SECRETARIAT: K. ROTHENBACHER (EPMF, BELGIUM)

24 MARCH 2015, 15:00 – 18:45 CET
METALS CONFERENCE CENTRE – ALUMINIUM ROOM
RUE DU DUC 100 – 1150 BRUSSELS (BELGIUM)

PGM Tox Experts Meeting

Minutes

1 Welcome and 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. Phil Copestake apologized; he could not attend the meeting due to illness.

1.3 Approval of the agenda

The Agenda was approved. The slides presented during the meeting are available in Annex 2.

1.4 Approval of the minutes of the last meeting (9 Oct 2014) including status of action points

The minutes of the last meeting were approved.

Decision: It was agreed to update ITS addenda now (WCA and bibra)

Action: PMC to follow up on outstanding action points

- **Continue discussion on way forward for alpha, beta-unsaturated ketone with bibra (relevant to Palladium (II) di(4-oxopent-2-en-2-oate))**
- **Discuss the speciation of RuCl3 with Dave Boyd**
- **Update water solubility HHPA in ITS matrix**

2 Substance identification and sameness of PGMs - update

2.1 ID cards

No discussion was required on this agenda point

2.2 Sameness: Update on diammonium hexachlororuthenate vs TETRADORu

No discussion was required on this agenda point

2.3 Inventory update

PMC presented the most recent tonnage band changes:

- Rh(NO3)3: increase from 1-10t/y to 10-100t/y
- Dihydrogen hexahydroxyplatinate, compound with 2-aminoethanol (1:2): : increase from 1-10t/y to 10-100t/y
- Karstedt Concentrate: PMC may have to take over the dossier in order to cover the 10-100 tpa data requirements
- Dipotassium hexachloropalladate: increase from 10-100 tpa to 100-1000 tpa. This change was only confirmed the day before the meeting and is thus not considered in the ITS yet
- Ruthenium trichloride: increase from 1-10t/y to 10-100t/y. This change was only confirmed the day before the meeting and is thus not considered in the ITS yet
- **Action: PMC to add another change in scope: IrCl4 will be replaced by 'reaction mass of iridiumtetrachloride and iridium trichloride' (1-10 tpa)**

- The meeting reminded the registrant that in case there is new a multiconstituent sample, the registrants will need to retrospectively correct their pre-registration
- **Action: registrants of 'reaction mass of iridiumtetrachloride and iridium trichloride' to review if their pre-registration needs updating**
- Tetraammonium decachloro-mu-oxodiruthenate(4-) as the recently defined actual species will replace Ammonium hexachlororuthenate as the entity for registration (same tonnage band = 10-100 tpa)

3 PGM testing programme

3.1 Outstanding p/c tests – update

WCA gave an update on the outstanding p/c tests. The tests are ongoing; most tests have been completed or are in reporting stage now.
IrCl4 has been part of the testing programme. Similar to the Ru compound, there was no change in the actual test substance, but further evaluation indicated that the 80% rule was not met and therefore a registration as multi-constituent substance will be required.

Action: WCA to

- **Change the substance name on the ITS matrix to 'reaction mass of iridiumtetrachloride and iridium trichloride' as discussed above**
- **Discuss with the CROs if it is possible to change the substance name of the test substance substance in test reports**
- **Request an updated certificate of analysis from sample provider**

Action: WCA to update ITS matrix to reflect that an Annex III exemption for HHPA compound with 2AE no longer applies)

3.2 PGM ecotoxicity testing

WCA reported the progress to date of the ecotoxicity testing programme.

On Diamminedichloropalladium (DDP) it was noted that the NOEC of the test on *Daphnia* Reproduction is considered reliable despite considerable substance loss since the NOEC has been derived based on averaged measured data, and has therefore been corrected for this.

New test requirements:

Dihydrogen hexahydroxyplatinate with 2-aminoethanol (HHPA-2AE): tonnage increase to 10-100 tpa

- A test on **daphnia** was agreed at the previous meeting, pending confirmation of the tonnage increase. This is now confirmed and the test should thus be started.
- Since the compound has a significantly higher water solubility (it is supplied as solution) than HHPA, it is not recommended to read across ecotoxicity effects data from HHPA. Therefore in addition to the daphnia test, the **PGM tox experts group recommends to also conduct tests on algae, fish and an ASRIT test**

Hexachloroplatinic Acid (CPA):

- There is a data gap for an **ASRIT** test. The group recommends to conduct this test. The result will then be read across to diammonium hexachloroplatinate

Diammonium sodium hexakis (nitrito-N)rhodate

- There is a data gap for an ASRIT test. The group recommends to conduct this test
- An algal test was agreed at the last Working Group meeting because based on the Daphnia result read across from Rh trinitrate did not seem appropriate. Read across will be reassessed following receipt of algal result and if not appropriate an acute fish study will be required

Rhodium tri-nitrate

- There is a data gap for an **ASRIT** test. The group recommends to conduct this test

RuCl3: tonnage increase to 10-100 tpa

- Read across from other Ru substance data was not considered appropriate. There is a data gap for a tests on **algae + fish + ASRIT**. The group recommends to conduct these tests

The following table summarizes the recommended new tests:

Substance	**Test**			
Diammonium Sodium Hexakis (nitrito-N) Rhodate	acute algae		ASRIT	(acute fish)[1]
HHPA - compound with 2-AE	acute algae	acute daphnia	ASRIT	acute fish
CPA			ASRIT	
Ru dimer	acute algae	acute daphnia	ASRIT	acute fish
Rh(NO3)3			ASRIT	
RuCl3	acute algae		ASRIT	acute fish
Colour code	*approved*	*recommend to approve*		

- Dipotassium hexachloropalladate – test requirements due to tonnage increase
  - For the environmental endpoints, chronic fish, bioaccumulation and soil toxicity tests (for plants, invertebrates and soil microorganisms) will be required (testing proposals). Although under REACH Annex IX only short-term terrestrial tests are required, conducting chronic tests may be more appropriate for use in PNEC derivation.
  - It was previously agreed to read across ecotoxicity data of DDP on a worst-case basis. Pd (IV) substances have been demonstrated to rapidly decompose to Pd (II) substances, therefore read across from DDP is considered to be appropriate for Pd (IV) substances. Therefore the tests should be conducted on DDP
  - The group discussed whether the above approach should be followed or if a water accommodated fraction (WAF) of KHCPd should be tested (KHCPd is not stable in water). However, these results would only be applicable to KHCPd while the DDP data can be read across to all other Pd compounds. The group decided that testing DDP will be most appropriate

[1] In case the acute algae test indicates that read across is not appropriate

- It was recommended to submit the dossier without undue delay as most of the data is ready
- **Action: PMC to discuss with WCA/EBRC if additional ES work is needed. This work should be prioritized**

3.3 PGM genotoxicity testing

3.3.1 Rh(III) genotoxicity

A thorough discussion on Rh(III) genotoxicity took place (cf slides 30-35).

- Positive genotoxicity findings were observed for all Rh-substances, except Rh trinitrate (solid), with a trend evident from the more strongly positive results evident with Rh compounds with simple solution behaviour and high solubility to the marginally positive situation evident for compounds with more complex predicted solution behaviour, e.g. rhodium sulphate.
- At the last expert mtg it was agreed to conduct an Ames test on rhodium sulphate as a referee compound
  - The test result was positive, though only just above the strain revertant thresholds for positivity
  - A solution in sulphuric acid was tested; no solid $Rh_2(SO_4)_3$ was available for testing
  - PMC informed the group that no TSCA 8(e) notification had been filed in this case, since the result was in line with known mutagenic effects of Rh(III). There were no objections from the expert group on this.
- Next steps
  - **Decision: If both Ames tests were conducted on solids the group recommends to conduct an additional Ames test on Rh nitrate solution which is the major form manufactured within the sector.**
  - **Action: PMC to check if existing Ames tests on Rh nitrate were conducted on solids or solutions** [Post meeting note: done; all tests were done on solids. PMC will therefore proceed with an Ames test]

3.4 PGM acute/repeated dose testing

All scheduled repeated dose toxicity RDT) tests have completed their in-life phases, completed the pathology work, and are in the reporting stage now. Draft reports have been circulated in advance of the meeting for review.

Discussion of RDT reports/ initial results

- No fundamental disagreements/ concerns regarding the study reports were raised
- **Action: PMC to circulate updated study reports – data tables for ammonium hexachloroplatinate**
- **Action: participants to send any editorial comments/ questions in writing to RSA/ PMC by 2 April**

Currently available results are summarized in the following table:

		NOAEL in mg/kg bw/d	
OECD	**422**	**407**	**421**
Diammonium Sodium Hexakis (nitrito-N) Rhodate	1000 (systemic, dev., reprotox)	-	-
Palladium dihydroxide	1000 (systemic) 1000 (reprotox)	-	-
Diammonium Hexachloropalladate	-	30 (local effects) 100 (systemic)	100
Tetraamminepalladium(2+)dichloride	4 (systemic) 100 (reprotox)	-	-
Diamminedichloropalladium	> 300 (systemic, dev., reprotox)	-	-
Ammonium hexachloroplatinate Alert: classification change; STOT RE1!	-	10	30 (general tox.) 30 (reprotox) 100 (pups)
Hexahydroxyplatinic acid	1000 (general tox.) 1000 (reprotox/ pups)	-	-
Tetraammine platinum nitrate	-	-	250 (general tox.) 1000 (reprotox/ pups)

Discussion of initial study results

- Diammonium Hexachloropalladate (AHCPd): discussion if a STOT classification for local effects in the G.I. tract is required. The group concluded that this is likely not required
- **Action: PMC to confirm with bibra/RSA that a STOT classification is unnecessary and document the associated rationale based on TGD guidance**
- Tetraamminepalladium(2+)dichloride (TPdCl2): the systemic effects observed are similar to effects seen in a comparable historical study with Tetraamminepalladium hydrogen carbonate (note: an out of scope substance). No classification is expected
- Palladium (II) di(4-oxopent-2-en-2-oate): the report was agreed in general. No classification is expected
- Diammonium sodium hexakis(nitrito-N)rhodate: the report was agreed in general. No classification is expected
- Palladium dihydroxide: the report was agreed in general. No classification is expected
- Dihydrogen hexahydroxyplatinate: the report was agreed in general. No classification is expected
- Diammonium hexachloroplatinate
    - A classification of STOT RE1 will be required. This is considered scientifically justified for application to all other soluble hexachloroplatinate salts

- **Action: PMC to consider if there is a need to submit a TSCA fyi letter on this [post meeting note: an FYI letter was sent to US EPA in Dec. 2014]**
- **Action: PMC to alert PGM WG at 25 March meeting [post-meeting note: done]**
- **Action: PMC to ask bibra to update classification in ITS matrix**
- **Action: PMC to discuss with bibra if a classification for reproductive toxicity is needed. The group was undecided on this point**

Discussion of testing requirements due to increases in tonnage band

- Dihydrogen hexahydroxyplatinate compound with 2-Aminoethanol
  - Data on acute oral toxicity is available [Antonelli (2001): OECD 423, LD50 > 2000 mg/kg bw]. **Action: PMC to ask bibra to judge the reliability of this study and evaluate if any signs of toxicity were reported in the acute study which might inform in respect of planned repeat dose studies**
  - It was discussed if read across from the separate HHPA and 2-aminoethanol moieties is appropriate. The group decided that there is not sufficient evidence to support this, as the substance properties are significantly different (e.g., water solubility). Therefore, the following tests will be required:
  - Irritation**: EpiSkin** test, BCOP, followed by
  - Sensitisation: **LLNA** test
  - RDT/ genotoxicity: the expert group recommends to conduct a 28d feeding study acc. to **OECD 407, combined with an in-vivo genotoxicity test (micronucleus assay)**. The latter is required for HHPA due to previous positive in vitro genotoxicity study outcomes, and this approach will minimise redundant in vivo testing. It was recommended to submit a testing proposal for both tests as in-vivo genotoxicity testing falls under Annex IX. These tests will therefore be on hold until they are approved by ECHA.
- Dipotassium hexachloropalladate
  - The group recommended to conduct a **toxicokinetics study**, before further tests are carried out
  - Testing proposals will be required for a **90d RDT study** and a **prenatal developmental toxicity** study
  - Based on the existing RDT outcomes, and interpreting the latest TGD guidance, probably no Extended one generation reproductive toxicity study (EOGRTS) will be needed. The group recommended to submit a waiver for this endpoint and recommend to reassess when data from the 90d and prenatal studies are available
- Rhodium trinitrate
  - Read across of RDT data from Diammonium Sodium Hexakis (nitrito-N) Rhodate was not considered appropriate. There is therefore a need for an **additional RDT test based on a OECD 422 protocol**
- RuCl3
  - Read across from other Ru data was not considered possible. Therefore, the following studies will be required
  - Genotoxicity (**Ames, in vitro micronucleus test, hprt test**)
  - Sensitisation: it was suggested to submit a waiver for an **LLNA**
  - RDT study based on a **OECD 422 protocol**

4 Current status of PNEC and DNEL derivation

4.1 PNEC derivation

No discussion was required on this agenda point

4.2 DNEL derivation

No discussion was required on this agenda point

5 CLP update, CLP notifications

No discussion was required on this agenda point

6 Project Planning

6.1 Overall project plan

No discussion was required on this agenda point

6.2 New study requirements

No discussion was required on this agenda point

7 AOB, next meetings/calls and closing remarks

7.1 RMOs for chloroplatinates

No discussion was required on this agenda point – item separately addressed at the PGM WG meeting.

David Boyd informed the meeting that ECHA is in the process of revising their guidance on substance identification. This may impose additional work to characterise some UVCBs, such as PGM nitrates.
Action: PMC secretariat to review the new guidance once available and report back to the group.

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Annexes

1. Agenda & list of participants
2. Slides presented at the meeting

Actions

Table 1. Actions agreed at the 24 March PGM Tox Experts Group meeting in Brussels

	What?	Who?	When?
1.	Follow up on outstanding action points - Continue discussion on way forward for ABUK with bibra - Discuss the speciation of RuCl3 with Dave Boyd - Update water solubility HHPA in ITS matrix	PMC Sec	Q2 2015
2.	Add another change in scope: IrCl4 will be replaced by 'reaction mass of iridiumtetrachloride and iridium trichloride' (1-10 tpa)	PMC Sec	Q2 2015
3.	Registrants of 'reaction mass of iridiumtetrachloride and iridium trichloride' to review if their pre-registration needs updating	PGM WG	Q2 2015
4.	Change the substance name (IrCl4) on the ITS matrix to 'reaction mass of iridiumtetrachloride and iridium trichloride' as discussed above	WCA	Q2 2015
5.	Confirm with the CROs if it is possible to change the substance name of the test substance	WCA	Q2 2015
6.	Request updated CoA from sample provider	PMC Sec	Q2 2015
7.	Update ITS matrix to reflect that an Annex III exemption for HHPA compound with 2AE no longer applies	WCA	Q2 2015
8.	Discuss with WCA/EBRC if additional ES work is needed on KHCPd	PMC	Q2 2015
9.	Check if existing Ames tests on Rh nitrate were conducted on solids or solutions	PMC	done
10.	Initiate Ames test on Rh nitrate solution	PMC Sec	Q2 2015
11.	Circulate updated study reports – data tables for AHCPt	PMC	ASAP
12.	Send any editorial comments/ questions on RDT study reports in writing to RSA/ PMC	PGM WG	by 2 April 2015
13.	AHCPd: discuss potential need for STOT cl. of AHCPd with bibra/ RSA	PMC	Q2 2015
14.	AHCPt classification STOT RE1: consider if there is a need to submit a TSCA fyi letter on this	PMC	Done
15.	AHCPt classification STOT RE1: alert PGM WG at 25 March meeting	PMC	Done
16.	AHCPt classification STOT RE1: Ask bibra to update C/L in ITS matrix	PMC	April 2015
17.	AHCPt classification STOT RE1: discuss with bibra if a classification on reprotox is needed.	PMC	April 2015
18.	HHPA compound with 2AE: ask bibra to judge the reliability of Antonelli (2001) study and confirm if any signs of toxicity were observed	PMC	30 Apr 2015
19.	Review the new guidance on substance ID and report back to the group.	PMC	Once available