European Precious Metals Federation

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# PGM Tox Experts & Work Group Meeting

1 April 2019 | Brussels, Belgium

European Precious Metals Federation

# Welcome & Introduction

# Confidentiality and Competition law

# Tour-de-table and apologies

| DO | DON'T |
|---|---|
| **Application of competition law** | |
| Art. 101 and 102 TFEU may be applicable to the conclusion of any preliminary agreement and activities of any preliminary phase. | Don't assume that conflicts with competition law are excluded simply by the fact that the Association's Articles of Association and Internal Rules complies with the provisions of the REACH Regulation. |
| **Consultation in Matters of Competition Law** | |
| Consult an in-house legal expert or the compliance officer of your company/association or an external lawyer whenever there are uncertainties respecting compliance with competition law.<br>Stop all meetings/discussions which are not in compliance with these Compliance Guidelines until a legal expert has been involved. | Don't assume that these Compliance Guidelines deal with all competition law issues exhaustively. Basically, compliance with Art. 101 and 102 TFEU can be determined only on the basis of market impact in each individual case. These Compliance Guidelines may therefore be regarded only as a means of providing general conduct recommendations. |
| **Activities in any preliminary phase and at any other stage of operation of the Association** | |
| Restrict cooperation within the scope of the preliminary phase to the initially defined goals and purposes of the cooperation. | Pursuant to Art. 101 and 102 TFEU, activities which have the object of the effect of preventing, restricting and/or distorting competition are prohibited within the scope of the Association's Articles of Association and Internal Rules, including:<br>- Coming to agreement, including arrangements or collusions, about prices, markets and customers (see Art. 101 paragraph 1 a)-e) TFEU);<br>- Joint boycotting of other companies;<br>- The unjustified unequal treatment of trade partners;<br>- The abusive exploitation of a dominating market position. |
| **Exchange of Confidential Information** | |
| Involve a Trustee for the exchange of Confidential Information. | The exchange of Information concerning market behaviour and having the object or the effect of preventing, restricting and/or distorting competition is inadmissible; in particular, this relates to:<br>- Production capacities;<br>- Productions or sales volumes;<br>- Import volumes;<br>- Market shares;<br>- Price policy;<br>- Distribution and marketing terms;<br>- Marketing strategies;<br>- Information regarding the relationship with suppliers. |
| **Documentation on Cooperation** | |
| Keep minutes of all meetings which detail the subject of the meeting.<br>In case of uncertainty, have the contents of the minutes reviewed by an external legal expert prior to sending them to all Members.<br>Stop all meetings which are not in compliance with these Guidelines until a legal expert has been involved. | |

# Approval of the agenda

1. Welcome and Introduction *(09.00 – 09.20)*
   - Reminder on Confidentiality and Competition law
   - Tour de table and apologies
   - Approval of the agenda
   - Approval of the minutes of the last meeting (9 October 2018) and status of action points

2. Second MISA Workshop : key conclusions / workplan *(09.20 – 09.30)*

3. Palladium & Compounds *(09.30 – 10.30)*
   - Update ongoing testing
   - Budget and workplan 2020

Coffee break (10.30 – 10.45)

4. Platinum and compounds *(10.45 – 11.30)*
   - Update ongoing testing
   - Workplan 2019 + setting priorities for 2020

**FOR APPROVAL**

# Approval of the agenda *(cont'd)*

5. Rhodium & Compounds *(11.30 – 12.00)*
   - Update ongoing testing
   - Workplan 2019 + setting priorities for 2020

Lunch break (12.00 – 13.00)

6. Ruthenium and compounds *(13.00 – 13.30)*
   - Update ongoing testing
   - Workplan 2019 + setting priorities for 2020

added **7. Gold Metal**

8. Workplan and draft budget 2020 *(13.30 – 13.40)*

9. AOB, next meeting(s) and closing remarks *(13.40 – 14.00)*
   - ES for communication
   - **LR change due to Brexit**
   - **IPA testing program**
   - QICAR project under ETAP

added

**FOR APPROVAL**

# Approval of minutes of the last meeting

Final draft minutes of the meeting on 9 October 2018, circulated on 16 October 2018

**FOR APPROVAL**

# Status action points (1/4)

| ACTION | WHO? | WHEN? | STATUS |
|---|---|---|---|
| Check internally which technique can be used for palladium speciation | Companies | <21 October 2018 | *Ongoing (cfr further in slides)* |
| Include Exposure Scenarios in Chesar and link OC/RMM to standard phrases (ESCom catalogue) | EPMF secretariat | Cfr tiered approach slide 11 | ✓ 1st batch circulated (cfr further in slides) |
| Draft MISA workplan with actions agreed during meeting | EPMF secretariat | <15 November 2018 | ✓ Shared with ECHA 8 Nov |
| Rediscuss update PGM metal dossiers to replace current waivers based on bioelution data | EPMF secretariat + companies | 1 April 2019 (spring BtB meeting) | *Ongoing (cfr further in slides)* |
| Communicate about classification PdO and/or Rh2O3 for oxidizing properties (if required) | EPMF secretariat | After receipt testing report | ✓ Shared with members 18/10 |
| Check if effects in DRF PdCl2 are not palatability effects, and gavage should be used instead. | EPMF secretariat & RSA | <end Oct 2018 | ✓ *Checked - reporting ongoing*<br>*'There was an initial reduction in food consumption for the female animals of the high dose group (10000 ppm $PdCl_2$ in the diet) at the start of treatment which recovered after the first week of the study.* ***The pattern of the reduced food consumption and lower body weight was consistent with a palatability effect****.'* |

# Status action points (2/4)

| ACTION | WHO? | WHEN? | STATUS |
|---|---|---|---|
| Draft justification document for direct in vivo skin sensitization testing (and not in vitro as first tier) | Johnson Matthey | <end Nov 2018 | *Ongoing (cfr further in slides)* |
| Agree on dosing for full OECD422 assay with Pdacac | EPMF secretariat+companies | <21 October 2018 | ✓ Full study started (1st dosing 13 March; 0-3-10-30 mg/kg/d) |
| Decide to continue RDT/Repro screening assay with PtN | EPMF secretariat+companies | once PtN SID/ sameness is clarified | *Ongoing, dpd outcome SID clarification (cfr further slides)* |
| Finalise RAJR HHPA group + send to members for review | EPMF secretariat +companies | <end Oct 2018 | *Ongoing (1st draft available, to be shared)* |
| Send PtN test samples to Evonik for 195Pt NMR analysis | PtN registrants | <21 October 2018 | ✓ *Samples sent by all registrants* |
| Develop manufacturing process/reaction scheme for PtN | PtN registrants | once PtN SID/ sameness is clarified | ✓ *SID finalised (cfr further in slides)* |

# Status action points (3/4)

| ACTION | WHO? | WHEN? | STATUS |
|---|---|---|---|
| Inform with candidate testing labs for iv mutagenicity testing on price + experience with metals | EPMF secretariat | <end Nov 2018 | ✓ *(cfr further in slides)* |
| Check internally on other candidate labs for iv mutagenicity testing + inform about preferred testing lab | companies | <end Oct 2018 | ✓ No additional labs contacted |
| Inform EPMF secretariat about agreement renaming Karstedt Concentrate to ‚1,3-diethenyl-1,1,3,3-tetramethyldisiloxane and its platinum(0) complexes'. | KC registrants | <21 October 2018 | ✓ All registrants responded, ECHA SID process ongoing |
| Karstedt Concentrate LR to update dossier | Heraeus | <end Oct 2018 | ✓ Dossier updated |
| Update KC SID card following dossier updates | EPMF secretariat | <end Nov 2018 | ✓ SID card updated 12 Nov |
| Draft RAJR for Rh(III) mutagenicity and have TP+RAJR reviewed by Mark Raffray | EPMF secretariat + Mark Raffray | <end Nov 2018 | ✓ Dossier updated (submission pending) |

# Status action points (4/4)

| ACTION | WHO? | WHEN? | STATUS |
|---|---|---|---|
| Check if RhI3 dissolution work can be done in house | Companies | <end Oct 2018 | ✓ Umicore agreed to test |
| Perform RhI3 dissolution work by company or in external testing lab | EPMF secretariat | <end 2018 | *Ongoing at Umicore* |
| Review proposal for additional TD testing of organic metal salts vs organometals | Companies | <21 October 2018 | *Ongoing (cfr further in slides)* |
| Include budget for additional TD testing in 2019 budget | EPMF secretariat | <end Oct 2018 | ✓ Included in 2019 budget |
| Inform EPMF Secretariat if nanoPGMs need registrations under REACH | Companies | ASAP and at latest <end 2018 | ✓ No need to change dossiers for inclusion nanoPGMs |

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# Second MISA Workshop

# Key conclusions (1/2)

- Good IND participation to MISA:
  - 18 consortia
  - 321 substances

- ECHA positive on MISA (organisation, participation and IND engagement)

- **ECHA positive on format and quality EPMF HH workplan**

- Non-MISA participation metals in focus of ECHA / MS

  → serious requests for additional testing & dossier revisions

# Key conclusions (2/2)

- **2nd MISA workshop** 7 Feb in Helsinki (ECHA premises)
- Focus on **environmental** endpoints
  - IND to complete Self-Assessment Tool
  - 4 topics identified by EM and ECHA:
    - read-across
    - ERV/PNEC derivation
    - bioaccumulation and Secondary Poisoning
    - difficult-to-test substances.
- **3 EPMF presentations**:
  - BAF and BCF for data-poor metals
  - ERV/PNEC derivation for data-poor metals
  - QICARs for data-poor metals (*project under ETAP – cfr later in meeting*)
- 25 key learnings drafted by EM / ECHA + meeting minutes

# Workplan

- EPMF **ENV workplan** drafted & shared with membership 1 March
  → no input received
  → submitted to ECHA 18 March (<29 March deadline)

- **Key actions** identified (*cfr further in slides*):
  - Drafting RAJR (read-across justification reports) + addressing counter-ion effect (*addressed under ETAP*)
  - Proper documentation TDp in dossier
  - Organic metal salts: generate 24h TDp data to show rapid dissociation
  - Update and refine PNEC/ERV (cfr ongoing Pd ecotox testing & lit review)
  - Review sediment & soil assessments: Equilibrium-Partitioning ~screening (OK if RCR is 'low')
  - Derivation BAF/BCF for Pt (cfr STOT-RE classification)
  - Update AnnexIII to VII: need to generate further ecotox data

- Actions partly covered in 2019 budget or included in draft 2020 budget

# Palladium and compounds

# Update ongoing testing

- **Palladium monoxide**
  - Oxidising properties (BAM, 2018)
    - **CLP/GHS: Oxidising solid cat 1 (H271)**
    - **TDG: Class 5.1 'Oxidising substances', Packaging group I**
  - Bioelution (ECTX, 2018)
    - Gastric: 2h release <0.00028%
    - Perspiration: 168h release <0.0028%

# Update ongoing testing

- **Tetraamminepalladium dichloride**
  - Algae tox (Fraunhofer, 2018)
    - EC50 (yield): 3.12 µg Pd/L
    - EC10 (yield) 2.11 µg Pd/L
    - NOEC: 2.46 µg Pd/L
  - *Daphnia* reproduction (Fraunhofer, 2019)
    - EC10 (reproduction) 35.7 µg Pd/L
    - NOEC: 42.7 µg Pd/L
  - ASRIT (Fraunhofer, 2019)
    - EC50: 44.6 mg TI/L (TI = 42% Pd)
    - EC10: 16.4 mg TI/L
    - NOEC: 15.9 mg TI/L
  - AMES (Covance, 2018)
    - Negative

# Update ongoing testing

- **Palladium di(4-oxopent-2-en-2-oate)**
  - Algae tox (Fraunhofer, 2018)
    - EC50 (yield): 11.2 µg Pd/L
    - EC10 (yield): 5.19 µg Pd/L
    - NOEC: 4.64 µg Pd/L
  - *Daphnia* reproduction (Fraunhofer, 2019)
    - EC10 (reproduction) 1.9 µg Pd/L
    - NOEC: 1.6 µg Pd/L
  - ASRIT (Fraunhofer, 2019)
    - EC50: 119.25 mg TI/L (TI = 42% Pd) *! extrapolated value !*
    - EC10: 6.68 mg TI/L
    - NOEC: 5.14 mg TI/L

# Update ongoing testing

- **Palladium di(4-oxopent-2-en-2-oate)**
  - RDT / Repro screening (OECD422, LPT):
    - 14-d DRF - dosing 1:
      - 0 – 100 – 300 – 1000 mg/kg/d (gavage)
      - MD & HD: prematurely sacrificed TD6
      - LD: excess of MTD for main study

      → Uncertainly for dose setting full test
    - 14-d DRF – dosing 2:
      - 0 – 30 – 60 mg/kg/d (gavage)
      - HD excess of MTD for main study

      Agreed dose setting by TE: 0 – 3 – 10 – 30 mg/kg/d
    - main study:
      - experimental initiation (oestrus cycle monitoring: 27 Feb
      - 1st application: 13 March

# Update ongoing testing

- **Palladium di(4-oxopent-2-en-2-oate)**
  - RDT / Repro screening (OECD422, LPT) – status TD29
    - 1 female died at GD25
      - Necropsy revealed reddish discoloured thymus, red discoloured lungs, inflated and empty intestines, very thin stomach mucosa.
      - No changes in behaviour, external appearance or faeces and no differences in BW were noted for remaining females of high dose group

# Update ongoing testing

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      - no changes in behaviour, external appearance or faeces and no differences in BW were noted for remaining females of high dose group

Test-item related?
Wait for all data…

    - Observations TD29:
      - one high dose male noted with breathing sounds on TD 28.
      - no changes noted for the female animals.
    - Body weight TD29
      - high dose males: BW remains slightly decreased (6.1% below control group, statistically not significant).
      - no changes for the female animals.
    - Food consumption
      - dose-dependently reduced food consumption for male animals of the intermediate and high dose group between TD 22 & 28 (12.6% and 25.1% below value of control group, statistically significant at $p < 0.05$ or 0.01).
      - for female animals, reductions for intermediate dose group (14.1% below control, not statistically significant) and for high dose group (22.6% below control, statistically significant at $p < 0.01$).

# Update ongoing testing

- **Palladium di(4-oxopent-2-en-2-oate)**
  - RDT / Repro screening (OECD422, LPT) – status TD29

Figure 1 Body weight of male animals
daily mean values

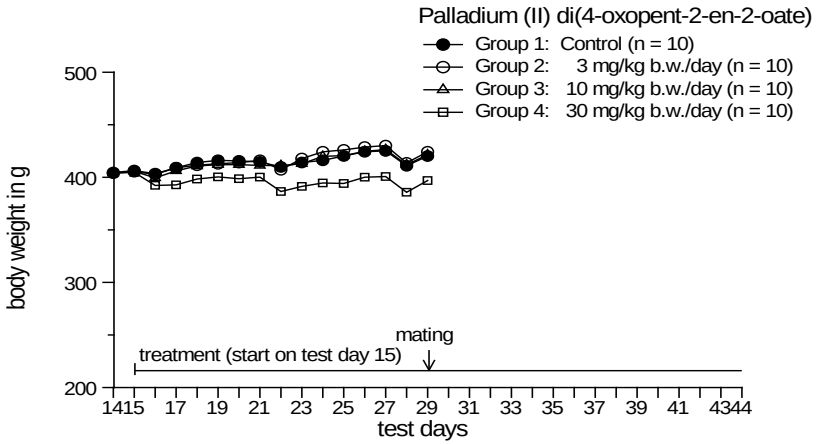



Figure 2 Body weight of female animals - Pre-mating period
daily mean values

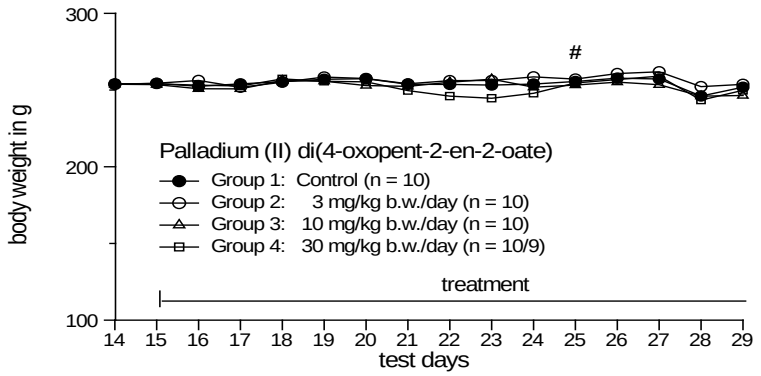



Figure 5 Food consumption of male animals - Pre-mating period
weekly mean values

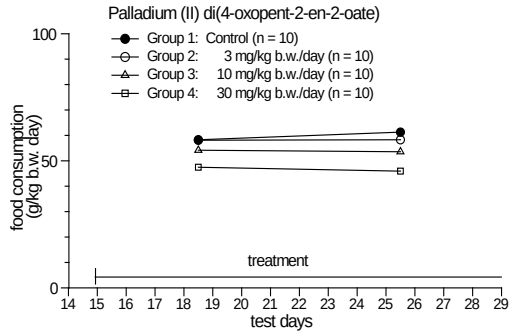
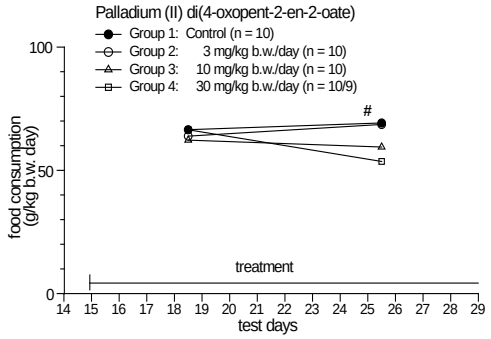



Figure 6 Food consumption of female animals - Pre-mating period
weekly mean values



# Update ongoing testing

- **Palladium dichloride:**
  - AMES (Covance, 2018)
    - Negative
  - In vitro gene mutation at *tk* locus (Covance, 2018)
    - Negative
  - RDT / Repro screening (OECD407/421, LPT):
    - 14-d DRF:
      - 0 – 1000 – 3000 – 10000 mg/kg diet
      - HD: males prematurely sacrificed TD9, female BW recovered during 2$^{nd}$ week
      - Effective TI intake:
        - 78 – 222 – 367 mg/kg/d for males
        - 82 – 250 – 707 mg/kg/d for females

# Update ongoing testing

- **Palladium dichloride:**
  - RDT / Repro screening (OECD407/421, LPT):
    - 14-d DRF:
      - HD in excess of MTD for males
      - HD well tolerated by females

      → dosing full study to be discussed soon
    - Ongoing stability assessment:
      - Weylchem (LPT subcontractor lab) not capable to detect TI in food
      - Scienceport contacted by EPMF (used by CitoxLab in past)
        - Initially difficulties to recover from diet – interference with (organic?) residues in the extract

        …but… '*we can now recover the test item in much better dry form,and after dissolution obtain a much better signal*'

        …awaiting feasibility report (expected soon!)

# Update ongoing testing

- **Disodium tetrachloropalladate:**
  - Skin sensitization (LPT)
    - In vivo skin sensitization
    - **Results showing skin sensitization potential**

*'In conclusion, under the present test conditions, the test item Disodium Tetrachloropalladate,* ***showed a positive response****. The Stimulation Index (SI) of the BrdU labelling index* ***exceeded the threshold-value of 1.6*** *at the highest concentration of 5%(w/w) (in this case SI = 1.881) and no obvious signs of irritation were observed. This* ***may indicate skin sensitizing properties*** *of the test item Disodium Tetrachloropalladate.'*

- Draft report just received

**→ TSCA notification required?**

(cfr. substance currently skin sensit 1A via RA)

**FOR APPROVAL**

# Update ongoing testing

- **Disodium tetrachloropalladate:**
  - RDT / Repro screening (OECD407/421, LPT):
    - 14-d DRF:
      - 0 – 1000 – 3000 – 10000 mg/kg diet
      - HD:
        - reductions BW, BW gain, food consumption for males
        - Reduction absolute weight liver and kidneys for males, but no sign. Effect on relative weight. Considered to be related with reduced BW and not indicative of target organ tox.
      - Mean TI intake:
        - 77 – 232 – 609 mg/kg/d for males
        - 87 – 260 – 794 mg/kg/d for females

        → dosing full study to be discussed soon

# Update ongoing testing

- **Disodium tetrachloropalladate:**
  - RDT / Repro screening (OECD407/421, LPT):
    - Ongoing stability assessment:
      - Weylchem (LPT subcontractor lab) not capable to detect TI in food
      - Scienceport contacted by EPMF (used by CitoxLab in past)

‘*Good results for recovery from diet and IR detecti*on’

…awaiting feasibility report (expected soon!)

# Update ongoing testing

- **Pd ecotox dataset**

  = newly generated data, *XX (N)* = nominal concentrations

| *in µg Pd/L* | DDP | K2PdCl4 | H2PdCl4 | TAPd Cl2 | TAPd HCO3 | PdCl2 | Pdacac | Pd nitrate |
|---|---|---|---|---|---|---|---|---|
| *Short term tox (EC50)* | | | | | | | | |
| fish | 154 | | >20 | | 189 | | | 46400 |
| Daphnia | 35,2 | | 29 | | 46,5 | 13 | 76 | 680 |
| Algae | 2,03 | *30 (N)* | 4,4 | 3,12 | *23,6 (N)* | 5,7; 7 | 11,2 | 25,2 |
| ASRIT | 30700 | | | 18800 | 12500 | | 41200 | |
| *Long-term tox (EC10)* | | | | | | | | |
| Daphnia | >14,3 | | | 35,7 | | | 1,6 | |
| Algae | 1,43 | *30 (N)* | 2,9 | 2,11 | *11,9 (N)* | | 5,19 | 15,6 |

# Update ongoing testing

- **Pd ecotox dataset**
  - **Aims**: **improve ecotox dataset, review PNEC / ERV** setting & check if appropriate to **split in different groups**

| *in µg Pd/L* | DDP | K2PdCl4 | H2PdCl4 | TAPd Cl2 | TAPd HCO3 | PdCl2 | Pdacac | Pd nitrate |
|---|---|---|---|---|---|---|---|---|
| *Short term tox (EC50)* | | | | | | | | |
| fish | 154 | | >20 | | 189 | | | 46400 |
| Daphnia | 35,2 | | 29 | | 46,5 | 13 | 76 | 680 |
| Algae | 2,03 | *30 (N)* | 4,4 | 3,12 | *23,6 (N)* | 5,7; 7 | 11,2 | 25,2 |
| ASRIT | 30700 | | | 18800 | 12500 | | 41200 | |
| *Long-term tox (EC10)* | | | | | | | | |
| Daphnia | >14,3 | | | 35,7 | | | 1,6 | |
| Algae | 1,43 | *30 (N)* | 2,9 | 2,11 | *11,9 (N)* | | 5,19 | 15,6 |
| | Cl-coordinated Pd(II/IV) cmpds | | | TAPd cmpds | | 'Uncomplexed' Pd cmpds | | |

# Update ongoing testing

- **Pd ecotox dataset**
  - Most sensitive species = algae, **no indication of difference** between different groups

| *in µg Pd/L* | DDP | K2PdCl4 | H2PdCl4 | TAPd Cl2 | TAPd HCO3 | PdCl2 | Pdacac | Pd nitrate |
|---|---|---|---|---|---|---|---|---|
| *Short term tox (EC50)* | | | | | | | | |
| fish | 154 | | >20 | | 189 | | | 46400 |
| Daphnia | 35,2 | | 29 | | 46,5 | 13 | 76 | 680 |
| Algae | 2,03 | *30 (N)* | 4,4 | 3,12 | *23,6 (N)* | 5,7; 7 | 11,2 | 25,2 |
| ASRIT | 30700 | | | 18800 | 12500 | | 41200 | |
| *Long-term tox (EC10)* | | | | | | | | |
| Daphnia | >14,3 | | | 35,7 | | | 1,6 | |
| **Algae** | **1,43** | *30 (N)* | **2,9** | **2,11** | *11,9 (N)* | | **5,19** | **15,6** |
| | Cl-coordinated Pd(II/IV) cmpds | | | TAPd cmpds | | 'Uncomplexed' Pd cmpds | | |

# Update ongoing testing

- **Pd ecotox dataset**
  - **Pd speciation in ENV = Pd(II) hydroxides, little free ion**:

1/ **expert opinion** '*Instability of palladium (IV) in the Environment*' by **D Boyd (2013)**

[*It is therefore concluded that* ***Pd(IV) will not survive in biological and environmental systems*** *due to its inherent instability, ease of reduction and its ability to reductively form strong complexes with organic nitrogen and sulphur containing moieties*.]

2/ **Fortin 2011** [*the* ***aqueous speciation of Pd is largely dominated by a single species at circumneutral pH: Pd(OH)2****. Chloro-complexes can also form but in significant proportions only at acidic pHs. It should be noted here that, according to these calculations, free Pd2+ ion concentrations are well below the atto-mol/L (10-18 mol/L) level and even below zepto-mol/L (10-21 mol/L) at pH > 7*.]

3/ **Le Faucheur 2019** [*The speciation of the data-poor metals in the algal experimental media was* ***dominated by the formation of neutral hydroxo-complexes*** *(~100%), e.g., […], $Pd(OH)_2^0$, $Pt(OH)_2^0$, $Rh(OH)_3^0$ and $Ru(OH)_3^0$ […] The* ***free ion species*** *of the data-poor metals were present at* ***very low levels*** *in the exposure media*.]

→ **same conclusion <u>for daphnid and fish</u> media, and <u>for all test compounds</u>**

# Update ongoing testing

- **Pd ecotox dataset**
  - **Proposal**:
    - **No split** in different groups (cfr. speciation to same species)
    - **Merge all Pd tox data** into 1 dataset
    - Use **average values** where possible

      → increase of PNECs (!!) compared to current situation
    - Have **ERV & PNEC review/derivation done by ARCHE** (10K included in 2019 budget)

      → *EPMF dataset + outcome lit review*

      → *use of compartment specific data where possible (e.g. sediment, soil)*

      → *ensure all 'common' metal approaches are implied, rather than using current worst-case situation*

**FOR APPROVAL**

# Update ongoing testing

- **Rapid dissociation Organic Metal Salts** (cfr 2018 autumn BtB meeting + conclusions MISA ENV WS)
  - Test OMS via 24h TDp screening test to show rapid dissociation

    → if OK, then assess as other metal cmpds (incl. potential contribution of counter-ion)

    → if not rapidly dissociating, assess as organometal cmpd (i.e. substance specific testing)

  - Test cost (ECTX offer 2018):
    - **5378.6 €** (incl 50€ shipment) for first sample
    - **3920.9 €** for each additional sample

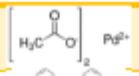
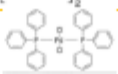
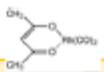
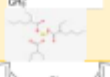
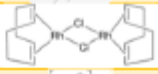
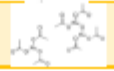
  - **Action point companies**: '*Review proposal for additional TD testing of organic metal salts vs organometals*'

    → 1 reply…

# Update ongoing testing

- **Rapid dissociation Organic Metal Salts**

**3 potential candidates to test**

| *Name* | *CAS* | | *Water solub (OECD105)* | |
|---|---|---|---|---|
| Palladium(II) acetate | 3375-31-3 |  | 922 (Harlan 2011) | ← test |
| Dichlorobis(triphenylphosphine)palladium | 13965-03-2 |  | 0,066 (Harlan 2011) | |
| Tetrakis(triphenylphosphine)palladium | 14221-01-3 |  | <0,12 (Gregory 2014) | |
| Carbonyl(pentane-2,4-dionato-O,O')(triphenylphosphine)rhodium | 25470-96-6 |  | <0,024 (Harlan 2011) | |
| Carbonylhydrotris(triphenylphosphine)rhodium | 17185-29-4 |  | <0,051 (Harlan 2011) | |
| Dicarbonyl(pentane-2,4-dionato-O,O')rhodium | 14874-82-9 |  | 650 (Gregory 2014) | |
| Rhodium tris(2-ethylhexanoate) | 20845-92-5 |  | 9,8 (Gregory 2014) | |
| Di-μ-chloro-bis(hapto-1,5-cyclooctadiene)dirhodium(I) | 12092-47-6 |  | 1560 (Harlan 2011) | |
| Tris(triphenylphosphine) rhodium (I) chloride | 14694-95-2 |  | <0,09 (Harlan 2011) | |
| Rhodium (III) acetate *(UVCB!)* | 42204-14-8 |  | 404x10^3 (Winde 2011) | ← test |
| Hexakis[mu-(acetato-O:O')]-μ3-oxo-triangulo-triruthenium acetate / Ruthenium acetate | 55466-76-7 |  | 660x10^3 (Gregory 2014) | ← *test?* |

**FOR APPROVAL**

***cfr AOB – registration dormant***

# Update ongoing testing

- **Rapid dissociation Organic Metal Salts**
  - **Proposal**:
    - **Test (2 or) 3 acetates** via 24h TDp protocol

      (approx 4400 € testing cost/sample in case of 3)
    - Depending on outcome:
      - Apply ENV RA approach with other metal cmpds, OR
      - Generate substance specific test data (algae + acute daphnia) when updating Annex III to VII

      (approx 6000€ + 7000€ testing cost/sample)

    - For all **other substances listed, generate substance specific test data** (algae + acute daphnia) when updating Annex III to VII

**FOR APPROVAL**

# Update ongoing testing

- **Skin sensitization waiver:**
  - Data gaps PtO, $Rh_2O_3$, $RuO_2$ and $Na_2PdCl_4$
  - Agreement to test directly *in vivo* (LLNA, OECD442B) instead of *in vitro* (cfr. minutes of BtB meetings 2017-2018)
  - JM proposal to **draft waiving statement** for in vitro assays

*In Vitro methods are available to address the end-point of skin sensitisation as described in OECD guidance Document 256 & ECHA 2018 "How to use new or revised in vitro test methods to address skin sensitisation", although these methods are not currently suitable to establish skin sensitisation potency. "Currently, there is no generally approved and/or validated way how to combine results obtained from in chemico and in vitro methods to assess the skin sensitisation potency. Some approaches on how to combine the in vitro data have been described in the ECHA Guidance (Appendix r.7.3-4) and in the OECD guidance Document 256, Annex 1. Due to this, an OECD project has been launched in 2107 to assess how in vitro data obtained from these three key events and other data can be combined to conclude on the skin sensitisation potency classification with a defined approach."*

*Therefore, to establish Disodium tetrachloropalladate skin sensitisation potency, which is required for registration, the following testing will be conducted:*

*Skin Sensitisation: Local Lymph Node Assay: BrdU-ELISA, OECD 442B (2010)*

→ **Sent to TE on 26/3 for input.**

**Questions**: inclusion Kimber publications + argumentation of 'non-acceptability' of solid negative in vitro test dataset for metals (cfr. suggestions earlier meetings)?

# Update ongoing testing

- **Speciation analysis Pd cmpds**
  - RAAF compliant RAJR need to be drafted for various Pd groups
  - ‘Speciation to similar toxicologically active species’ need to be shown
  - For Pt, $^{195}$Pt NMR has been used

    → what technique can be used for Pd?
    - Raman? eg spectra TAPd cmpds show typical peak around 502 cm-1

    - *Umicore input pending*

# Workplan 2019-20

- Literature review HH (Pd cmpds)
- Ongoing RDT/Repro testing

  → include in REACH dossiers

  → revise read-across / grouping + RAJRs

  → revise DNELs & exposure scenarios
- Pd metal dossier: replace waivers based on substance inertness (cfr. MISA WP) – cfr. next slides

# Workplan 2020

- **Pd ITS matrix**
  - PC endpoints: all Pd metal specific data
  - ENV endpoints: filled using TDp & 'Pd-ion' data
  - HH data: **proposal to group Pd metal – PdO – Pd(OH)2**

| | **Pd metal** | **PdO** | **Pd(OH)2** |
|---|---|---|---|
| **Water solubility** | TD data (poorly soluble) | TD data (poorly soluble) | TD: max release 1,02 µg/L |
| **Dustiness** Total dustiness / Inhalable / Thoracic / Respirable fractions | DMT (2012) ***Pd black*** *457.02 / 296.34 / 103.03 / 36.73 mg/g* **Pd powder** 284.26 / 166.71 / 18.37 / 2.36 mg/g | DMT (2012) 566.83 / 335.63 / 44.27 / 6.3 mg/g | DMT (2012) 138.92 / 83.16 / 14.97 / 3.16 mg/g |
| **Respiratory tract deposition** Head / TB / Pulmonary / Total | wca (2012) ***Pd black*** *51.9 / 0.41 / 0.64 / 52.9%* **Pd powder** 45.8 / 0.12 / 0.08 / 46.0% | wca (2012) 46.3 / 0.12 / 0.085 / 46.5% | wca (2012) 46.6 /0.16 / 0.19 / 47.0% |
| **Bio-elution** (µg/m²) | ***Pd black*** *Gastric 2hr: 7019.0* *Dermal 24 hr: 27.93* *Dermal 168 hr: 84.8* **Pd powder** Gastric 2hr: 13978.3 Dermal 24 hr: 131.97 Dermal 168 hr: 137.3 | ECTX, (2018**)** Gastric 2hr: <3,1 Perspiration (168h): <3,1 | Gastric 2hr: 3819.3 Dermal 24 hr: 51.32 Dermal 168 hr: 127.8 |

# Workplan 2020

| | Pd metal | PdO | Pd(OH)2 |
|---|---|---|---|
| Skin irritation *in vitro* | in vivo data | In vivo data | **RA from Pdacac,** OECD 439<br>[See also in vivo] |
| Eye irritation *in vitro* | In vivo RA data | In vivo data | In vivo RA data |
| Skin sensitisation | Arcelin, 1992<br>OECD 406 not sensitising<br>+ Bio-elution and T/D data | Waive based on T/D data (insoluble) | **RA Pdacac**, OECD 429 LLNA<br>**Skin Sens. 1** |
| *In vitro* gene mutation study in bacteria | RA /WoE from available data<br>RA from Pd dinitrate OECD 471, -ve | Read-across from Pd dinitrate<br>Verspeek-Rip (2003) OECD 471, -ve | **RA from Pd dinitrate** OECD 471, -ve |
| Acute toxicity, oral route | RA from PdO<br>No classification | Published data (Holbrook et al., 1975)<br>LD50>4.9 g/kg bw | **RA from Pd dinitrate**<br>**Acute tox 4 (oral)** |
| Skin irritation *in vivo* | OECD 406 (Modified OET) not irritant<br>+ Bio-elution and T/D data | not required at this tonnage<br>Cambell et al., 1975 (Tested form unspecified) - no classification | RA from palladium monoxide, non irritant |
| Eye irritation *in vivo* | RA from PdO<br>+T/D data available | not required at this tonnage<br>Hysell et al. 1974<br>No reaction after 3 d; No classification | **RA from Pdacac**, OECD 405<br>**Eye Dam. 1** |
| *In vitro* cytogenicity in mammalian cells | RA /WoE proposed<br>RA from Pd dinitrate OECD 487, -ve | not required at this tonnage | **RA from Pd dinitrate**, OECD 487, -ve |
| *In vitro* gene mutation study in mammalian cells | RA /WoE proposed<br>RA from Pd dinitrate OECD 476, -ve | not required at this tonnage | **RA from Pd dinitrate** OECD 476, -ve |
| Acute toxicity, inhalation | Waive: not a relevant route of exposure | not required at this tonnage. Waive: not a relevant route of exposure | Waive: not a relevant route of exposure |
| Acute toxicity, dermal route | Data waiver | not required at this tonnage | **RA from TAPd HCO3**<br>**RA from Pd (acac)2** In no classification |
| Short-term repeated dose toxicity oral/ dermal/ inhalation | RA from palladium dihydroxide NOAEL 1000 mg/kg bw/day (systemic; reprotox)<br>+Bio-elution and T/D<br>No systemic DNELs required | not required at this tonnage | Tested form: powder<br>OECD TG422 - NOAEL 1000 mg/kg bw/day (systemic; repro-dev) |
| Reproductive toxicity | | not required at this tonnage | |
| Toxicokinetics, metabolism and distribution | Proposed absorptions<br>Oral: 100%<br>Dermal 10%<br>Inhalation: 100% | not required at this tonnage | Proposed absorptions<br>Oral: 100%<br>Dermal 10%<br>Inhalation: 100% |

# Workplan 2020

## Get rid of RA from Pdacac (cfr. ongoing testing) & Pd nitrate (UVCB)

| | Pd metal | PdO | Pd(OH)2 |
|---|---|---|---|
| Skin irritation *in vitro* | in vivo data | In vivo data | **RA from Pdacac,** OECD 439<br>[See also in vivo] |
| Eye irritation *in vitro* | In vivo RA data | In vivo data | In vivo RA data |
| Skin sensitisation | Arcelin, 1992<br>OECD 406 not sensitising<br>+ Bio-elution and T/D data | Waive based on T/D data (insoluble) | **RA Pdacac**, OECD 429 LLNA<br>**Skin Sens. 1** |
| *In vitro* gene mutation study in bacteria | RA /WoE from available data<br>RA from Pd dinitrate OECD 471, -ve | Read-across from Pd dinitrate<br>Verspeek-Rip (2003) OECD 471, -ve | **RA from Pd dinitrate** OECD 471, -ve |
| Acute toxicity, oral route | RA from PdO<br>No classification | Published data (Holbrook et al., 1975)<br>LD50>4.9 g/kg bw | **RA from Pd dinitrate**<br>**Acute tox 4 (oral)** |
| Skin irritation *in vivo* | OECD 406 (Modified OET) not irritant<br>+ Bio-elution and T/D data | not required at this tonnage<br>Cambell et al., 1975 (Tested form unspecified) - no classification | RA from palladium monoxide, non irritant |
| Eye irritation *in vivo* | RA from PdO<br>+T/D data available | not required at this tonnage<br>Hysell et al. 1974<br>No reaction after 3 d; No classification | **RA from Pdacac**, OECD 405<br>**Eye Dam. 1** |
| *In vitro* cytogenicity in mammalian cells | RA /WoE proposed<br>RA from Pd dinitrate OECD 487, -ve | not required at this tonnage | **RA from Pd dinitrate,** OECD 487, -ve |
| *In vitro* gene mutation study in mammalian cells | RA /WoE proposed<br>RA from Pd dinitrate OECD 476, -ve | not required at this tonnage | **RA from Pd dinitrate** OECD 476, -ve |
| Acute toxicity, inhalation | Waive: not a relevant route of exposure | not required at this tonnage. Waive: not a relevant route of exposure | Waive: not a relevant route of exposure |
| Acute toxicity, dermal route | Data waiver | not required at this tonnage | **RA from TAPd HCO3**<br>**RA from Pd (acac)2** In no classification |
| Short-term repeated dose toxicity oral/ dermal/ inhalation | RA from palladium dihydroxide NOAEL 1000 mg/kg bw/day (systemic; reprotox)<br>+Bio-elution and T/D<br>No systemic DNELs required | not required at this tonnage | Tested form: powder<br>OECD TG422 - NOAEL 1000 mg/kg bw/day (systemic; repro-dev) |
| Reproductive toxicity | | not required at this tonnage | |
| Toxicokinetics, metabolism and distribution | Proposed absorptions<br>Oral: 100%<br>Dermal 10%<br>Inhalation: 100% | not required at this tonnage | Proposed absorptions<br>Oral: 100%<br>Dermal 10%<br>Inhalation: 100% |

# Workplan 2020

- Proposal to **generate Pd(OH)2 specific test data**:

| | Cost / assay (euro) |
|---|---|
| In vitro skin irritation | 3000 |
| In vitro eye irritation | 3500 |
| Skin sensitisation (in vivo?) | 5500 |
| In vitro gene mutation in bacteria | 5500 |
| In vitro cytogenicity (micronucleus) | 17000 |
| In vitro mamm cell gene mutation (tk) | 13000 |
| Acute tox (oral) | 5500 |
| Study monitoring (Approx 60h) | 10000 |
| Test substance (approx 50g) | 5000 |
| ***TOTAL*** | ***+/- 70000*** |

**FOR APPROVAL**

# Budget 2020

| | |
|---|---|
| **11. Pd metal** | **17.805 €** |
| | |
| **11.1 REACH registration** | **0 €** |
| **11.2 REACH dossier maintenance** | **10.500 €** |
| **11.3 REACH evaluation** | **0 €** |
| **11.4 REACH classification & labelling** | **0 €** |
| **11.5 REACH authorisation** | **0 €** |
| **11.6 Internal and external fixed Scientific Managers** | **6.505 €** |
| **11.7 IUCLID IT hosting system** | **400 €** |
| **11.8 Knowledge Management tool + hosting** | **400 €** |
| | |
| **12. Pd compounds** | **199.586 €** |
| | |
| **12.1 REACH registration** | **0 €** |
| **12.2 REACH dossier maintenance** | **140.000 €** |
| **12.3 REACH evaluation** | **0 €** |
| **12.4 REACH classification & labelling** | **0 €** |
| **12.5 REACH authorisation** | **0 €** |
| **12.6 Internal and external fixed Scientific Managers** | **48.786 €** |
| **12.7 IUCLID IT hosting system** | **400 €** |
| **12.8 Knowledge Management tool + hosting** | **400 €** |
| **12.10 Science budget** | **10.000 €** |

# COFFEE BREAK

# Platinum and compounds

# Update ongoing testing

- **Platinum dioxide:**
  - Skin sensitization (LPT)
    - In vivo skin sensitization
    - Draft report available, not skin sensitizing
  - AMES (Covance, 2018)
    - Negative

# Update ongoing testing

- **Platinum nitrate:**
  - RDT / Repro screening (OECD407/421, LPT):
    - 14-d DRF:
      - PtN tested as solid

        0 – 300 – 1000 – 3000 mg/kg diet on TD 1-14

        0 – 10000 – 7000 – 3000 mg/kg diet on TD 15-29
      - No premature deaths
      - HD: Reduced BW for males and females, but related to reduced food intake (ie, not considered adverse)
      - Mean TI intake:
        - TD 1-14: 21– 70 – 214 mg/kg/d for males, 24 – 78 – 249 mg/kg/d for females
        - TD 15-29: 194 – 426 – 580 mg/kg/d for males, 235, 536, 782 mg/kg/d for females

  → **study on hold due to ECHA SID questions**

# Update ongoing testing

- **Platinum nitrate:**
  - TP for in vivo mutagenicity included
  - TP investigation preceeded by **SID check**

  - June 2018: ECHA questions on SID:
    - Identity main constituent (e.g. Pt oxidation state)
    - Reaction scheme
    - Additional analytics to support

  - **195Pt NMR**:
    - 4 solutions analysed
      - Pt(IV) dominant (>90%), little to no signal in Pt(II) region
      - Pt(OH)x(NO3)y monomeric or polymeric species
      - Spectra some level of similarity, but also differences (~reflecting UVCB nature)

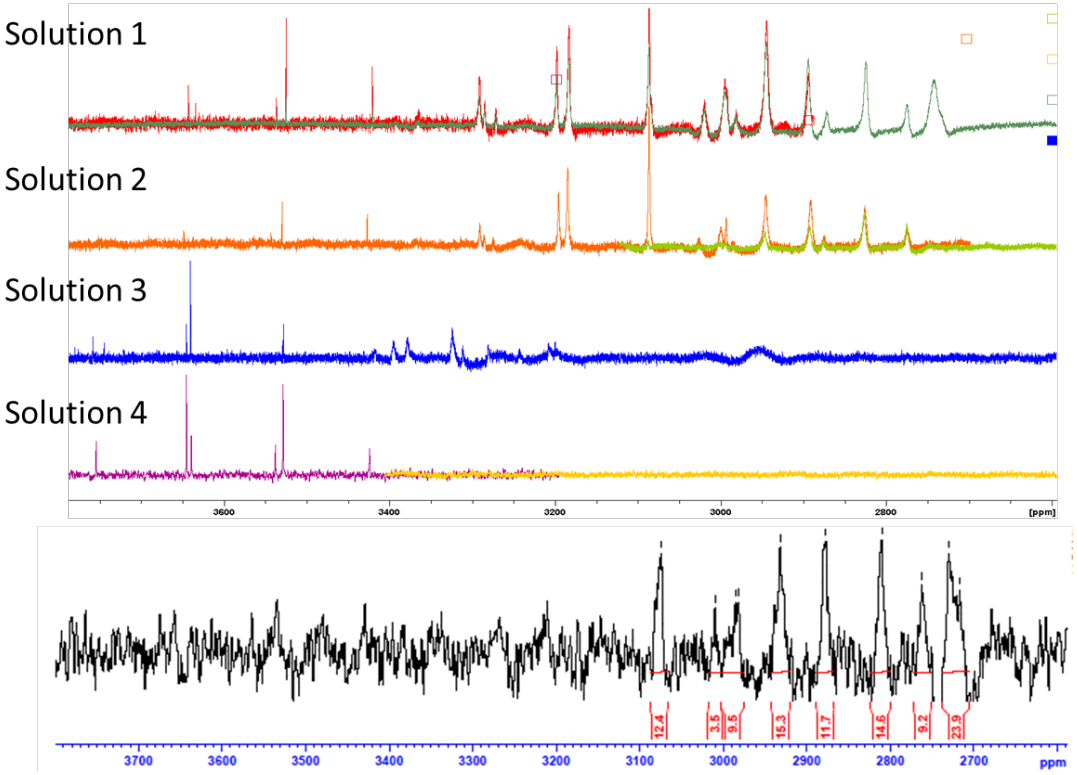
# Update ongoing testing

- **Platinum nitrate:**
  - **195Pt NMR:**
    - 1 solid analysed
      - No NMR signal in Pt(II) and Pt(IV) region
      - Vasilchenko: '*due to complex mixture of mono- and polymeric species*'
    - Redissolved solid (in diluted $HNO_3$) – similar spectrum to solutions 1-3
  - **PDF (Pair Distribution Function)**
    - 1 solid analysed
    - Support for Pt-hydroxo-nitrato clusters identified by Vasilchenko et al (i.e. Pt(IV) species)
  - **EXAFS/XANES:**
    - 1 solid & 1 solution analysed
    - Considered **no suitable** technique for PtN SID by Tox Experts

      Cfr.

# Update ongoing testing

- **Platinum nitrate:**



# Update ongoing testing

- **Platinum nitrate:**
  - **Way-forward:**
    - Registration strategy remains, i.e. solid registered and solutions considered as mixture
    - Update IU section 1.2 with revised manufacturing process / reaction scheme

      *! Each registrant to include himself company specific details !*
    - Update IU section 1.4 with revised analytics:
      - Pt NMR spectra for each registrant
      - PDF analysis for registrant with solid sample
    - New identifiers requested:
      - '***Platinum(IV) aqua hydroxo nitrato complexes***'
    - 1 company will leave joint-registration (sameness questioned)
  - Email to ECHA (29/3) by LR to check agreement with proposal
  - LR to resubmit updated dossier ASAP after approval
  - Co-reg will be informed when they need to take action

# Update ongoing testing

- **Platinum nitrate:**
  - **Way-forward:**
    - RDT/Repro screening:
      - Sameness solid vs solution confirmed
      - **Proposal to take up DRF, and continue as originally agreed**
        (i.e. solid PtN as test item)

**FOR APPROVAL**

# Update ongoing testing

- **Testing Proposals in vivo mutagenicity testing**
  - **Draft decisions** received for 3 TPs:
    - TAPt-group (with TAPt chloride as proposed test item (TI))
    - Dipotassium tetrachloroplatinate
    - Hexachloroplatinate-group (with diammonium HClPt as proposed TI)
  - **Public consultation** launched for
    - Hexahydroxoplatinate-group (with HHPA-2AE as proposed TI)
  - **SID investigation PtN** ongoing, public consultation expected soon

# Update ongoing testing

- **Testing Proposals in vivo mutagenicity testing**
  - Revised DD received for TAPt TP (Proposal for Amendment by DK):
    - Referring to discussion in MSC-RAC workshop (Oct 2018): '*for comet assay, gonadal tissue cells should be collected and processed into slides and these should be stored in order to limit additional animal testing*.'
    - PfA1: **slides** shall be prepared from single cell/nuclei suspensions from **gonadal tissues** & stored for up to 5 years. In case a **positive result** is obtained from any of the somatic tissues in the Comet assay the **gonadal slides shall be analysed**.
    - PfA2: Adjust the discussion of gonadal sampling in Appendix 1: Reasons to reflect Pfa 1 and include that: "*A negative or inconclusive result in whole gonads cannot be used to conclude on the germ cell genotoxicity as the sensitivity of the comet in gonadal cells has not been validated to detect germ cell genotoxicity*."

**→ registrant input <8 April – AGREE OR ANY INPUT TO PROVIDE?**

**FOR APPROVAL**

# Update ongoing testing

- **Testing Proposals in vivo mutagenicity testing**
  - **Offers** requested from **LPT & Covance**
    - **LPT**: '*we have numerous experience conducting the Comet Assay combined with in vivo Micronucleus testing. We already have established protocols and performed studies for your requested tissues more than 10 studies. Three of the tests were with metals*'
    - **Covance**: '*We have wide experience with various classes of pharmaceuticals and chemicals, however, experience with metal salts is limited. We have historical control ranges for the requested tissues: liver, glandular stomach, duodenum and gonad*.'

***LPT and Covance have historical control data for tissues requested, experience with metals 'limited' for both***

# Update ongoing testing

- **Testing Proposals in vivo mutagenicity testing**

  **assumed setup**: rats (1 gender), oral admin, three admin (0 – 24 – 45h), sacrifice/ sampling at 48h, 3 treatment groups+neg/pos control

| | LPT | Covance |
|---|---|---|
| DRF | 3500 | **£**32215<br>+2160 for TK |
| Main study | 43000 | |
| TK reporting (6 timepoints) | 8000 (+360 per additional timepoint)<br>+ 3500 for TK evaluation | |
| Additional tissue (gonads) | 5800 (sampling+storage)<br>or 7800 (sampling+direct scoring) | **£**10955+8575+5865 |
| Formulation analysis | ***NOT INCLUDED!*** | *£10170+4170+1800+2000* |
| Histological analysis (required in case of pos results) | 1350 (per tissue and per sex) | |
| Analytics: method development + validation$ | 12000 | included |
| Analysis blood samples | 18000 (+3000 per additional timepoint) | included |
| **TOTAL** | **90-95K €** | **£75-80K** |

*if corrosive TI, histopath and comet scoring might be required in DRF – price increase
$method development + validation once for all Pt tests? Plus **12,5% price reduction if all genetox ordered**

# Update ongoing testing

- **Testing Proposals in vivo mutagenicity testing**

  **assumed setup**: rats (1 gender), oral admin, three admin (0 – 24 – 45h), sacrifice/ sampling at 48h, 3 treatment groups+neg/pos control

| | LPT | Covance |
|---|---|---|
| DRF | 3500 | |
| Main study | 43000 | £32215 +2160 for TK |
| TK reporting (6 timepoints) | 8000 (+360 per ad… …epoint) + 3500 … …luation | |
| Additional tissue (gonads) | …mpling+storage) …sampling+direct scoring) | £10955+8575+5865 |
| Formulation analysis | ***NOT INCLUDED!*** | *£10170+4170+1800+2000* |
| Histological analysis (required in ca… …esults) | 1350 (per tissue and per sex) | |
| Analytics: method develop… …idation$ | 12000 | included |
| Analysis blood s… | 18000 (+3000 per additional timepoint) | included |
| **TOTAL** | **90-95K €** | **£75-80K** |

Tentative numbers – need thorough investigation for final/definitive numbers

*if corr…sive TI, histopath and comet scoring might be required in DRF – price increase
$method development + validation once for all Pt tests? Plus **12,5% price reduction if all genetox ordered**

# Workplan 2020

- Literature review HH (chloroplatinates, Pt cmpds, Karstedt Conc)

- Ongoing RDT/Repro testing PtN

  → include in REACH dossiers

  → revise DNELs & exposure scenarios (where required at all)

- Pt metal dossier: replace waivers based on substance inertness (cfr. MISA WP) – cfr next slides

# Workplan 2020

- **Pt ITS matrix**
  - PC endpoints: all Pt metal specific data
  - ENV endpoints: filled using TDp & ‘Pt-ion’ data
  - HH data: **proposal to group Pt metal – PtO2**

| | **Pt metal** | **PtO2** |
|---|---|---|
| **Water solubility** | TD data (poorly soluble) | TD data (poorly soluble) |
| **Dustiness**<br>Total dustiness / Inhalable / Thoracic / Respirable fractions | DMT (2012)<br>**Pt black**<br>205.45; 157.25; 126.22; 60.55 mg/g<br>**Pt sponge**<br>72.65; 41.92; 3.38; 0.49 mg/g | No data |
| **Respiratory tract deposition**<br>Head / TB / Pulmonary / Total | wca (2012)<br>**Pt black**<br>72.3; 1.8; 6.0; 80.1%<br>**Pt sponge**<br>43.9; 0.098; 0.053; 44.1% | No data |
| **Bio-elution** (µg/m²) | ***Pt black***<br>*Gastric 2hr: 15.1*<br>*Dermal 24 hr: 26.67*<br>*Dermal 168 hr: 48.3*<br>**Pt powder**<br>Gastric 2hr: 22.4<br>Dermal 24 hr: 8.73<br>Dermal 168 hr: 18.2 | No data |

# Workplan 2020

**Generate bioelution data for PtO2? (gastric + perspiration; approx 6000€ testing cost)**

- **Pt ITS matrix**
  - PC endpoints: all Pt metal specific data
  - ENV endpoints: filled using TPp & 'Pt-ion' data
  - HH data: **proposal to group Pt metal – PtO2**

| | **Pt metal** | **PtO2** |
|---|---|---|
| **Water solubility** | TD data (poorly soluble) | TD data (poorly soluble) |
| **Dustiness**<br>Total dustiness / Inhalable / Thoracic / Respirable fractions | DMT (2012)<br>**Pt black**<br>205.45; 157.25; 126.22; 60.55 mg/g<br>**Pt sponge**<br>72.65; 41.92; 3.38; 0.49 mg/g | No data |
| **Respiratory tract deposition**<br>Head / TB / Pulmonary / Total | wca (2012)<br>**Pt black**<br>72.3; 1.8; 6.0; 80.1%<br>**Pt sponge**<br>43.9; 0.098; 0.053; 44.1% | No data |
| **Bio-elution** (µg/m²) | ***Pt black***<br>*Gastric 2hr: 15.1*<br>*Dermal 24 hr: 26.67*<br>*Dermal 168 hr: 48.3*<br>**Pt powder**<br>Gastric 2hr: 22.4<br>Dermal 24 hr: 8.73<br>Dermal 168 hr: 18.2 | **No data** |

# Setting priorities for 2020

## Proposal to test 2 in vitro muta assays and RDT/Repro screening

| | Pt metal | PtO2 |
|---|---|---|
| Skin irritation *in vitro* | See in vivo<br>Possibility of conducting in vitro irritancy/corrosivity tests using particulate Pt | Data waiver - in vivo data available |
| Eye irritation *in vitro* | See in vivo<br>Possibility of conducting in vitro irritancy/corrosivity tests using particulate Pt | Data waiver - in vivo data available |
| Skin sensitisation | Waive based on T/D data (insoluble) | Tested form: solid - OECD442B, NEGATIVE |
| *In vitro* gene mutation study in bacteria | Waive based on bio-elution data - no classification | Tested form: solid – Ames OECD471, NEGATIVE |
| Acute toxicity, oral route | Waive based on bio-elution & T/D data with support from PtO2 no classification. | Tested form: powder – not classified |
| Skin irritation *in vivo* | Waive based on bio-elution & T/D data with support from PtO2 - no classification | Tested form unspecified<br>- concluded that the test substance failed to give any indication of irritation (score 0) on both intact and abraded skin (mean of reactions at 24 and 72 hours).<br>WoE changed to Key |
| Eye irritation *in vivo* | Waive based on bio-elution & T/D data with support from PtO2 - no classification | Tested form: powder<br>not irritating |
| *In vitro* cytogenicity in mammalian cells | Waive based on bio-elution data - no classification | not required at this tonnage |
| *In vitro* gene mutation study in mammalian cells | Waive based on bio-elution data - no classification | not required at this tonnage |
| Acute toxicity, inhalation | Waive: not a relevant route of exposure | not required at this tonnage |
| Acute toxicity, dermal route | Waive based on bio-elution and T/D data (insoluble) | not required at this tonnage |
| Short-term repeated dose toxicity oral/ dermal/ inhalation | Waive based on bio-elution and T/D data | Limited published data available |
| Reproductive toxicity | | not required at this tonnage |
| Toxicokinetics, metabolism and distribution | Proposed absorptions<br>Oral: 0.5%<br>Dermal 10%<br>Inhalation: 100% | not required at this tonnage<br>Moore et al., 1975 Retention in rats following inhalation exposure |

# Setting priorities for 2020

## Proposal to test 2 in vitro muta assays and RDT/Repro screening

| | Pt metal | PtO2 |
|---|---|---|
| Skin irritation *in vitro* | See in vivo<br>Possibility of conducting in vitro irritancy/corrosivity tests using particulate Pt | Data waiver - in vivo data available |
| Eye irritation *in vitro* | See in vivo<br>Possibility of conducting in vitro irritancy/corrosivity tests using particulate Pt | Data waiver - in vivo data available |
| Skin sensitisation | Waive based on T/D data (insoluble) | Tested form: solid - OECD442B, NEGATIVE |
| *In vitro* gene mutation study in bacteria | Waive based on bio-elution data - no classification | ted form: solid – Ames OECD471, NEGATIVE |
| Acute toxicity, oral route | Waive based on bio-elution & T/D data with support fro<br>PtO2 no classification. | Tested form: powder – not classified |
| Skin irritation *in vivo* | Waive based on bio-elution & T/D data with support f<br>PtO2 - no classification | Tested form unspecified<br>- co uded that the test substance failed to give any i ation of irritation (score 0) on both intact and abr ed skin (mean of reactions at 24 and 72 hours).<br>WoE changed to Key |
| Eye irritation *in vivo* | Waive based on bio-elution & T/D data with suppo rom<br>PtO2 - no classification | Tested form: powder<br>not irritating |
| *In vitro* cytogenicity in mammalian cells | Waive based on bio-elution data - no classifi on | not required at this tonnage |
| *In vitro* gene mutation study in mammalian cells | Waive based on bio-elution data - no classi tion | not required at this tonnage |
| Acute toxicity, inhalation | Waive: not a relevant route of expos | not required at this tonnage |
| Acute toxicity, dermal route | Waive based on bio-elution and T/D data (insoluble) | not required at this tonnage |
| Short-term repeated dose toxicity oral/ dermal/ inhalation | Waive based on bio-elution and T/D data | Limited published data available |
| Reproductive toxicity | | not required at this tonnage |
| Toxicokinetics, metabolism and distribution | Proposed absorptions<br>Oral: 0.5%<br>Dermal 10%<br>Inhalation: 100% | not required at this tonnage<br>Moore et al., 1975 Retention in rats following inhalation exposure |

# Workplan 2020

- Literature review HH (chloroplatinates, Pt cmpds, Karstedt Conc)
- Ongoing RDT/Repro testing PtN

  → include in REACH dossiers

  → revise DNELs & exposure scenarios (where required at all)
- Pt metal dossier: replace waivers based on substance inertness
  - Bioelution: 6000 €
  - In vitro mutagenicity: 35000 €
  - RDT/Repro screening: 250000 €

# Workplan 2020

- Literature review HH (chloroplatinates, Pt cmpds, Karstedt Conc)
- Ongoing RDT/Repro testing PtN

  → include in REACH dossiers

  → revise DNELs & exposure scenarios (where required at all)
- Pt metal dossier: replace waivers based on substance inertness
  - Bioelution: 6000 €
  - In vitro mutagenicity: 35000 €
  - RDT/Repro screening: 250000 €
- Bioaccumulation/bioconcentration potential Pt:
  - Cfr STOT-RE1 classification ClPt
  - Proposal to perform literature review first – 15000 €
- Update ENV assessment (PNEC/ERV & ES) where required following 2018 lit review
- Follow-up TP in vivo muta & KC EOGRTS

# Workplan 2020

- Literature review HH (chloroplatinates, Pt cmpds, Karstedt Conc)
- Ongoing RDT/Repro testing PtN

  → include in REACH dossiers

  → revise DNELs & exposure scenarios (where required at all)
- Pt metal dossier: replace waivers based on substance inertness
  - Bioelution: 6000 €
  - In vitro mutagenicity: 35000 €
  - RDT/Repro screening: 250000 €
- Bioaccumulation/bioconcentration potential Pt:
  - Cfr STOT-RE1 classification ClPt
  - Proposal to perform literature review first – 15000 €
- Update ENV assessment (PNEC/ERV & ES) where required following 2018 lit review
- Follow-up TP in vivo muta & KC EOGRTS

? PRIORITIES ?

**FOR APPROVAL**

# Budget 2020

| | |
|---|---|
| **7. Pt metal** | **315.062 €** |
| | |
| 7.1 REACH registration | 0 € |
| 7.2 REACH dossier maintenance | 298.000 € |
| 7.3 REACH evaluation | 0 € |
| 7.4 REACH classification & labelling | 0 € |
| 7.5 REACH authorisation | 0 € |
| 7.6 Internal and external fixed Scientific Managers | 16.262 € |
| 7.7 IUCLID IT hosting system | 400 € |
| 7.8 Knowledge Management tool + hosting | 400 € |
| | |
| **8. Chloroplatinates** | **55.062 €** |
| | |
| 8.1 REACH registration | 0 € |
| 8.2 REACH dossier maintenance | 38.000 € |
| 8.3 REACH evaluation | 0 € |
| 8.4 REACH classification & labelling | 0 € |
| 8.5 REACH authorisation | 0 € |
| 8.6 Internal and external fixed Scientific Managers | 16.262 € |
| 8.7 IUCLID IT hosting system | 400 € |
| 8.8 Knowledge Management tool + hosting | 400 € |

# Budget 2020

| | |
|---|---|
| **9. Karstedt** | **30.062 €** |
| | |
| **9.1 REACH registration** | **0 €** |
| **9.2 REACH dossier maintenance** | **13.000 €** |
| **9.3 REACH evaluation** | **0 €** |
| **9.4 REACH classification & labelling** | **0 €** |
| **9.5 REACH authorisation** | **0 €** |
| **9.6 Internal and external fixed Scientific Managers** | **16.262 €** |
| **9.7 IUCLID IT hosting system** | **400 €** |
| **9.8 Knowledge Management tool + hosting** | **400 €** |
| | |
| **10. Pt compounds (others)** | **126.493 €** |
| | |
| **10.1 REACH registration** | **0 €** |
| **10.2 REACH dossier maintenance** | **50.000 €** |
| **10.3 REACH evaluation** | **0 €** |
| **10.4 REACH classification & labelling** | **0 €** |
| **10.5 REACH authorisation** | **0 €** |
| **10.6 Internal and external fixed Scientific Managers** | **65.693 €** |
| **10.7 IUCLID IT hosting system** | **400 €** |
| **10.8 Knowledge Management tool + hosting** | **400 €** |
| **10.9 Science budget** | **10.000 €** |

# Rhodium and compounds

# Update ongoing testing

- **Dirhodium trioxide**
  - Oxidising properties (BAM, 2018)
    - **CLP/GHS: Oxidising solid cat 1 (H271)**
    - **TDG: Class 5.1 'Oxidising substances', Packaging group I**
  - Acute tox, oral (LPT, 2018)
    - LC50>2000 mg/kg
    - Not classified
  - In vitro skin irrit/corr (LPT, 2019)
    - Epiderm, non-irritant
  - In vitro eye irrit/corr (*draft report available*)
    - BCOP, non-irritant & non corrosive
  - Skin sensit (*draft report available*)
    - Test repeated (strange response with increasing dosing), issue with positive control
    - Not sensitising (*draft report available*)

# Workplan 2019-20

- Update Annex III to VII as approved (cfr. testing to be initiated this year)
- Update ENV assessment (PNEC/ERV & ES) where required following 2018 lit review
- Follow-up in vivo TP

? PRIORITIES ?

**FOR APPROVAL**

# Budget 2020

| | |
|---|---|
| **13. Rh metal** | **17.934 €** |
| | |
| **13.1 REACH registration** | **0 €** |
| **13.2 REACH dossier maintenance** | **10.500 €** |
| **13.3 REACH evaluation** | **0 €** |
| **13.4 REACH classification & labelling** | **0 €** |
| **13.5 REACH authorisation** | **0 €** |
| **13.6 Internal and external fixed Scientific Managers** | **6.634 €** |
| **13.7 IUCLID IT hosting system** | **400 €** |
| **13.8 Knowledge Management tool + hosting** | **400 €** |
| | |
| **14. Rh III compounds** | **95.552 €** |
| | |
| **14.1 REACH registration** | **0 €** |
| **14.2 REACH dossier maintenance** | **35.000 €** |
| **14.3 REACH evaluation** | **0 €** |
| **14.4 REACH classification & labelling** | **0 €** |
| **14.5 REACH authorisation** | **0 €** |
| **14.6 Internal and external fixed Scientific Managers** | **49.752 €** |
| **14.7 IUCLID IT hosting system** | **400 €** |
| **14.8 Knowledge Management tool + hosting** | **400 €** |
| **14.9 Science budget** | **10.000 €** |

# Budget 2020

| 15. Rh compounds (others) | 52.384 € |
|---|---|
| | |
| 15.1 REACH registration | 0 € |
| 15.2 REACH dossier maintenance | 35.000 € |
| 15.3 REACH evaluation | 0 € |
| 15.4 REACH classification & labelling | 0 € |
| 15.5 REACH authorisation | 0 € |
| 15.6 Internal and external fixed Scientific Managers | 16.584 € |
| 15.7 IUCLID IT hosting system | 400 € |
| 15.8 Knowledge Management tool + hosting | 400 € |

# LUNCH BREAK

# Ruthenium and compounds

# Update ongoing testing

- **Ruthenium(IV) dioxide**
  - In vitro skin irrit/corr (LPT, 2018)
    - Epiderm, non-irritant
  - Skin sensit (*draft report available*)
    - Not sensitising
  - AMES (Covance, 2018)
    - Negative

# Workplan 2019-20

- Literature review HH (Ru cmpds)
- Update Annex III to VII as approved (cfr. testing to be initiated this year)
- Ru metal dossier: replace waivers based on substance inertness

# Workplan 2019-20

**Generate bioelution data for RuO2? (gastric + perspiration; approx 6000€ testing cost)**

- **Ru ITS matrix**
  - PC endpoints: all Ru metal specific data
  - ENV endpoints: filled using TPp & ‘Ru-ion’ data
  - HH data: **proposal to group Ru metal – RuO2**

| | **Ru metal** | **RuO2** |
|---|---|---|
| **Water solubility** | TD data (poorly soluble) | TD data (poorly soluble) |
| **Dustiness**<br>Total dustiness / Inhalable / Thoracic / Respirable fractions | DMT (2012)<br>**Ru black**<br>401.12; 265.11; 119.36; 33.36 mg/g<br>**Ru powder**<br>48.48; 32.8; 16.6; 5.32 mg/g | No data |
| **Respiratory tract deposition**<br>Head / TB / Pulmonary / Total | wca (2012)<br>**Ru black**<br>53.2; 0.6; 0.81; 54.6%<br>**Ru powder**<br>54.9; 0.69; 0.89; 56.4% | No data |
| **Bio-elution** (µg/m²) | **Ru black**<br>Gastric 2hr: 4.5<br>Dermal 24 hr: 1.93<br>Dermal 168 hr: 1.89<br>**Ru powder**<br>Gastric 2hr: N/D<br>Dermal 24 hr: 0.136<br>Dermal 168 hr: 0.2 | No data |

# Workplan 2019-20

| | Ru metal | RuO2 |
|---|---|---|
| Skin irritation *in vitro* | See in vivo | Tested form: solid - OECD439<br>NEGATIVE |
| Eye irritation *in vitro* | See in vivo | NA- in vivo data available |
| Skin sensitisation | Waive based on bio-elution and T/D data (insoluble) | Tested form: solid - OECD442B<br>not skin sensitizing<br>reporting ongoing |
| *In vitro* gene mutation study in bacteria | Waive based on bio-elution and T/D data | Tested form: solid - Ames OECD471<br>NEGATIVE |
| Acute toxicity, oral route | Waive: based on bio-elution and T/D data with support from RuO2 - no classification. | Collier (1982a). Safepharm. OECD 401, LD50 > 2000 mg/kg bw. |
| Skin irritation *in vivo* | Waive based on bio-elution and T/D data | Not required at this tonnage |
| Eye irritation *in vivo* | Waive based on bio-elution and T/D data with support from RuO2 - no classification | Collier (1982b), OECD 405, Overall irritation score (unwashed group) = 21. Overall irritation score (washed group) = 15. not irritating |
| *In vitro* cytogenicity in mammalian cells | Waive based on bio-elution and T/D data | Not required at this tonnage |
| *In vitro* gene mutation study in mammalian cells | Waive based on bio-elution and T/D data | Not required at this tonnage |
| Acute toxicity, inhalation | Waive: Enabling studies indicate not a relevant route of exposure | Not required at this tonnage |
| Acute toxicity, dermal route | Waive based on bio-elution and T/D data (insoluble) | Not required at this tonnage |
| Short-term repeated dose toxicity oral/ dermal/ inhalation | Waive based on bio-elution and T/D data | Not required at this tonnage |
| Reproductive toxicity | | Not required at this tonnage |
| Toxicokinetics, metabolism and distribution | Proposed absorptions<br>Oral: 1%<br>Dermal 10%<br>Inhalation: 100% | Not required at this tonnage<br><br>Willard et al., 1957 Distribution of RuO2 in mice following injection |

# Workplan 2019-20

## Proposal to test 2 in vitro muta assays and RDT/Repro screening

| | Ru metal | RuO2 |
|---|---|---|
| Skin irritation *in vitro* | See in vivo | Tested form: solid - OECD439<br>NEGATIVE |
| Eye irritation *in vitro* | See in vivo | NA- in vivo data available |
| Skin sensitisation | Waive based on bio-elution and T/D data (insoluble) | Tested form: solid - OECD442B<br>not skin sensitizing<br>reporting ongoing |
| *In vitro* gene mutation study in bacteria | Waive based on bio-elution and T/D data | Tested form: solid - Ames OECD471<br>NEGATIVE |
| Acute toxicity, oral route | Waive: based on bio-elution and T/D data with support f[illegible]n RuO2 - no classification. | Co[illegible]r (1982a). Safepharm. OECD 401, LD50 > 2000 mg/kg bw. |
| Skin irritation *in vivo* | Waive based on bio-elution and T/D data | Not required at this tonnage |
| Eye irritation *in vivo* | Waive based on bio-elution and T/D data with suppo[illegible]rom RuO2 - no classification | C[illegible]er (1982b), OECD 405, Overall irritation score (un[illegible]ed group) = 21. Overall irritation score (washed group) = 15. not irritating |
| *In vitro* cytogenicity in mammalian cells | Waive based on bio-elution and T/D data | Not required at this tonnage |
| *In vitro* gene mutation study in mammalian cells | Waive based on bio-elution and T/D da | Not required at this tonnage |
| Acute toxicity, inhalation | Waive: Enabling studies indicate not a releva[illegible]route of exposure | Not required at this tonnage |
| Acute toxicity, dermal route | Waive based on bio-elution and T/D data (insoluble) | Not required at this tonnage |
| Short-term repeated dose toxicity oral/ dermal/ inhalation | Waive based on bio-elution and T/D data | Not required at this tonnage |
| Reproductive toxicity | | Not required at this tonnage |
| Toxicokinetics, metabolism and distribution | Proposed absorptions<br>Oral: 1%<br>Dermal 10%<br>Inhalation: 100% | Not required at this tonnage<br><br>Willard et al., 1957 Distribution of RuO2 in mice following injection |

# Workplan 2019-20

- Literature review HH (Ru cmpds)
- Update Annex III to VII as approved (cfr. testing to be initiated this year)
- Ru metal dossier: replace waivers based on substance inertness
  - Bioelution: 6000 €
  - In vitro mutagenicity: 35000 €
  - RDT/Repro screening: 250000 €
- Update ENV assessment (PNEC/ERV & ES) where required following 2018 lit review

# Workplan 2019-20

- Literature review HH (Ru cmpds)
- Update Annex III to VII as approved (cfr. testing to be initiated this year)
- Ru metal dossier: replace waivers based on substance inertness
  - Bioelution: 6000 €
  - In vitro mutagenicity: 35000 €
  - RDT/Repro screening: 250000 €
- Update ENV assessment (PNEC/ERV & ES) where required following 2018 lit review

? PRIORITIES ?

**FOR APPROVAL**

# Budget 2020

| | |
|---|---|
| **16. Ru metal** | **267.934 €** |
| 16.1 REACH registration | 0 € |
| 16.2 REACH dossier maintenance | 260.500 € |
| 16.3 REACH evaluation | 0 € |
| 16.4 REACH classification & labelling | 0 € |
| 16.5 REACH authorisation | 0 € |
| 16.6 Internal and external fixed Scientific Managers | 6.634 € |
| 16.7 IUCLID IT hosting system | 400 € |
| 16.8 Knowledge Management tool + hosting | 400 € |
| | |
| **17. Ru compounds** | **42.439 €** |
| | |
| 17.1 REACH registration | 0 € |
| 17.2 REACH dossier maintenance | 18.500 € |
| 17.3 REACH evaluation | 0 € |
| 17.4 REACH classification & labelling | 0 € |
| 17.5 REACH authorisation | 0 € |
| 17.6 Internal and external fixed Scientific Managers | 13.139 € |
| 17.7 IUCLID IT hosting system | 400 € |
| 17.8 Knowledge Management tool + hosting | 400 € |
| 17.10 Science budget | 10.000 € |

# Gold metal

# Workplan 2020

- Au metal dossier: replace waivers based on substance inertness

# Workplan 2020

## Proposal to test

| | Au metal |
|---|---|
| Skin irritation *in vitro* | Waive based on bio-elution and T/D data |
| Eye irritation *in vitro* | Waive based on bio-elution and T/D data |
| Skin sensitisation | OECD406 (GPMT) – not sensitizing |
| *In vitro* gene mutation study in bacteria | OECD471 – not mutagenic |
| Acute toxicity, oral route | Waive based on bio-elution and T/D data |
| Skin irritation *in vivo* | Waiver |
| Eye irritation *in vivo* | Waiver |
| *In vitro* cytogenicity in mammalian cells | Waive based on bio-elution and T/D data |
| *In vitro* gene mutation study in mammalian cells | Waive based on bio-elution and T/D data |
| Acute toxicity, inhalation | Waive: not a relevant route of exposure |
| Acute toxicity, dermal route | Waive based on bio-elution and T/D data (insoluble) |
| Short-term repeated dose toxicity oral/ dermal/ inhalation | Waive based on bio-elution and T/D data |
| Reproductive toxicity | |
| Toxicokinetics, metabolism and distribution | Proposed absorptions<br>Oral: 1%<br>Dermal 10%<br>Inhalation: 100% |

# Workplan 2020

- Au metal dossier: replace waivers based on substance inertness
  - In vitro skin irrit/corr: 3000
  - In vitro eye irrit/corr: 3500
  - Acute tox, oral: 5500
  - In vitro cytogenicity in mamm cell: 17000
  - In vitro gene mutation in mamm cell: 13000
  - RDT/Repro screening: 250000
  - Study monitoring: 10000
  - Cost test item: ????

- Update ENV assessment (PNEC/ERV & ES) where required following 2018 lit review

# Workplan 2020

- Au metal dossier: replace waivers based on substance inertness
  - In vitro skin irrit/corr: 3000
  - In vitro eye irrit/corr: 3500
  - Acute tox, oral: 5500
  - In vitro cytogenicity in mamm cell: 17000
  - In vitro gene mutation in mamm cell: 13000
  - RDT/Repro screening: 250000
  - Study monitoring: 10000
  - Cost test item: ????

? PRIORITIES ?

- Update ENV assessment (PNEC/ERV & ES) where required following 2018 lit review

**FOR APPROVAL**

# Budget 2020

| | |
|---|---|
| **3. Au metal** | **331.884 €** |
| | |
| **3.1 REACH registration** | **0 €** |
| **3.2 REACH dossier maintenance** | **314.500 €** |
| **3.3 REACH evaluation** | **0 €** |
| **3.4 REACH classification & labelling** | **0 €** |
| **3.5 REACH authorisation** | **0 €** |
| **3.6 Internal and external fixed Scientific Managers** | **16.584 €** |
| **3.7 IUCLID IT hosting system** | **400 €** |
| **3.8 Knowledge Management tool + hosting** | **400 €** |
| | |
| **4. Au compounds** | **30.092 €** |
| | |
| **4.1 REACH registration** | **0 €** |
| **4.2 REACH dossier maintenance** | **21.000 €** |
| **4.3 REACH evaluation** | **0 €** |
| **4.4 REACH classification & labelling** | **0 €** |
| **4.5 REACH authorisation** | **0 €** |
| **4.6 Internal and external fixed Scientific Managers** | **8.292 €** |
| **4.7 IUCLID IT hosting system** | **400 €** |
| **4.8 Knowledge Management tool + hosting** | **400 €** |
| **4.9 Science budget** | **0 €** |

European Precious Metals Federation

# Workplan and draft budget 2020

# Workplan

Cfr previous slides.

# Draft budget 2020

| | |
|---|---|
| **5. Ag cyanide/Potassium dicyanoargentate** | **33.062 €** |
| | |
| 5.1 REACH registration | 0 € |
| 5.2 REACH dossier maintenance | 16.000 € |
| 5.3 REACH evaluation | 0 € |
| 5.4 REACH classification & labelling | 0 € |
| 5.5 REACH authorisation | 0 € |
| 5.6 Internal and external fixed Scientific Managers | 16.262 € |
| 5.7 IUCLID IT hosting system | 400 € |
| 5.8 Knowledge Management tool + hosting | 400 € |
| 5.9 Science budget | 0 € |
| | |
| **6. Potassium dicyanoaurate** | **18.931 €** |
| | |
| 6.1 REACH registration | 0 € |
| 6.2 REACH dossier maintenance | 10.000 € |
| 6.3 REACH evaluation | 0 € |
| 6.4 REACH classification & labelling | 0 € |
| 6.5 REACH authorisation | 0 € |
| 6.6 Internal and external fixed Scientific Managers | 8.131 € |
| 6.7 IUCLID IT hosting system | 400 € |
| 6.8 Knowledge Management tool + hosting | 400 € |
| 6.9 Science budget | 0 € |

# Draft budget 2020

| | |
|---|---|
| **18. Ir metal** | **14.617 €** |
| | |
| **18.1 REACH registration** | **0 €** |
| **18.2 REACH dossier maintenance** | **10.500 €** |
| **18.3 REACH evaluation** | **0 €** |
| **18.4 REACH classification & labelling** | **0 €** |
| **18.5 REACH authorisation** | **0 €** |
| **18.6 Internal and external fixed Scientific Managers** | **3.317 €** |
| **18.7 IUCLID IT hosting system** | **400 €** |
| **18.8 Knowledge Management tool + hosting** | **400 €** |
| | |
| **19. Ir compounds** | **23.117 €** |
| | |
| **19.1 REACH registration** | **0 €** |
| **19.2 REACH dossier maintenance** | **19.000 €** |
| **19.3 REACH evaluation** | **0 €** |
| **19.4 REACH classification & labelling** | **0 €** |
| **19.5 REACH authorisation** | **0 €** |
| **19.6 Internal and external fixed Scientific Managers** | **3.317 €** |
| **19.7 IUCLID IT hosting system** | **400 €** |
| **19.8 Knowledge Management tool + hosting** | **400 €** |

European Precious Metals Federation

# AOB, next meeting(s) and closing remarks

# ES for communication

- Request to develop workplan on Exposure Scenarios (ESs)
  - Allow/facilitate direct incorporation of REACH ESs in company eSDS
  - Improve/align readability of ESs.
- **Workplan**:
  - transfer all ESs into CHESAR to facilitate the automatic creation of eSDS
  - tiered approach:
    - **Tier 1** - **Q3-Q4 2018**: substances for which occupational assessment has been performed in Chesar

  - Documents sent end of January, **almost no feedback received**

# ES for communication

| Tier 1 | Tier 2 | Tier 3 |
|---|---|---|
| Tetrachloroauric acid | Hexachloroplatinic acid | Tetraamminepalladium(2+) diacetate |
| Potassium dicyanoargentate | Dihydrogen hexahydroxyplatinate. compound with 2-aminoethanol (1:2) (in solution) | Disodium tetrachloropalladate |
| Silver cyanide | Dipotassium hexachloroplatinate | Palladium dinitrate (UVCB!) |
| Potassium dicyanoaurate | Diammonium hexachloroplatinate | Palladium dihydroxide |
| Diamminedichloropalladium | Dihydrogen hexahydroxyplatinate | Diammonium hexachloropalladate |
| Dihydrogen tetrachloropalladate(2-) (in solution) | Diammonium sodium hexakis(nitrito-N)rhodate | Dipotassium hexachloropalladate |
| Palladium (II) di(4-oxopent-2-en-2-oate) | Ruthenium trichloride. hydrate | Platinum dinitrate (UVCB!) |
| Tetraamminepalladium(2+) dichloride | Tetraammonium decachloro-mu-oxodiruthenate(4-) | Palladium dichloride |
| Platinum. 1.3-diethenyl-1.1.3.3-tetramethyldisiloxane complexes / Karstedt concentrate (UVCB!) | | |

# ES for communication

- **Workplan**:
  - transfer all ESs into CHESAR to facilitate the automatic creation of eSDS
  - tiered approach:
    - **Tier 1** - **Q3-Q4 2018**: substances for which occupational assessment has been performed in Chesar
    - **Tier 2 - Q1-Q2 2019:** substances not yet in CHESAR. but where no changes in risk assessment are anticipated in a short term
    - **Tier 3 - Q3-Q4 2019 :** substances not yet in CHESAR. but where changes in risk assessment are anticipated (eg. ongoing review Pd PNEC. ongoing mammalian tox testing)
- **Budget and resources**:
  - **2019:** work will be done internally

? PRIORITIES ?

**FOR APPROVAL**

# LR change due to Brexit

- As a result of Brexit discussions, need to change Lead Registrant positions from JM

| Name of the substance | Identification numbers | | Tonnage band | Proposed NEW LR |
|---|---|---|---|---|
| | CAS | EC | | |
| Tetraamminepalladium (II) nitrate | 13601-08-6 | 237-078-2 | 1-10 t/a (Annex III) | **Heraeus** |
| Tetraammineplatinum dichloride | 13933-32-9 | 237-706-5 | 1-10 t/a (Annex III) | **Heraeus** |
| *Diammonium hexachloroplatinate* | *16919-58-7* | *240-973-0* | *10-100 t/a* | ***dormant*** |
| Dihydrogen hexahydroxyplatinate | 51850-20-5 | 257-471-2 | 10-100 t/a | **BASF** |
| Iridium | 7439-88-5 | 231-095-9 | 1-10 t/a (Annex III) | **Heraeus** |
| Carbonyl(pentane-2,4-dionato-O,O')(triphenylphosphine)rhodium | 25470-96-6 | 247-015-0 | 1-10 t/a (Annex III) | **Umicore** |
| *Hexakis[mu-(acetato-O:O')]-μ3-oxo-triangulo-triruthenium acetate / Ruthenium acetate* | *55466-76-7* | *259-653-7* | *1-10 t/a (Annex III)* | ***dormant*** |

**FOR APPROVAL**

# IPA testing program

- IPA considering to work on Platinum tail pipe emissions from catalytic converters of cars.

  → for discussing during IPA ESTF meeting later this week (South Africa.

  - Clarification of project by joint EPMF – IPA members?
  - Potential conflicts with EPMF testing program?

# QICAR project under ETAP

- QICAR = Quantitative Ion-Character Activity Relationship
  = QSAR-like approach for metals
- QSAR: model predictions for organic molecules

molecular **structure** of *target* chemical

*properties of structurally similar source chemicals*

predicted '***property***' of *target* chemical

*'property': phys-chem endpoints ($K_{ow}$, boiling point…), effects data…*
*global use e.g. OECD QSAR Toolbox, US EPA EPISuite*

# QICAR project under ETAP

- QICAR = Quantitative Ion-Character Activity Relationship

**physicochemical parameter(s)** of *target* metal (cmpd)

*Properties/effects + phys-chem parameter(s) of source metal (cmpds)*

predicted **property/effect** of *target* metal (cmpd)

- QICARs being developed since 1950's
  - Review for Environment and Climate Change Canada (ECCC; 2011)
    - Metals of concern ('MoC'): Bi, PGMs, Lanthanides
    - Identify best performing models + prioritize MoC

  + recent papers authored by Chinese researchers

# QICAR project under ETAP

- Typical **metal characteristics** as potential predictors:

| | |
|---|---|
| **physical properties** | *atomic weight – AW, atomic volume – V, density - ρ, melting point – MP, polarizability - α, molar refractivity – MR, atom size (AR/AW)* |
| **electronic structure** | *atomic number – AN, ionization energy and potential – IP and ΔIP, respectively, and electron affinity – E** |
| **redox properties** | *oxidation number – ox, standard electrode potential -$E_0$ and electrochemical potential, $\Delta E_0$* |
| **binding properties** | *ionic radius – r, covalent radius – CR, Van der Waals radius – Vdw, and electronegativity – $\chi_m$* |
| **indices** | *ionic potential – z/r, ionic index – $z^2/r$, covalent index $\chi_m{}^2 r$, covalent binding stability – Δβ, Pearson softness parameter – $\sigma_p$ and absolute value of the first hydrolysis constant – log $K_{OH}$* |

# QICAR project under ETAP

- **Temporal conclusions** from existing literature:
  - many endpoints covered
  - many metals covered
  - models 'well predictive'

**… BUT …**

  - Quality of source data questionable
  - no / limited data for data-poor
  - metal speciation data lacking

2017: Metals' industry initiative to further invest in QICAR
- use quality-checked data
- measured data (EC50) for model organism
- *data-rich* and *data-poor* metals
- metal speciation

# QICAR project under ETAP

- '***Application of Quantitative Ion Character- Activity Relationships (QICARs) to Data-Poor Metals***' at INRS (Institut National de la Recherche Scientifique, Canada)

- Focus on **acute freshwater toxicity** to algae, daphnids and fish

- Researchers:
  - Dr Séverine Le Faucheur
  - Prof Claude Fortin
  - Prof Peter Campbell

- Data provided by metals' industry or through bibliographic research:
  - ***'data-rich'* metals**: Ag, Ca, Cd, Co, Cu, K, Mg, Mn, Na, Ni, Pb, Zn
    → to ***build*** model
  - ***'data-poor'* metals**: Al, Au, Ge, In, Ir, Pd, Pt, Re, Rh, Ru
    → to ***test*** model

# QICAR project under ETAP

- Acute tox data for algae, daphnids and fish
- Only studies with **measured** metal concentrations
- Details on
  - test species,
  - experimental conditions (exposure duration, temperature),
  - measured responses (growth inhibition; immobilization; mortality) and
  - exposure media composition (initial and final pH, hardness, concentrations of major cations & anions, dissolved organic carbon)

# QICAR project under ETAP

- WHAM VII and Visual MINTEQ
- Thermodynamic data much **better constrained for data-rich** than data-poor

| | $M^{z+}$ | $M(OH)_n$ | $M(CO_3)_n$ | $M(Cl)_n$ | $M(SO_4)_n$ | $M(X)_n$ | M-DOM |
|---|---|---|---|---|---|---|---|
| Ag | 41-99% | <1% | 0 | <1-55% | <1% | - | 0 |
| Ca | 98% | <1% | <1% | 2% | <1% | - | 0 |
| Cd | 9-83% | <1% | <1% | <1-3% | <1-2% | 11-62% [$CdHPO_4$] | 0 |
| Co | 3-80% | <1% | 19-97% | <1% | <1-6% | - | <1-7% |
| Cu | <1-68% | <1-15% | 3-93% | <1% | <1-4% | - | 0-78% |
| K | 99% | <1% | <1% | <1% | <1% | - | 0 |
| Mg | 100% | <1% | <1% | <1% | <1% | - | <1% |
| Mn | 97% | <1% | <1% | <1% | <1% | - | 0 |
| Na | 97-99% | <1% | <1% | <1% | <1-3% | - | 0 |
| Ni | <1-57% | <1% | <1-43% | <1% | <1-3% | - | <1-100% |
| Pb | <1-23% | <1% | <1-66% | <1% | <1% | - | 32-98% |
| Zn | 35-100% | <1-54% | 0-17% | <1% | 0-7% | - | <1-4% |

| | $M^{z+}$ | $M(OH)_n$ | $M(CO_3)_n$ | $M(Cl)_n$ | $M(SO_4)_n$ | $M(X)_n$ | M-DOM |
|---|---|---|---|---|---|---|---|
| Au(I) | <1% | <1% | <1% | <1% | <1% | 100% [$Au(CN)_2^-$] | 0 |
| Ge(IV) | <1% | 100% [$Ge(OH)_4^0$] | <1% | <1% | <1% | 0 | 0 |
| In(III) | <1% | 100% [$In(OH)_3^0$] | <1% | <1% | <1% | 0 | 0 |
| Pd(II) | <1% | 100% [$Pd(OH)_2^0$] | <1% | <1% | <1% | 0 | 0 |
| Pt(II) | <1% | 100% [$Pt(OH)_2^0$] | <1% | <1% | <1% | 0 | 0 |
| Rh(III) | <1% | 100% [$Rh(OH)_3^0$] | <1% | <1% | <1% | 0 | 0 |
| Ru(III) | <1% | 100% [$Ru(OH)_3^0$] | <1% | <1% | <1% | 0 | 0 |

(*example for algae exposure media*)

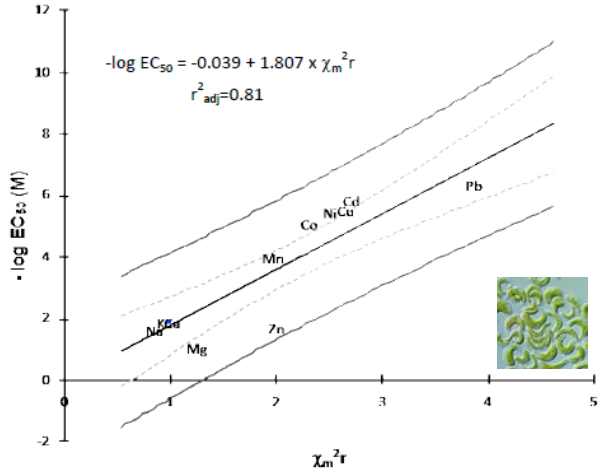
Free metal ion proportions **vary widely**

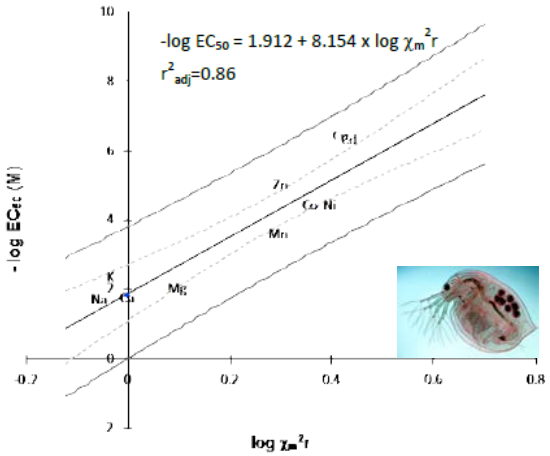
- Consistently high proportions for Ca, K, Na, Mg and Mn
- Variable for other metals, depending on medium composition: influence of pH (e.g. Cu, Zn), Cl (e.g. Ag), $CO_3$ (e.g. Pb, Ni), DOM (e.g. Cu)…
- Consistently very low (<<1%): dominated by neutral hydroxocomplexes for **data-poors ($X(OH)_y^0$)**

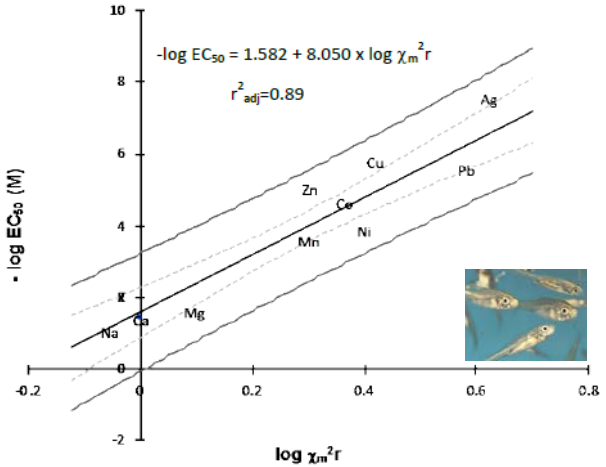
  ! *except precious metals cyanides: remained as e.g. $Au(CN)_2^-$*

# QICAR project under ETAP

- Very **good correlations between $\chi_m^2 r$ and toxicity** of *data-rich* metals
  - → $r^2$adj values >0.8
  - → for all organisms
  - → 'grouped' and single species models, except for *O. mykiss*



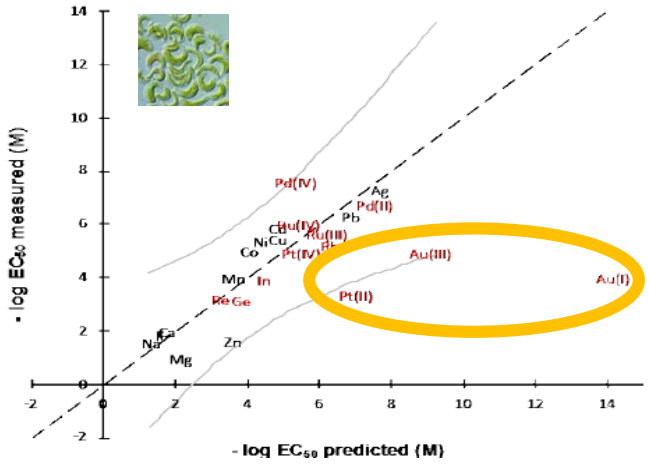



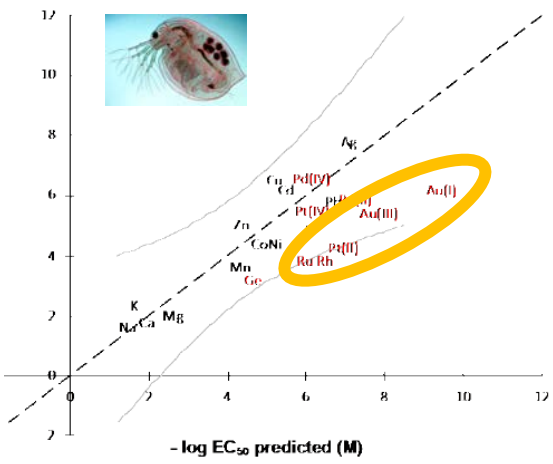
# QICAR project under ETAP

- **Predictions for *data-poor* metals were not as good**:
  - → predictions being borderline or not within 95% PI
  - → predictions outside PI tend to fall in lower right quadrant, i.e. **OVERprediction of toxicity**

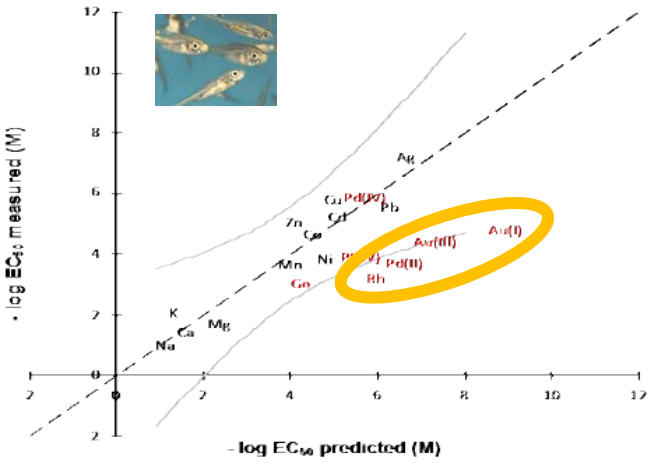
algae: Au, Pt(II)




daphnids: Au, Pt(II), Rh, R




fish: Au, Pd(II), Rh



# QICAR project under ETAP

- **Poor predictive power for *data-poor* metals**:
  1. **Less robust** toxicity data: extracted from very few experimental tests

  2. Model predictions involve **extrapolation**:
     $\chi_m^2 r$ (*data-rich* metals) 0.88 (Na) - 4.28 (Ag) vs. Au(III) 4.90, Au(I) 7.89
     → poorer model performance?

$\chi m^2 r$ →

| 0,73 | 0,88 | 0,93 | 1,00 | 1,06 | 1,24 | 1,91 | 1,99 | 2,01 | 2,03 | 2,09 | 2,14 | 2,30 | 2,52 | 2,53 | 2,64 | 2,71 | 3,00 | 3,00 | 3,05 | 3,29 | 3,29 | 3,48 | 3,86 | 3,87 | 4,16 | 4,28 | 4,90 | 7,89 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Li(I) | Na | K | Ca | Sr(II) | Mg | Re(VII | Mn | Zn | Ga(III) | Re(V) | Ge(IV) | Co | Ni | In(III) | Cu | Cd | Pd(IV) | Ru(IV) | Pt(IV) | Ir(III) | Ru(III) | Rh(III) | Pb | Pt(II) | Pd(II) | Ag | Au(III) | Au(I) |

  3. **Complex molecules** for toxicity testing + specific **chemistry** (complexation behaviour)

# QICAR project under ETAP

- ***Predictions for data-poor*** metals based on free ion:
  - **marked deterioration** of the predictive ability of the QICAR models
  - systematic **UNDERestimation** of toxicity of elements for which speciation could be calculated:
    - $Au(CN)_2^-$ anion
    - polyhydroxo-species
- unusual result **reflection of distinctive speciation** of these metals?
  1. free metal ion at vanishingly low concentrations (< $10^{-15}$ M)
  2. except $Au(CN)_2^-$, metal cation present almost entirely as neutral polyhydroxo-species ($Au(OH)_3^0$, $Ge(OH)_4^0$, $In(OH)_3^0$, $Pd(OH)_2^0$, $Pt(OH)_2^0$, $Rh(OH)_3^0$ and $Ru(OH)_3^0$)
- **MLR** did not improve predictive power

***DRAFT REPORT BEING REVIEWED BY SPONSORS – AVAILABLE SOON***

# QICAR project under ETAP

- QICARs: **resource intensive** to develop, **easy** to apply
- QICARs work **well for *data-rich*** metals
- QICARs to date work **less well for *data-poor*** metals
- ***Data-poor*** metals:

  QICARs have **potential to estimate ecotoxicity**, but weaknesses identified:

  - Few experimental data available to test the QICAR predictions
  - Lack of information about thermodynamics / environmental chemistry / geochemistry

# QICAR project under ETAP

- Potential future steps to take?
  - **refinement acute model**
    ~extend database data-poor metals (thermodynamic + ecotoxic)
    ~include more data-poor metals
  - **chronic aquatic effects**
  - **other 'environments'**: soil, sediment, marine environments
- Potential applications;
  - **Identification of outliers**
    - toxicity values lying outside the QICAR prediction intervals (flag values that merit further scrutiny or possible retesting)
  - **Comparison of effects**
    - QICARs are 'easy to use' (quick indication of predicted (or 'expected') effect, or compare predicted effects to prioritize)
  - **Refinement of assessments**
    - Mixture toxicity (eg, '*What metal will drive the effects ?*'
    - Influence of environmental parameters (temperature, DOC, pH…)

# Next meeting(s)

- Upcoming Events:
  - EPMF General Assembly: **5-6 June 2019, Bordeaux, France**
  - Autumn Back-to-Back meeting: **8-10 October 2019**, **Brussels, Belgium**
  - EPMF General Assembly: **3 December 2019, Brussels, Belgium**

# Closing remarks

# THANK YOU

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