready for submission in 2013.

3. **PM CN- project**
   - **3.1. Scope.** Due to changes in PMC Members' REACH inventories two changes were made to the scope of the PM CN- project: increase of tonnage band of silver cyanide and removal of potassium tetrakis (Cyano-C) aurate compound. The need for testing on silver cyanide will be considered by WCA and included in the final ITS report (AP13). As regards the on-going physico-chemical testing work on the tetrakis compound, WCA will investigate the pros and cons of stopping or finalising the work and revert to PMC with a request for decision (AP8).
   - **3.2. Progress on agreed tests (physico-chemical, dustiness, eco-toxicology).** Cf. item 2.3 above. According to the sample provider of potassium dicyanoargentate the sample was sent to Brixham on 7 Dec 2011; it has so far not arrived at the test house and the test programme on this material may hence be delayed by several weeks if the sample is not received before the 16 Dec 2011 (AP9). The PM CN- compounds are not included in the bio-elution testing programme as this test is relevant for sparingly soluble compounds looking at metal cations; more specific research based on dissociation in aqueous solutions and other information may be more relevant for precious metals cyanides. However, two of the compounds have been added to the dustiness testing programme, which is being run as part of the PGM dustiness testing programme. **Post-meeting note:** *Silver cyanide was also added to the dustiness testing scope.*
   - **3.3. Discussion on limitations/possibilities to measuring free cyanide.** Although measuring free cyanide may be difficult depending on the level of detection/sensitivity of the method use, the overall analytical performance and the requirement of specific instruments and conditions, it is not impossible and should not prevent the testing programme to proceed. Intertek has been subcontracted by Brixham to perform the analytical work on their behalf; the aim of such work is to derive EC50 for the tested compound and compare this with the sensitivity of the analytical method used. It was agreed to use the dose-range finding study as a checkpoint to confirm whether any significant (analytical) issues may arise with measuring free cyanide in test media (AP10).
   - **3.4. Next steps for mammalian toxicity endpoints.** In order to support and validate the current modelling of the toxicity of precious metals cyanides, the results of the ecotox and dustiness tests should be used. Only after that will it be possible to evolve the mammalian toxicity programme of the PM CN- project (Mar 2012?), which should now also consider silver cyanide information requirements and toxicity profile (AP11).
   - **3.5. Updated paper on modelling.** The existing paper will be updated in order to include PMC's comments; the update as such will not take place before the results of the ecotox testing programme become available, as these will allow validating or informing the proposed approach. In the event the results become available in a tiered manner, the document may be updated in a stepwise manner too (AP12). This document will be kept separate from the ITS report and will be kept 'alive' and updated as necessary; it could constitute a document to be uploaded onto the relevant IUCLID 5 files to justify PMC's approach in fulfilling the REACH information requirements for precious metals cyanides.
   - **3.6. ITS finalisation and timeline of PM CN- project.** Once the testing requirements for silver cyanide are identified the ITS report will be updated with the information available at the time. Subsequent tiers in the testing strategy work will be documented as addenda to the final ITS report (expected end Feb 2012) (AP13). Unless testing cannot proceed as expected, and assuming exposure data collection and assessment for CSR preparation can be done in 2012, the files would be ready for submission in 2013.

4. **AOB and closing remarks.** All actions of the last conference calls (7 Jun and 21 Oct 2011) have been

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progressed with and addressed during the call. It was agreed to host the next conference call on 8 Feb 2012 at 10h30 am CET. The objective of this call will be to follow-up on the actions listed in Table 1 below and update participants on the overall progress and timeline of both projects (AP14).

Table 1. Actions agreed at the 13 Dec 2011 Au+PM CN- WG conference call

	What?	Who?	When?
Au			
1.	Call Evonik to confirm receipt of information request e-mail and follow-up on available information/interest in sharing data with PMC. **Post-meeting note:** *Evonik confirms having information but due to workload and limited resources cannot respond to PMC's request before end Jan 2012. Confidentiality Agreement template has meanwhile been sent to Evonik.*	CB	Done
2.	Contact companies involved in pharmaceutical applications of Au compounds to identify availability of additional information	CB+WCA	ASAP
3.	Perform literature search on sodium/potassium/ammonium tetrachloroaurate, gold trichloride, triiodide, tribromide and trinitrate in order to gather sufficient information on systemic toxicity to fulfill acute, subacute and reprotox information requirements and derive a DNEL	WCA	End Jan 2012
4.	Use ecotox dose-range finding study results as checkpoint to determine potential pH issues	WCA	Jan 2012
5.	Check possibility for sample provider of Gold provide a powder form fulfilling the conditions of the bio-elution testing protocol	CB	ASAP
6.	Evolve mammalian toxicity testing programme on the basis of the discussions on pH-related issues with D. Kirland and bio-elution test results	WCA	Jan 2012 on-going
7.	Prepare final ITS report including items below and circulate to Au+PM CN-WG: - Final annex III assessment for Aurio and Balsams compounds	WCA	End Feb 2012
PM CN-			
8.	Inform PMC on pros and cons of stopping or continuing the on-going testing programme on potassium tetrakis (Cyano-C) aurate at Harlan	WCA	ASAP
9.	Contact sample provider of potassium dicyanoargentate, clarify status of sample provision/obtain tracking number, and inform likely delay of testing programme. **Post-meeting note:** *Feed-back from sample provider indicates sample has been sent on 12 Dec 2011 and no tracking number exists.*	CB	Done
10.	Use ecotox dose-range finding study results as checkpoint to determine: - Potential pH issues - Potential difficulty to measure free cyanide - Dissociation behaviour in aqueous solutions to inform the mammalian toxicity testing programme - Likely validation of the mixture toxicity modelling approach - Need to perform validation ecotox tests on silver cyanide	WCA	Jan 2012
11.	Evolve mammalian toxicity testing programme on the basis of the discussions on pH-related issues with D. Kirland, ecotox dose-range finding study and dustiness test results	WCA	Jan 2012 on-going
12.	Update paper on mixture toxicity modelling including the items below and circulate to Au+PM CN- WG: - Replace reference to RCR by toxicity pressure or ratio	WCA	Jan 2012 on-going

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	- Include Klimisch rank of used references - Describe Annex III exemption more largely/completely - (Provisional) Evidence/information/validation provided by the (draft) results of dose-range finding ecotox study - (Informal) feed-back from MS representatives on the acceptability of the method		
13.	Prepare final ITS report including items below and circulate to Au+PM CN-WG: - Inclusion of silver cyanide and potential testing requirements	WCA	End Feb 2012
General			
14.	Organise next Au + PM CN- WG conference call to follow-up on agreed actions and project progress	Au+PM CN- WG	8 Feb 2012, 10h30 am CET

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