Precious Metals Consortium

Precious Metals & Rhenium Consortium

PGM Tox Experts & Work Group Meeting

9 October 2018 | Brussels

Precious Metals Consortium

1. Welcome and introduction

1.1 Confidentiality and Competition law

1.2 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 Agreement 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 or an external lawyer whenever there are uncertainties respecting compliance with competition law. 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 Consortium	
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 this Agreement, including: - Coming to agreement, including arrangements or collusions, about prices, markets and customers (see Art. 101 paragraph 1 a)-e) TFEU); - Joint boycotting of other companies; - The unjustified unequal treatment of trade partners; - 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 : - Production capacities; - Productions or sales volumes; - Import volumes; - Market shares; - Price policy; - Distribution and marketing terms; - Marketing strategies; - Information regarding the relationship with suppliers.
Documentation on Cooperation	
Keep minutes of all meetings which detail the subject of the meeting. In case of uncertainty, have the contents of the minutes reviewed by an external legal expert prior to sending them to all parties of the Agreement. Stop all meetings which are not in compliance with these Guidelines until a legal expert has been involved.	

1.3 Approval of the agenda

1. Welcome and Introduction (11:00 – 11:30)
    1. Reminder on Confidentiality and Competition Law
    2. Tour de table and apologies
    3. Approval of the agenda
    4. Approval of the minutes of the last meeting (14 March 2018) and status of action points

2. PGM exposure scenario workplan : inclusion exposure scenarios in Chesar
3. First MISA workshop: key conclusions/learnings (new) (11:30 – 11:45)

4. Palladium and compounds (11:45 – 12:15)
    1. Update ongoing testing
    2. **Expert review Registration dossiers Pd / Pt (new)**

5. Platinum and compounds (12:15 – 13:00)
    1. Update ongoing testing
    2. Pt genotox : Status + way forward substance ID Pt nitrate
    3. **Karstedt Concentrate SID (new)**

Lunch break (13:00 – 14:00)

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

6. Rhodium and compounds (14:00-14:45)
    1. Update ongoing testing
    2. Rh(III) genetox : status & further actions

7. Ruthenium and compounds (14:45 -15:15)
    1. Update ongoing testing

8. Workplan and budget (15:15 – 15:30)

9. AOB. next meeting(s) and closing remarks (15:30 – 15:45)
    1. **Organic Metal Salts vs Organometallics (new)**

1.4 Approval of minutes & status action points

Final draft minutes of the meeting on 14 March 2018, circulated on 21 March 2018

APPROVED?

1.4 Approval of minutes & status action points

ACTIONS	Who ?	When?	Status
Update OFI trackers as proposed and agreed (Pd. Pt. Rh and Ru group substances)	PMC	ASAP	✓
Perform approved actions from the OFI tracker	PMC	Cfr. proposed timings in OFI	✓
Consult internally on PdO and Rh2O3 testing for oxidizing properties	Companies	<31 March	✓
Organise testing oxidizing properties (if no objections or (reference to) existing test data are received	PMC	April '18	✓
Check internally the relevance & express support to update the proposed AnnexIII dossiers.	Companies	<15 April	✓
Include update AnnexIII dossiers to AnnexVII dossiers (Pd. Pt. Rh. Ru and Ir group substances) in 2019 workplan & budget	PMC	<June GA meeting	✓
Check internally which technique can be used for palladium speciation	Companies	<31 March	*pending*
Update Pt nitrate dossier to include TP for in vivo genotox	PMC		✓
LR to submit Pt nitrate dossier	Heraeus		✓

1.4 Approval of minutes & status action points

ACTIONS	Who ?	When?	Status
Inform ECHA about inclusion TP in Pt nitrate dossier	PMC	ASAP after dossier update	✓
Communicate with ECHA about the Pt testing approach	PMC	tbc	✓
Develop a testing stategy for in vivo genotoxicity testing	PMC & companies	Q2-Q3 2018	*ongoing (cfr further)*
Organise Pt in vivo genotox testing	PMC & companies	<Q2 2019 (anticipated timing)	*ongoing (cfr further)*
Perform Pt in vivo genotoxicity testing	PMC	ASAP after ECHA approval (Q2 2019?)	*ongoing (cfr further)*
Inform members about the discussions with ECHA (meeting 15 March)	PMC		✓
Draft RA justification reports for HHPA group. incl. experimental testing	PMC & companies	<end 2018	*ongoing (cfr further)*
Update/finalise dirhodium trisulphate and rhodium tris(2-ethylhexanoate) dossiers	PMC	April 2018	✓
Check pH Rhodium trichloride hydrate	Companies	<15 April	✓

1.4 Approval of minutes & status action points

ACTIONS	Who ?	When?	Status
Draft TP for in vivo genotoxicity for rhodium trisulphate and include in the dossier	PMC	ASAP	*ongoing (cfr further)*
LR to submit rhodium trisulphate dossier	Umicore	ASAP once available	✓
Schedule a call and discuss about RhI3 solubilisation and speciation.	PMC and Johnson Matthey	Q2 2018	*pending*
Check ecotox data Ru(III) cmpds and order an acute ecotox test with the most sensitive species for tris(nitrato-O)nitrosylruthenium to confirm RA + add 10K euro to the 2019 budget.	PMC	Test to run in 2019	✓
Update iridium metal dossier from AnnexIII to AnnexVII + order bioelution testing	PMC	2019	✓
Check if dossiers of rhenium and gold group are candidate for update Annex III to VII	PMC	<June GA meeting	✓

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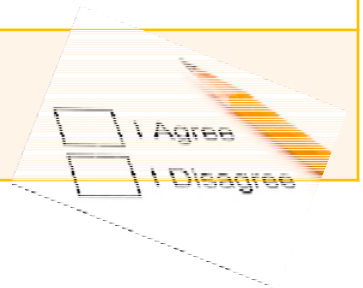
2. PGM exposure scenario workplan: inclusion ESs in Chesar

Inclusion exposure scenarios in Chesar

- 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
    - **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**:
  - **2018:** 18K € for linking conditions of use/operational conditions with standard phrases (EBRC contracted) - covered by available 2018 budget under "*Update of uses and exposure scenarios*"
  - **2019:** work will be done internally - no external budget will be required -

Inclusion exposure scenarios in Chesar

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!)		



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3. MISA – first workshop 2 October

MISA – first workshop 2 October

- EPMF participants: Katrien Arijs, Maxime Eliat, Jelle Mertens
- Company representatives: Steven Verberckmoes
- ECHA participation: Kimmo Louekari and Agnes Kovari (Evaluation Unit), Jos Mossink (Head of Unit – Substance Identification and Data Sharing)
- Others: Betty Hakkert and Petra van Kesteren (RIVM), Katrin Schutte (Eur. Comm.)
- **Agenda**:
  - **AM**: Plenary breakout session HH Read-Across

    aim: ECHA expectations, IND practice + exchange
  - **PM**: Breakout sessions:
    - HH Read-across

      aim: discuss AM + agreements to fulfil regulatory requirements
    - EOGRTS / Route of Exposure and Mutagenicity

      aim: ECHA expectations, IND practice, exchange + agreements to fulfil regulatory requirements

MISA – first workshop 2 October

- Key conclusions/learnings (1/2):
  - **Read-across/grouping:**
    - Clearly define background + boundaries of categories
    - Grouping:
      - Bioelution as tier 1
      - Bridging studies as tier 2
    - Test data need to be available for at least 1 worst-case group/category member
    - Read-across of data/classification to all group/category members (unless you can undoubtedly justify exemption)
    - Bioelution can not be used to fill datagaps (only as 'qualitative' information)
    - Ensure counter-ion effects on tox and bioavailability are properly considered

MISA – first workshop 2 October

- Key conclusions/learnings (2/2):
  - **EOGRTS/Genetox**
    - EOGRTS: 10-w premating proposed (~robustness, international data acceptance)
    - If 2-gen study available (dated <March 2015), this is sufficient to fill EOGRTS. If data indicate need for DIT/DNT cohort, then additional testing for these cohorts can be performed (OECD426 for DNT, unclear what test for DIT)
    - Dustiness testing/MMAD accepted as indicator for inhalation potential
    - Testing of corrosive substances preferably via oral route, and up to concentrations causing 'mild irritation'
    - Data requirements for nanos triggered by nano tonnage band, not for the 'merged tonnage' with the bulk-substance (***TO BE CONFIRMED BY ECHA!)***
    - Suggestion to be transparant in dossier:
      - Include wording why further testing is not warranted (eg PNDT, EOGRTS…)
      - Include reference to all studies considered (also KL3-4) + reason for exclusion
    - Exposure route selection by ECHA driven by PROCs

MISA – first workshop 2 October

- **Next steps**:
  - Template circulated to mention questions: generic + substance specific (<10 Oct)
  - Blog will be launched for follow-up Q&A
  - Detailed report (review by participants & ECHA) with key learnings
  - Consortia **workplan** to be submitted to ECHA <15 November
    - what will you do?
    - by when?

    → no details!

    → actions following the 2 Oct workshop only!

  - **Next workshop** on ENV (topics to be decided based on consortia self-assessments), early Feb 2019 in Helsinki

MISA – first workshop 2 October

- Key actions PGMs (1/2):
  - **Update PGM metal dossiers?**
    - Current waivers (lack of bioavailability) not sustainable
    - **Proposal**:
      - fill endpoints with **test data**
      - **group** metal + respective metal oxide (+ other poorly solubles?):
        - Metal+oxide poorly soluble (no bioelution data for PtO2 and RuO2)
        - New test data from update PGM oxides annex III → VII
        - Ongoing lit review HH/ENV for PGM metals + nanoform
      - rediscuss details in sping BtB meeting, schedule work in **2020**

        → main impact expected on Pt and Ru metal (10-100 tpa)

        → Pd covered by Pd(OH)2?

        → Rh metal (1-10 tpa) covered by ongoing Rh2O3 testing

        → Iridium (no Iridium oxide in EPMF scope): bioelution testing in 2019 workplan, proposal to keep in (as supporting evidence) – 15 k€

MISA – first workshop 2 October

- Key actions PGMs (2/2):
  - **Update RAJR where needed:**
    - Pd & Rh: speciation data to same ‘toxicologically active species’
    - Review existing RAJR (eg STOT RE2 classification TAPd)
  - **Review Rh(III) genetox strategy?**
    cfr further slides…

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4. Palladium and compounds

Update ongoing testing

- Short **Recap**:
  - Pd ecotox based on DDP
  - Refinement Pd PNEC ⟹ requirement for additional ecotox testing
  - Acute tox testing: algae most sensitive
  - Tiered testing:
    - **Algae** tox (OECD201) with TAPd dichloride (group of Pd(II) tetraammines) and Pdacac (group of uncomplexed Pd(II))
    - **Daphnia Reprotox** test (OECD211) and ASRIT (OECD209)
      - Pd(II) tetraammines: TAPd dichloride as representative test cmpd
      - Uncomplexed Pd(II): Pdacac as representative test cmpd
    - **Sediment** testing?
- Testing at Fraunhofer

Update ongoing testing

- **Algae** tox TAPd dichloride – very narrow window of toxicity

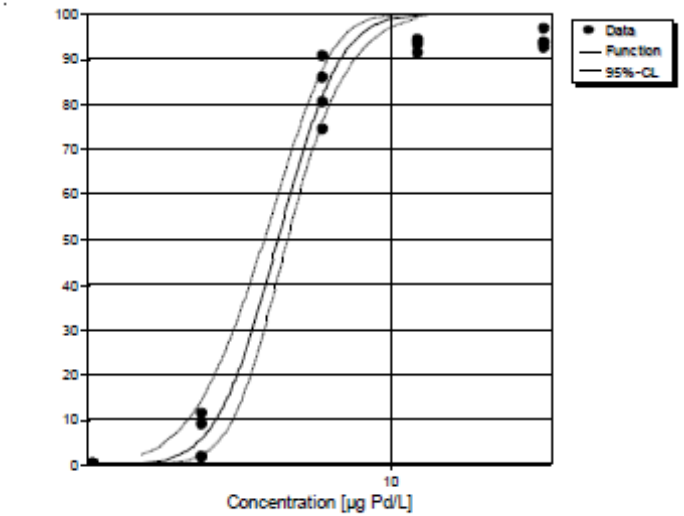


Figure 2: **Influence of mean measured Pd concentrations on percent inhibition of growth rate after 72 h (linear regression).**

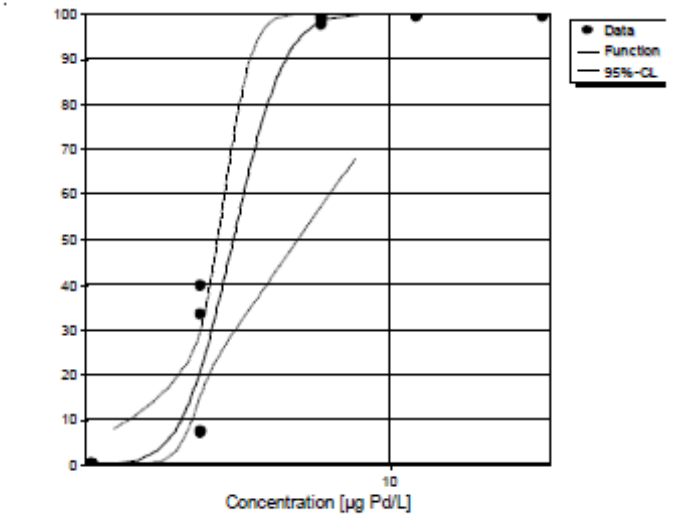


Figure 3: **Influence of mean measured Pd concentrations on percent inhibition of yield after 72 h (linear regression).**

Update ongoing testing

- **Algae** tox Pdacac

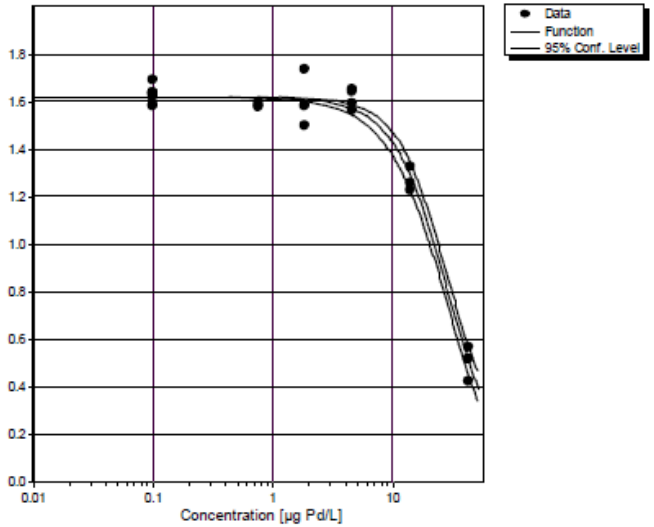


Figure 2: **Influence of mean measured Pd concentrations on percent inhibition of growth rate after 72 h (non-linear regression).**

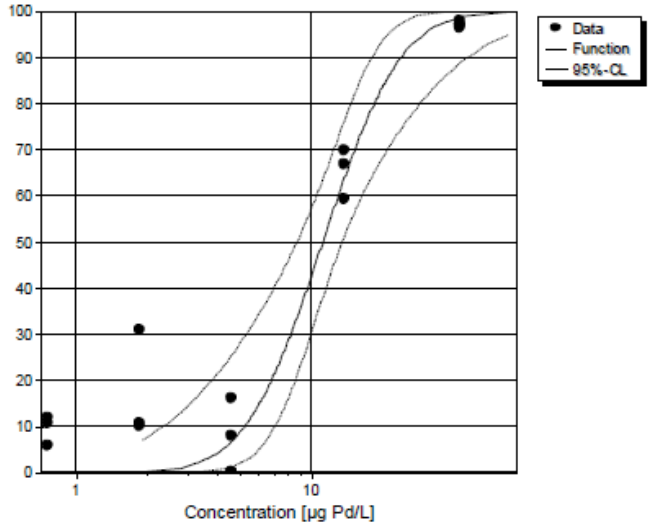


Figure 3: **Influence of mean measured Pd concentrations on percent inhibition of yield after 72 h (linear Probit regression).**

Update ongoing testing

- **Algae** tox - **summary**

	TAPd dichloride	**Pdacac**
Test doses (nominal)	0-6.25-12.5-25-50-100 µg TI/L	0-3.13-7.83-19.6-48.9-122 µg TI/L
Recovery@start/end	*48-84.4% / 34.7-61.6%*	*36.1-41.5% / 15.5-30.2%*
NOEC	5.68 µg TI/L	13.3 µg TI/L
as Pd	*2.46 µg Pd/L*	*4.64 µg Pd/L*
EC10	4.87 µg TI/L (yield)	14.9 µg TI/L (yield)
as Pd	***2.11 µg Pd/L***	***5.19 µg Pd/L***
EC50	7.20 µg TI/L (yield)	32.1 µg TI/L (yield)
as Pd	***3.12 µg Pd/L***	***11.2 µg Pd/L***

TI=Test Item

Update ongoing testing

- **Algae** tox [in µg **Pd**/L] - relationship **other Pd cmpds**

		NOEC	EC10	EC50
Cl-coord Pd(II/IV)	**DDP**	1.33	1.43	2.03
	H2PdCl4	1.4	NR	4.4
TAPd(II)	**TAPd(HCO3)2**	14	NR	24
	TAPdCl2	2.46	NR	3.12
Uncomplexed Pd(II)	**Pd nitrate**	23	NR	29
	Pdacac	4.64	NR	11.2
	(Pd (standard in HCl)	*NR*	*NR*	*5.7)*

- **<u>Pending questions</u>:**
  - Grouping still relevant?
  - Pd(x+)-ion driving toxicity, and not the 'coordinated complex' as hypothesized?

  To be answered as soon as all data get available…

Update ongoing testing

- **Daphnia reprotox** (21 day test) – **DRF** finalised

	TAPd dichloride	Pdacac
Test doses (nominal)	0-1-10-100 µg Pd/L (42.1% Pd)	0-3-30-300 µg Pd/L (34.9% Pd)
Observations	*30% inhib cumulative offspring@100 µg Pd/L*	*100% mortality@300 µg Pd/L after 48h*
	Immobility not affected	*Cumulative offspring not affected*
		15% reprod inhib@30 µg Pd/L
		Sign effect length@30 µg Pd/L
(NOEC	*10 µg Pd/L*	*≥30 µg Pd/L)**
(EC10	*6.5 µg Pd/L*	*75 µg Pd/L)**
Dosing full test	0-3.8-9.6-24.0-60.0-150 µg Pd/L	0-4.6-11.5-28.8-72-180 µg Pd/L

Indicative values (nominal concentrations. limited amount of underlying data)

- Full test running

Update ongoing testing

- **ASRIT** – **DRF** finalised

	TAPd dichloride	Pdacac
Test doses (nominal)	0-10-100-1000 mg TI/L (42.1% Pd)	0-10-100-1000 mg TI/L (34.9% Pd)
Observations	*28% inhib@10 mg TI/L*	*8% inhib@10 mg TI/L (1 replicate)*
	100% inhib@100 mg TI/L	*70% inhib@100 mg TI/L*
		80% inhib@1000 mg TI/L
Dosing full test	0-3.6-7.6-15.9-33.3-70 mg TI/L	0-5.14-10.8-22.7-47.6-100 mg TI/L

- Full test running

Update ongoing testing

- **PdO – bioelution** (@ECTX)
  - → *Bioelution data to strengthen dossier*
  - Gastric + perspiration
  - Sample manufactured + delivered
  - Draft study plans commented – testing scheduled end Sept – early Oct

- **PdO – oxidizing properties** (@BAM)
  - → *test data to replace waiving statement*
  - Sample tested
  - ***Classification as Oxidising solid (cat1 - H271)? To be confirmed)***

Update ongoing testing

- **PdCl2 – genotox testing** (@Covance)

  → *AMES: missing strain; in vitro MLA (tk; OECD490): WoE argumentation*

  - **AMES**:
    - Formulation in water
    - Toxicity observed at 80-250 µg/plate
    - No notable and concentration-related increases in revertant numbers were observed, and none that were significantly above the concurrent vehicle control

    No evidence of any PdCl2 mutagenic activity in this assay system ie, treatments up to toxic concentrations in the absence and in the presence of S-9.

  - **In vitro MLA (tk)**:
    - Formulation in water, 3-h treatment incubation
    - The MF of the concentrations plated (20-500 µg/ml -S9; 10-300 µg/ml+S-9) were all less than the sum of the mean control MF plus the global evaluation factor (GEF) + no statistically significant linear trends

    PdCl2 did not induce mutation at the tk-locus of L5178Y mouse lymphoma cells when tested up to toxic and/or precipitating concentrations in presence and absence of S-9.

Update ongoing testing

- **TAPdCl2 – genotox testing** (@Covance)

  → *AMES: missing strain*

  - **AMES**:
    - Formulation in water
    - Toxicity observed at 50-160 µg/plate
    - No notable and concentration-related increases in revertant numbers were observed, and none that were significantly above the concurrent vehicle control

    No evidence of any TAPdCl2 mutagenic activity in this assay system ie, treatments up to toxic concentrations in the absence and in the presence of S-9.

Update ongoing testing

- **Na2PdCl4 – in vivo skin sensitisation** testing (@LPT)

  → *confirm negative substance specific data to avoid RA from positive* RA group member

  - In vivo skin sensitization (OECD442B)
  - ***Results available end of cw 38, draft report available end of cw 39***

  ! Need to develop WoE argumentation ('in vitro testing not appropriate for metals')

Update ongoing testing

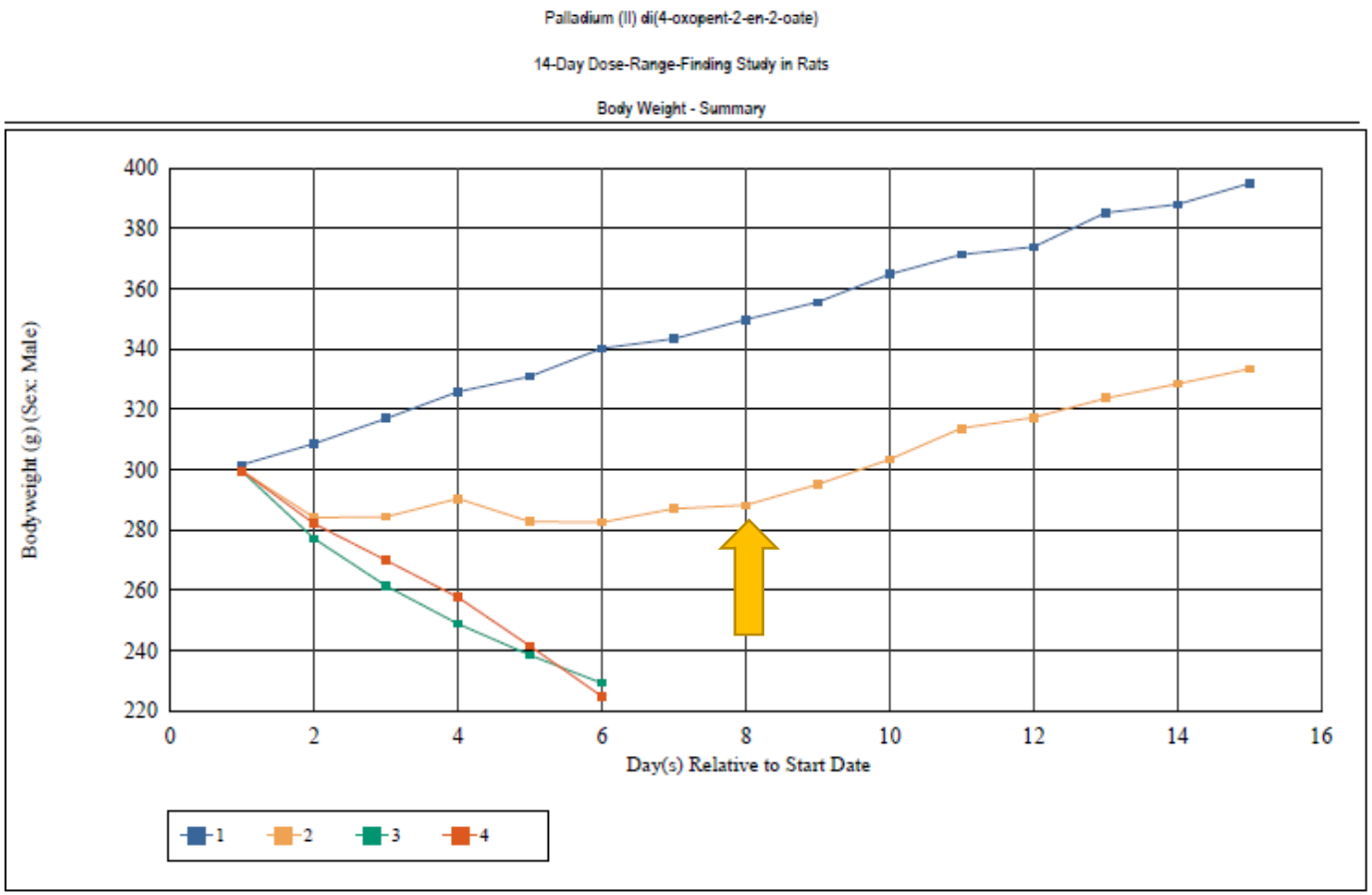
- **Pdacac – combined RDT/Reprotox screening** assay (OECD422)@LPT (1/6)
  → *currently RA from Pd(OH)2, potential contribution acac-ligand*
  - **DRF** study:
    - 100-300-1000 mg/kg/d, gavage, vehicle = corn oil
    - **Low dose group**:
      - One female dead on d8. At necropsy:
        - external inspection:
          - abdomen thickened
          - snout bloody
          - faeces at the anus
        - macroscopic findings:
          - small and large intestine: inflated and reddened
          - hypophysis reddened
          - stomach (wall): thin

        Necropsy findings are similar to those in the higher dose groups
      - Remaining males&females: recovering BW since day 8, clinical signs including salivation and decreased water consumption still present in all animals since that day

Update ongoing testing

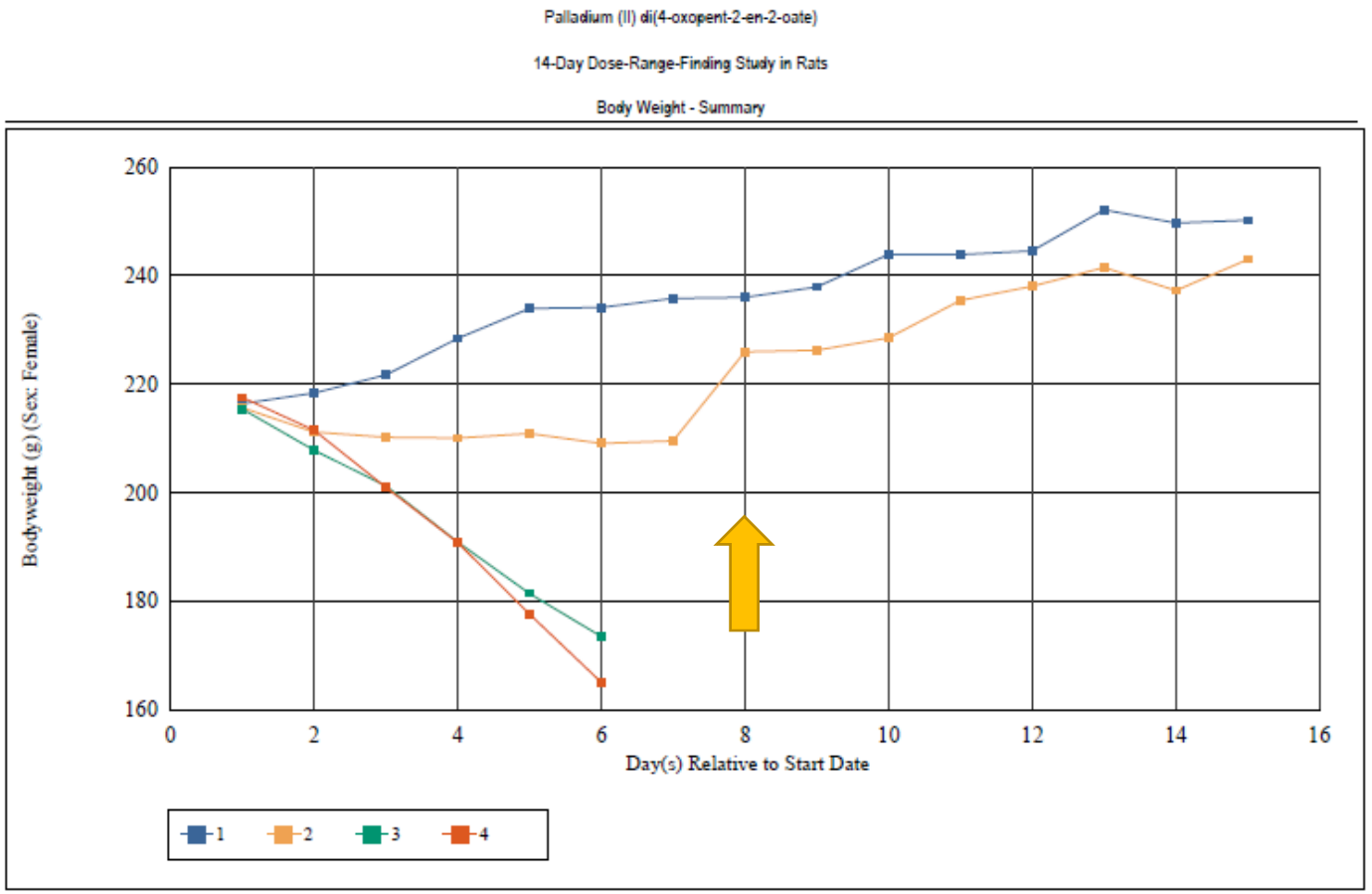
- **Pdacac – combined RDT/Reprotox screening** assay (2/6)

♂



Update ongoing testing

- **Pdacac – combined RDT/Reprotox screening** assay (3/6)



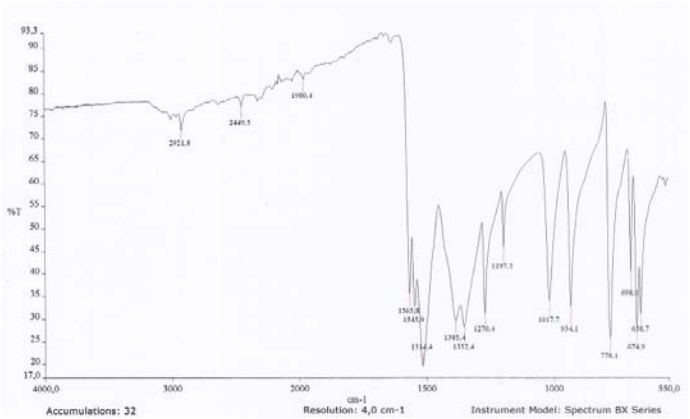
Update ongoing testing

- **Pdacac – combined RDT/Reprotox screening** assay (4/6)
  - **Mid and high dose** group:
    - Administration up to d5, **termination at d6**
    - Necropsy:
      - At external inspection, one or more findings from the list below:
        - bloody snout
        - faeces at the anus
        - anus area wet
        - bloody cantus of the eye (one eye or both eyes)
      - One or more macroscopic findings from the list below:
        - stomach tightly filled, inflated and/or enlarged
        - stomach (mucosa) reddened
        - stomach (mucosa) very thin or thickened
        - caecum reddened
        - caecum enlarged
        - caecum (walls) bloody
        - intestines reddened
        - intestines inflated

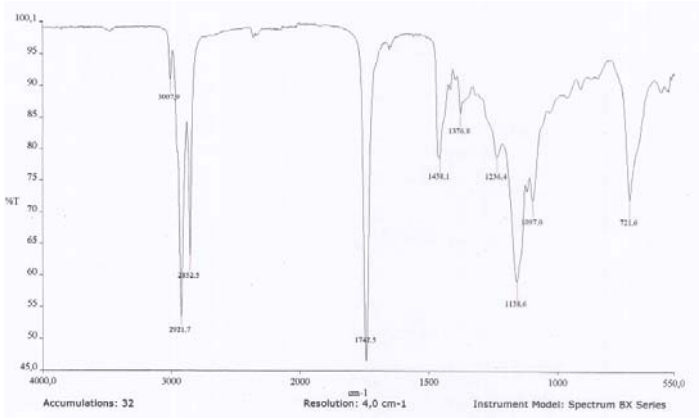
Update ongoing testing

- **Pdacac – combined RDT/Reprotox screening** assay (5/6)
  - Test item **stability shown** (*also 60 mg/ml stability shown*!)

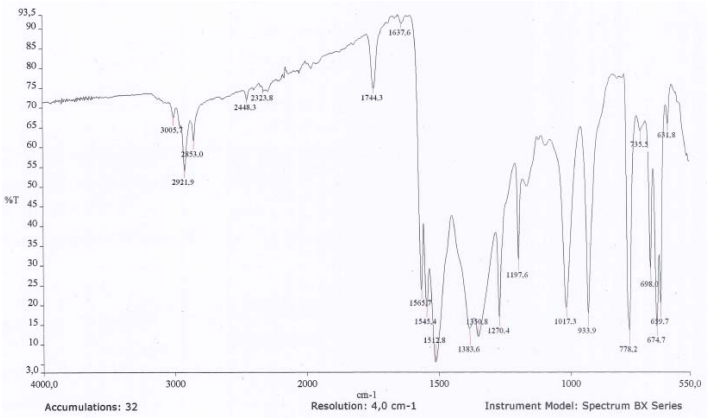
Pdacac



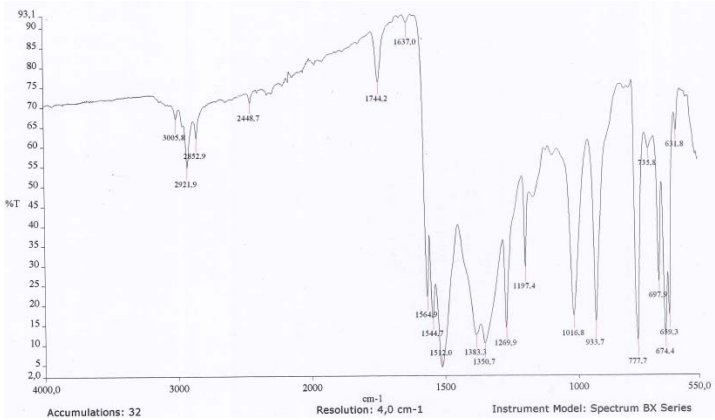
Vehicle



Pdacac 20 mg/ml, d0



Pdacac 20 mg/ml, d7



Update ongoing testing

- **Pdacac – combined RDT/Reprotox screening** assay (6/6)
  - Test item concentration/homogeneity ongoing

  - What's next?
    - Finalise ICP analysis
    - Reporting
    - Deciding on dosing regime for full test
    - …

Update ongoing testing

- **PdCl2 – RDT and Reprotox screening** assays (OECD407-421) @LPT (1/6)
  → *currently RA from Pd(OH)2 (sufficiently conservative approach?)*
  - **Prelim test** (*cfr. unclear tox behavior - anhydrous form vs hydrate*)
    - 1 male, 2 female
    - 500 mg/kg, gavage, 0.8% aqueous hydroxypropyl methylcellulose gel
    - 5d treatment, termination at d6
    - Findings:
      - Reflux, slight salivation
      - BW reduction after d5 (-5% for ♂, -10% and – 14% for ♀) – test item related
      - Reduced food consumption – test item related
      - Black discoloured snout (lack of grooming?)
      - Stomach and caecum enlarged and tightly filled with black content
      - Thin gastric mucosa

Figure 1 Body weight of rats during a 5-day preliminary study

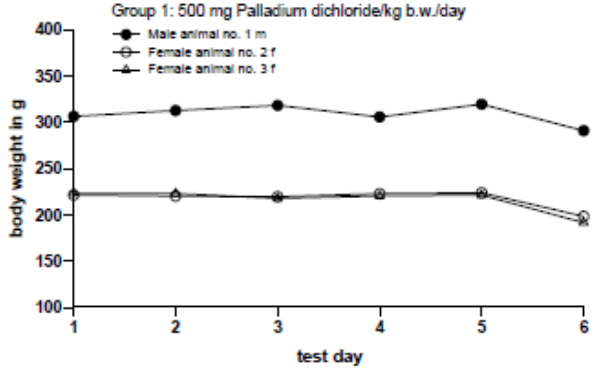
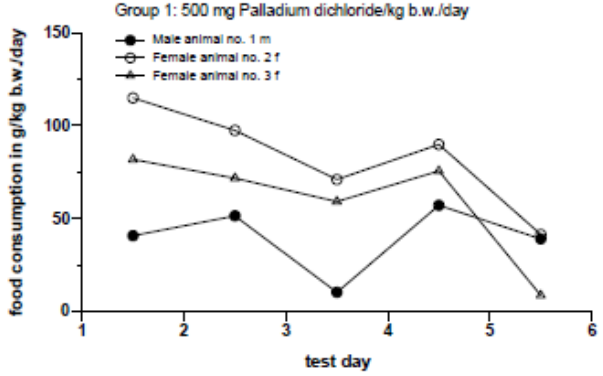


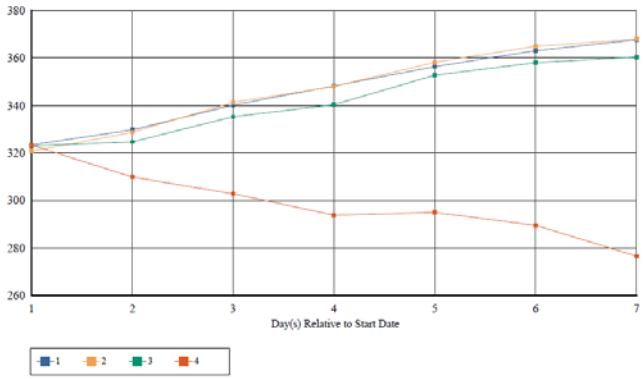
Figure 2 Food consumption of rats during a 5-day preliminary study



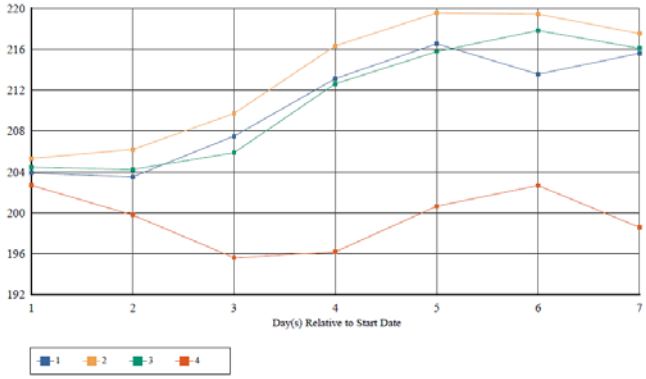
Update ongoing testing

- **PdCl2 – RDT and Reprotox screening** assays (2/6)
  - **DRF**:
    - *Dosing: '[…] if 500 mg/kg bw/day is tolerated without major effects for 5 days by gavage that it would be sensible to investigate 1000 mg/kg bw/day (10000 ppm) in the DRF study*."
    - Dosing levels: 1000 - 3000 - 10000 ppm in diet (corresponding to approx. 100-300-1000 mg/kg/d)
    - Test days 7-8 high dose group:
      - BW males continuously decreasing (-27%) vs BW females slight recovery
      - Food consumption males -55% vs females -30%
      - no test item-related influence on BW for low & mid dose group
      - no signs of systemic intolerance were noted at any dose level.

♂



♀



Update ongoing testing

- **PdCl2 – RDT and Reprotox screening** assays (3/6)
  - **DRF**:
    - Decision to **terminate high dose group,males at day 9,** and examine the stomach and GIT (special care for signs of irritation or other gross pathology findings)
    - At necropsy:
      - caecum: dark content (5 of 5 animals)
      - colon dark content (3 of 5 animals)
      - stomach (mucosa): thickened (1 of 5 animals)

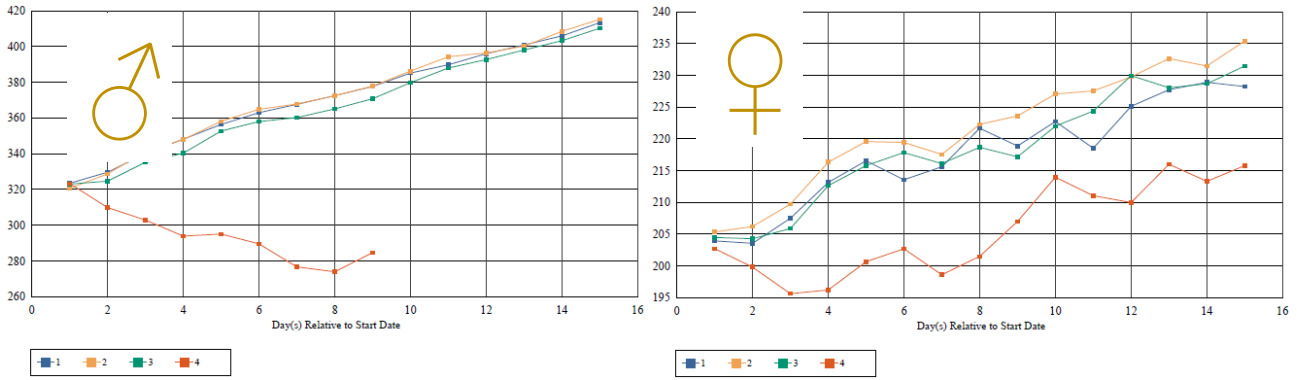
Update ongoing testing

- **PdCl2 – RDT and Reprotox screening** assays (4/6)
  - **DRF**:
    - Termination of remaining groups/animals at d14
    - High dose females:
      - equal findings as for the high dose male animals (prematurely sacrificed on d9)

Observation	*Group 3*		*Group 4*	
	Male	*Female*	*Male #*	*Female*
No pathological findings	*5 of 5*	*4 of 5*	-	*1 of 5*
Caecum: dark content	-	*1 of 5*	*5 of 5*	*4 of 5*
Colon: dark content	-	-	*3 of 5*	*3 of 5*
Thickened stomach mucosa	-	-	*1 of 5*	*1 of 5*

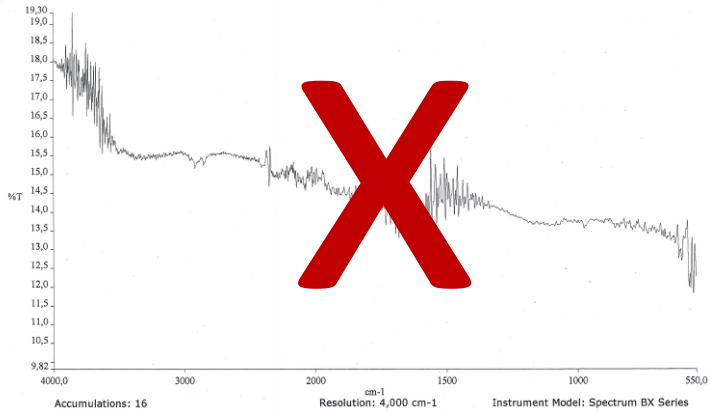
#: prematurely sacrificed on test day 9, due to a markedly reduced body weight.

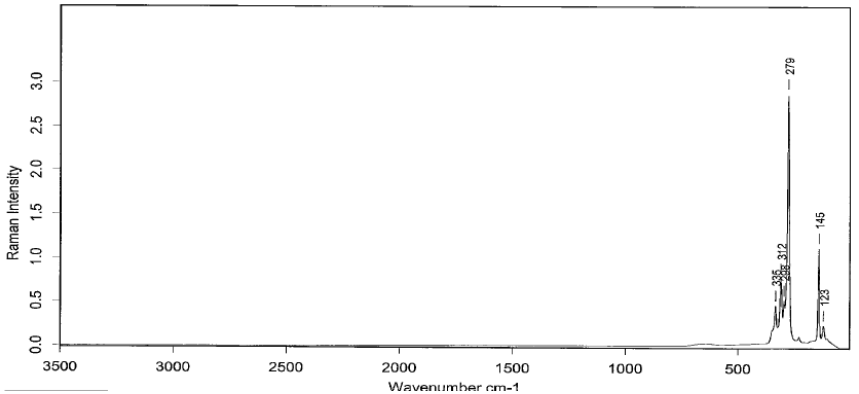
      - BW and food consumption slightly recovered, but not reaching values of other groups
      - discoloured faeces for few high dose females on a few test days
      - no changes in behavior or external appearance of the male and female animals.



Update ongoing testing

- **PdCl2 – RDT and Reprotox screening** assays (5/6)
  - **DRF**:
    - Test item stability:
      - FT-IR not suited
      - Suggestion Tox Experts:
        - Use **Raman** instead (Peaks <500 cm-1)
        - Analyse diet without pretreatment first. If not working, do CCl4 extraction and analyse dried pellet
        - XRD not suited (amorphous pellet?), XPS or SSNMR as alternatives





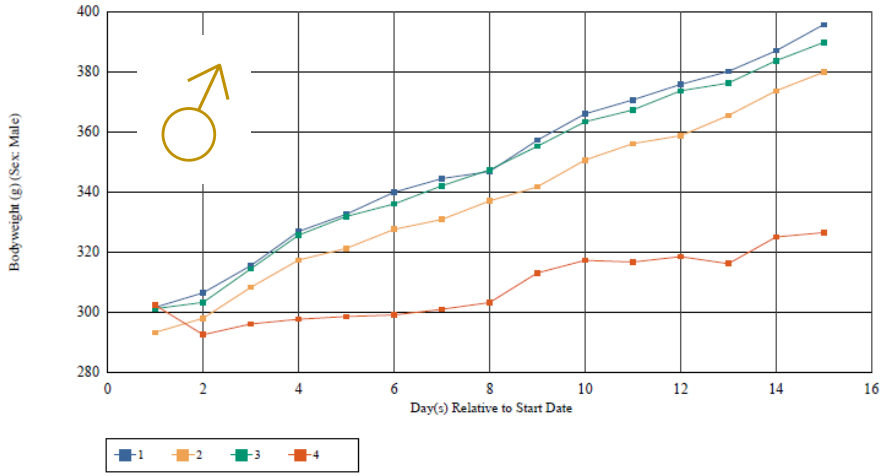
Update ongoing testing

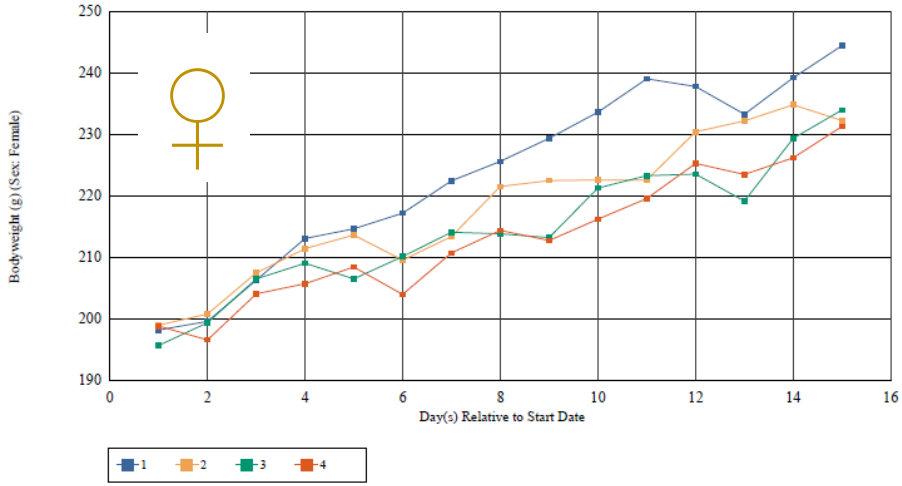
- **PdCl2 – RDT and Reprotox screening** assays (6/6)
  - **DRF**:
    - Test item stability
    - Test item concentration and homogeneity
    - Reporting
    - Deciding on dosing regime for full test

…

Update ongoing testing

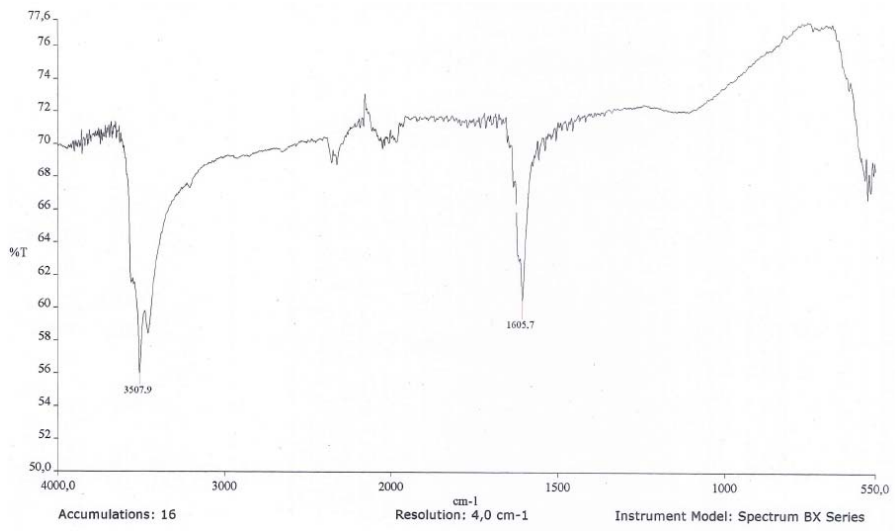
- **Na2PdCl4 – RDT&Reprotox screening** assays (OECD407-421) @LPT (1/3)
  → currently low KL ranked Moore et al (1975) study on K salt
  - **DRF**:
    - Dosing levels: 1000 - 3000 - 10000 ppm in diet (corresponding to approx. 100-300-1000 mg/kg/d)
    - No behavioural changes
    - High dose males: picked up lack of weight gain at d9
    - Findings at necropsy:
      - High dose group: enlarged caecum filled with dark content (2 male and 3 female animals)





Update ongoing testing

- **Na2PdCl4 – RDT&Reprotox screening** assays (2/3)
  - **DRF**:
    - Test item stability:
      - CCl4 extraction of diet, dry pellets
      - FT-IR on pellets



Update ongoing testing

- **Na2PdCl4 – RDT&Reprotox screening** assays (3/3)
  - **DRF**:
    - Test item stability
    - Test item concentration and homogeneity
    - Reporting
    - Deciding on dosing regime for full test

…

Update ongoing testing - summary

TAPdCl2	**ENV**	alg	***Finalised***
		Daphnia reprotox	***Ongoing***
		ASRIT	***Ongoing***
	HH	AMES	***Finalised***
Pdacac	**ENV**	alg	***Finalised***
		Daphnia reprotox	***Ongoing***
		ASRIT	***Ongoing***
	HH	RDT/Repro screening	***Ongoing***
PdO	**PC**	Oxid properties	***Finalised***
	HH	bioelution	***Ongoing***
PdCl2	**HH**	AMES	***Finalised***
		in vitro MLA (tk)	***Finalised***
		RDT/Repro screening	***Ongoing***
Na2PdCl4	**HH**	skin sensit	***Ongoing***
		RDT/Repro screening	***Ongoing***

Expert review registration dossiers Pd/Pt

- **DHI** contracted
- **4 groups** selected:
    - Hexachloroplatinates
    - Tetraamminepalladium compounds
    - Tetrachloropalladate
    - Hexachloropalladate

  → sensitizers (skin/resp), read-across, 'weak' ENV assessment, TP… included
- Focus = IUCLID dossier, CSR, justification documents

Expert review registration dossiers Pd/Pt

- Covered points:
  - technical compliance with IUCLID format
  - waivers
  - read-across justifications and supporting documentation
  - classification
  - identification of the critical NOAECs/ NOAELs
  - derivation of DNELs / PNECs
  - exposure assessment
  - relevance and appropriateness of Risk Management Measures
  - Risk Characterisations, interpretation of RCRs

- Specific focus on critical endpoints, i.e. respiratory sensitisation of chloroplatinates and skin sensitisation of the palladium substances.

Expert review registration dossiers Pd/Pt

- **Main conclusions**:
  - Verify compliance waivers following update to IUCLID v6.1-2
  - Verify compliance when using read-across (ie, report source and target correctly)
  - Data lacking for possible local effects from LT exposure in the 3 Pd groups
  - Classify TAPdCl2 as STOT-RE2 via RA from TAPdHCO3
  - DNELs: include interspecies scaling factor of 4
  - DNEL H2PdCl4 inappropriately derived via read across
  - PNEC derivation Pd groups weak
  - Applicability metal-based Kd for metal complexes

Most conclusions already included in OFI tracker / workplan…

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5. Platinum and compounds

Update ongoing testing

- **PtO2 – genotox testing** (@Covance)

  → *AMES: missing data*

  - **AMES**:
    - No vehicle identified ⟹ suspensions in 1% Methyl Cellulose
    - Exp 1 treatments of strains TA98 (+S9) and TA100 (+S9): notable increases in revertant numbers:
      - approached (TA98) or exceeded (TA100) 2-fold the concurrent vehicle control level
      - some evidence of a concentration-relationship as they occurred at highest treatment concentration)

    → in both cases the increases were almost entirely attributable to a single elevated replicate plate count.

    + no comparable increases observed following either the plate incorporation or pre-incubation methodology treatments in Exp 2

    ⟹ single elevated plate counts were not considered a true compound-related effect

    Study was considered to have provided no evidence of any PtO2,hydrate mutagenic activity.

Update ongoing testing

- **PtO2 – in vivo skin sensitisation** testing (@LPT)

  → *no data available*

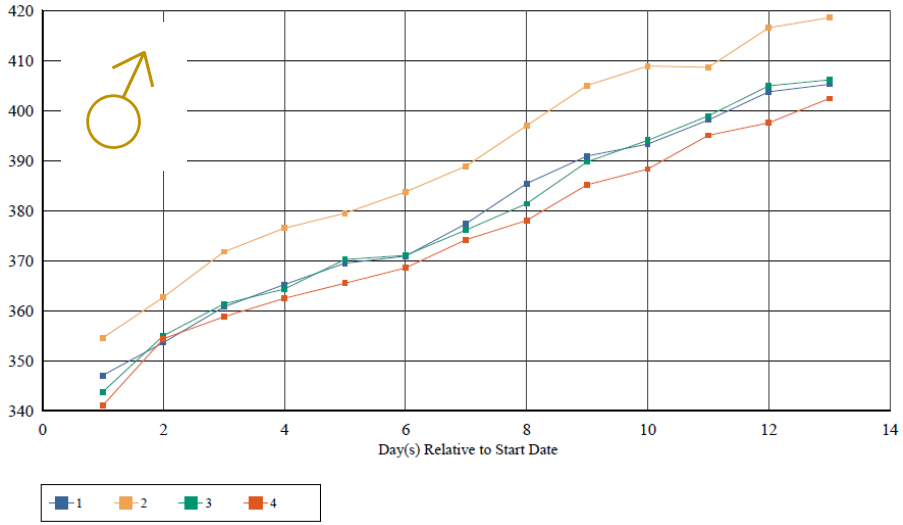
  - In vivo skin sensitization (OECD442B)

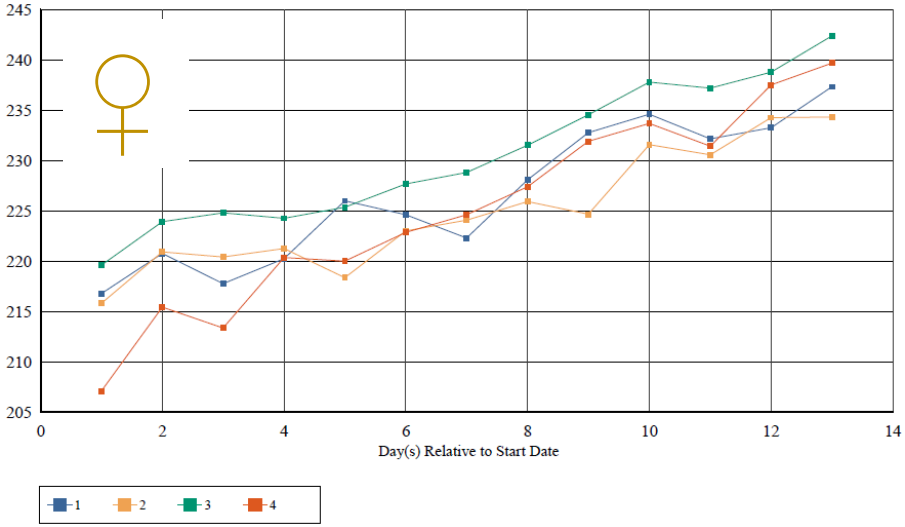
  - ***Results available end of cw 38, draft report available end of cw 39***

! Need to develop WoE argumentation ('in vitro testing not appropriate for metals')

Update ongoing testing

- **PtN – RDT and Reprotox screening** assays (OECD407-421) @LPT (1/5)
  → waiver based on corrosivity not sustainable
  - **DRF**:
    - Dosing levels: 300 - 1000 - 3000 ppm in diet (corresponding to approx. 30-100-300 mg/kg/d)
    - Test day 11 (of 14):
    - no clinical signs and no effects on body weight at any dosing level





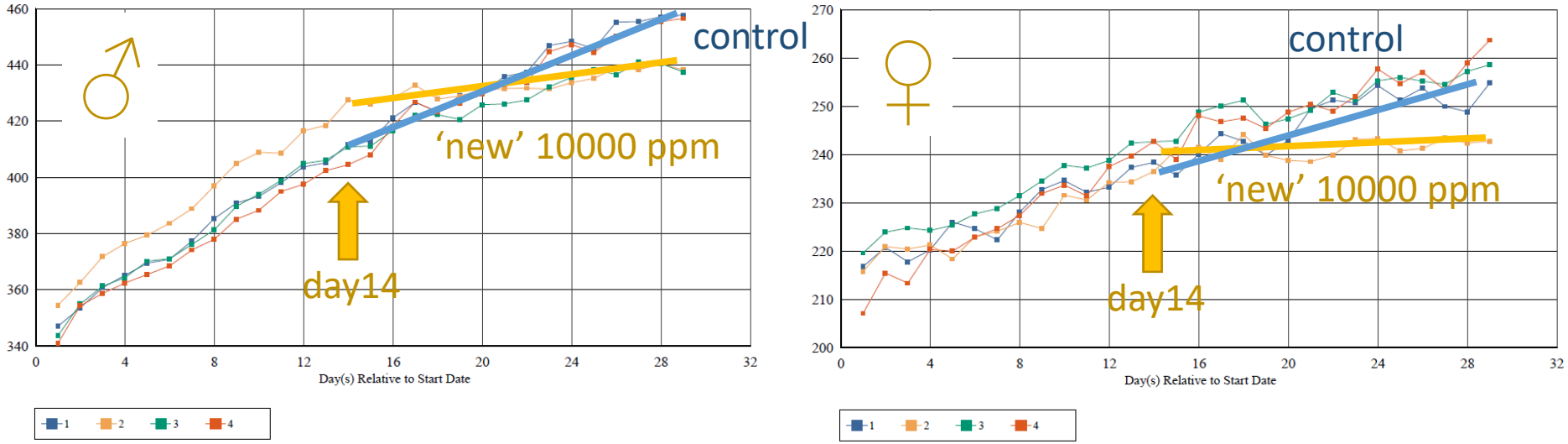
Update ongoing testing

- **PtN – RDT and Reprotox screening** assays (2/5)
  - **DRF**:
    - Decision to **extend DRF** with 14 additional days + **increase dosing** levels

	Days 1-14	Days 15-28
Control	0 ppm	0 ppm
Low dose	300 ppm →	**10000 ppm**
Mid dose	1000 ppm →	**7000 ppm**
High dose	3000 ppm	3000 ppm

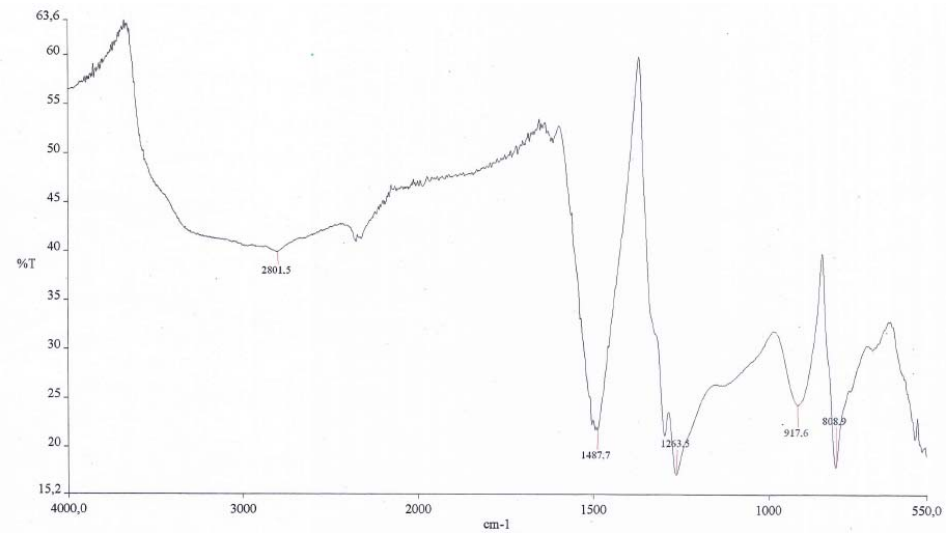
Update ongoing testing

- **PtN – RDT and Reprotox screening** assays (3/5)
  - DRF:
    - Necropsy: no test item-related changes.
    - Slight and statistically not significant reductions in BW (high dose,male: max -4.3%; high dose,female: -4,9%)
    - Only temporal reduced food consumption between d15 - 17 for mid and high dose.
    - No changes in behaviour, the external appearance and the consistency of the faeces



Update ongoing testing

- **PtN – RDT and Reprotox screening** assays (4/5)
  - **DRF**:
    - Test item stability:
      - FT-IR possible



Update ongoing testing

- **PtN – RDT and Reprotox screening** assays (5/5)
  - **DRF**:
    - Test item stability:
      - FT-IR possible

Cfr slides on SID investigation PtN

Update ongoing testing - summary

PtO2	**HH**	skin sensit	***Ongoing***
		AMES	***Finalised***
PtN	**HH**	RDT/Repro screening	***Ongoing***

Pt genotox : Status

- 5 **TP for in vivo genetox**

  → included in 9 dossiers

Genotoxicity Group	Substance covered in group	EC	Registration tonnage band	Registration date	Public consultation – deadline for submitting information
Pt(IV) anionic (*'hexachloroplatinates'*)	Diammonium hexachloroplatinate	240-973-0	10-100 t/a	Jan 2018	7/6/2018
	Hexachloroplatinic acid	241-010-7	10-100 t/a		11/5/2018
	Dipotassium hexachloroplatinate	240-979-3	10-100 t/a		11/5/2018
Pt(II) cationic £	Tetraammineplatinum dichloride	237-706-5	1-10 t/a (Annex III)	Dec 2017	16/4/2018
	Tetraammineplatinum dinitrate (in solution)	243-929-9	1-10t/a	Dec 2017	16/4/2018
Pt(IV) anionic (*'hexahydroxyplatinates'*)	Dihydrogen hexahydroxyplatinate, compound with 2-aminoethanol (1:2)	268-717-3	10-100 t/a	Jan 2018	*Not published yet*
	Dihydrogen hexahydroxyplatinate	257-471-2	10-100 t/a	June 2017	16/4/2018
Pt(IV) cationic *	Platinum dinitrate (*UVCB*)	242-383-9	10-100 t/a	June 2017	*Not published yet*
Pt(II) anionic	Dipotassium tetrachloroplatinate	233-050-9	1-10 t/a (Annex III)	Dec 2017	2/8/2018

** Underlined substance is proposed as source substance for in vivo mutagenicity/genotoxicity testing within the group*

£ This group contains the non-PMC substances Tetraammineplatinum diacetate and Tetraammineplatinum hydrogen carbonate (registered by Umicore as LR)

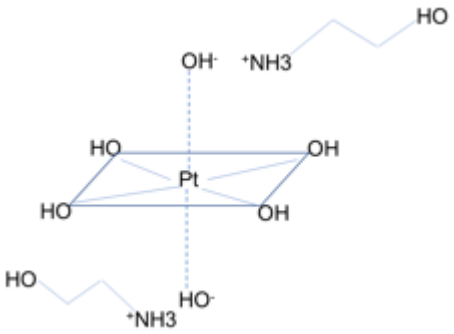
- Public consultations finalised for 3 TP/groups
- SID investigation integral part of TP assessment

  → **questions for HHPA-2AE and PtN** *(cfr next slides)*

Pt genotox : Status

- **SID questions HHPA-2AE** (1/2)
  - *Issue 1: Name and other identifier (identifiers and type of the substance)*
  - *Issue 2: Composition (how it was derived, role of 2-aminoethanol)*
  - *Issue 3: Spectral data and quantification*

  - **Clarification document** drafted by PMC/BASF (as LR)
    - Monoconstituent substance
    - **Protonated 2AE as counterion**
    - **No coordination** Pt-N under these conditio
    - Exists in narrow concentration window
    - Further evidence on composition:
      - Ramen
      - 13C NMR
      - 1H NMR
      - Elemental analysis
      - 2AE content in solution



<u>Informally</u> considered acceptable by ECHA

Pt genotox : Status

- **SID questions HHPA-2AE** (2/2)
  - Read-across HHPA-2AE to HHPA dossier, but no **read-across justification** document available
    - Being drafted by EMPF secretariat
    - Missing information: '*speciation to same toxicological species*?'

      → **Pt NMR analysis** ongoing with Evonik:
        - HHPA and HHPA-2AE in HCl solution (pH1,5)
        - 1h shaking, 1h settling

      (cfr. approach for TAPt cmpds)

Pt genotox : Status

- **SID questions PtN** (1/2)
  - *Issue 1: Name and other identifiers (well defined substance vs UVCB, manufacturing process description, reaction scheme)*
  - *Issue 2: Composition (identity of the main constituent)*
  - *Issue 3: Analytical information*

  - TE conf call 4 July: **4 main actions** identified
    1. Test PtN samples from all registrants with 195Pt NMR (solution and solid (+ redissolved solid))
    2. If required, test PtN samples with XANES/EXAFS
    3. Develop manufacturing process + reaction scheme
    4. Investigate elemental composition

Pt genotox : Status

- **SID questions PtN** (1/2)
  - **195Pt NMR testing** at Evonik (Hanau)
    - Request for test samples sent to companies
    - Test + reporting in Oct-Nov
  - **EXAFS/XANES**
    - Possible in University Karlsruhe (solid + solution)
    - PtN sample (solid + solution) sent for some preliminary analysis (quality of spectra, pretreatments required…)
    - Prelim analysis serving as basis for price offer
  - **Elemental analysis** samples unclear – under investigation by LR
  - **Manuf process/reaction scheme**: to be developed after SID has been clarified

    *Volunteers: Angela, Paul, Herbert – **others?***

! If SID clarified & sameness solid vs solution(s) agreed,

then RDT/Reprotox screening assay can continue.

If not…

Pt genotox : Status

- **Next steps**:
  - Public consultations finalised for 3 TP / groups, pending for 2 (HHPA-2AE and PtN)
    - HHPA-2AE expected to be launched soon
    - PtN pending on ongoing SID investigation
  - TP being processed for **3 groups** (TAPt, HexaClPt, TetraClPt)
    → expected to be referred to MSCA at **same time**
  - TP HHPA-group and PtN expected to be processed **later** and separate from the others
  - Testing Q2-3 2019?

Pt genotox : Status

Lab	OECD 474 In vivo micronucleus	OECD 489 Comet assay	OECD 474/489 combined	OECD 488 Transgenic gene mutation
Envigo UK Candidate lab?	27 rat studies (last 2 yrs) Sprague Dawley or Han Wistar 12 mouse CD1	Sprague Dawley or Han Wistar rats Predominately performed in the liver and duodenum tissues. Liver - 19 studies in 19 months, Duodenum - 14 studies in 19 months, **Kidney - 4 studies since 2017** Glandular stomach - 10 studies since 2011	can combine the OECD474 and 489 however we do not currently have experience with freezing tissues for analysis at a later date	*Do not offer this*
CiTox Lab Hungary	*Subcontracted*	*Subcontracted*	*Subcontracted*	*No subcontractor identified*
Eurofins, Germany	Performed routinely	Several studies performed in liver, lung, stomach, duodenum and colon. **Kidney could be stablished in 2-3 months**	Yes??	*Not established*
LPT Germany	Numerous experience	Numerous experience **Control data in all organs are available**	Numerous experience	*Not established*
Covance UK Candidate lab?	Good experience in rat & mouse. Historical data –vehicle & positive controls.	Good experience in rat & mouse. Historical data –vehicle & positive controls Wealth of background data in stomach, liver & duodenum, **less so in kidney**. Frozen tissues not validated.	Good experience in rat & mouse. Historical data – vehicle & positive controls	Mutamouse fully validated and operational.

KC SID clarification

- *Recap: conclusion from OECD422 assay:*
  - *Classify KC as Repr2*
  - *Include TP for EOGRTS*

- SID investigation part of TP assessment

- Questions raised by ECHA:
  - *Issue 1: Name and other identifiers (manufacturing process description, reaction scheme)*
  - *Issue 2: Composition (Variability)*
  - *Issue 3: Analytical information*

- **LR included clarifications** in dossier → ***informally* accepted by ECHA**

KC SID clarification

- **Pending issue: a new identifier/new substance name needed:**
  - **current identifier only relates to the complexes as such and not the other constituents** like the starting silane (can be present in high concentrations)
  - the oxidation state (Pt(0)) needs to be reflected in the name.

ECHA proposal : "*1,3-diethenyl-1,1,3,3-tetramethyldisiloxane and its platinum (0) complexes*"

KC SID clarification

- **Next steps:**
  - EC entry can be kept for now but statement needed in ‘remark’ field of reference substance in IUCLID section 1.1:

“*The EC number 242-383-9 currently assigned does not specifically correspond to the registered substance. This identifier cannot be modified or deleted at this stage in the present registration update for technical reasons*”

(number connected to registration in REACH-IT, and not technically possible to modify at this stage - unsure if need to change in the future)

  - move current CAS number to “Other identifiers”
  - provide a representative IUPAC (chemical) name in section 1.1.

- **In practice**, name ‘Karstedt Concentrate’ can still be used by companies, and registration remains valid/acceptable

KC SID clarification

For information - ballpark estimate for EOGRT assay (Citoxlab)

citoxlab
Safety and Health Research

Extended One Generation Reproductive Toxicity Rat -oral gavage (including 10 weeks premating exposure	OECD 443 / 12-15 months / ~7 kg	535 000
Supporting analysis (assuming 6 occasions). Additional occasion: 1213 Eur/occ.		7 278
Optional:		**Optional:**
Immunotox subgroups		50 547
Neurotox subgroups		106 155
Extension of Cohort 1B to mate the F1 animals to produce the F2 generation		79 015

→ *Capacity migth be an issue (cfr many requests + demanding)*

→ *7 kg test substance required (!?)*

Precious Metals Consortium

Precious Metals Consortium

6. Rhodium and compounds

Update ongoing testing

- **Rhodium trioxide – acute tox (oral), skin irrit/corr, eye irrit/corr, in vivo skin sensitisation** testing (@LPT)

  → *datagaps for update Annex III to VII*

  - Acute tox (oral)

    Scheduled Oct 2018

  - Skin irrit/corr

    Scheduled Sept-Oct 2018

  - Eye irrit/corr

    Scheduled Sept-Oct 2018

  - In vivo skin sensitization (OECD442B)

    Scheduled Oct 2018

    Develop WoE argumentation ('in vitro testing not appropriate for metals')

Update ongoing testing

- **Rhodium trioxide – oxidizing properties** (@BAM)
  → *test data to replace waiving statement*
  - Sample tested.
  - ***Classification as Oxidising solid (cat1 - H271)? To be confirmed)***

Rh(III) genotox : Status

- **AMES** testing **poorly water soluble Rh(III)** cmpds:
  - Rhodium trihydroxide
    - Suspensions in 0,5%MC

    Conclusion: Rhodium trihydroxide does not induce mutation

  - Rhodium trioxide
    - Suspensions in 0,5%MC

    Conclusion: Rhodium trioxide does not induce mutation

  - Rhodium tris(2-ethylhexanoate)
    - Formulation in tetrahydrofuran

    Conclusion: Rh tris(2EH) does not induce mutation

→ ***confirmation of Rh(III) genetox hypothesis for PWS Rh(III)***

Rh(III) genotox : Further actions

- **Rh(III) genetox database**

	Rh trichloride hydrate	Rh trinitrate (solid)	Rh trinitrate (liquid)	Rh acetate	Rh sulfate	Triammonium hexachloro rhodate	Dipotassium pentachloro rhodate	Diammonium sodium hexakis(nitrito-N) rhodate	Rh triiodide	Rh trioxide	Rh trihydroxide	Rh tris(2-ethyl-hexanoate)
Water solubility category	WS	WS	WS	WS	WS	WS	WS-MWS	MWS	PWS	PWS	PWS	PWS
Bioelution (gastric) (% dissolution)	101							95	0.014	0.00013	0.54	
Bacterial reverse mutation (Ames)	+ (n=4)	- (n=2)	+	+	+	+	+	-	+*	-	-	-
In vitro MN	+ (n=3)							-				
In vitro mammalian mutagenicity (hprt / tk)	+ (n=2)							-				
Other in vitro	+ (n=3)					+	+					
In vivo MN	+	-										

Solid neg responses

Self-classified as Muta2

Rh(III) genotox : Further actions

- **Rh(III) genetox database**

	Rh trichloride hydrate	Rh trinitrate (solid)	Rh trinitrate (liquid)	Rh acetate	Rh sulfate	Triammonium hexachloro rhodate	Dipotassium pentachloro rhodate	Diammonium sodium hexakis(nitrito-N) rhodate	Rh triiodide	Rh trioxide	Rh trihydroxide	Rh tris(2-ethyl-hexanoate)
Water solubility category	WS	WS	WS	WS	WS	WS	WS-MWS	MWS	PWS	PWS	PWS	PWS
Bioelution (gastric) (% dissolution)	101							95	0.014	0.00013	0.54	
Bacterial reverse mutation (Ames)	+ (n=4)	- (n=2)	+	+	+	+	+	-	+*	-	-	-
In vitro MN	+ (n=3)							-				
In vitro mammalian mutagenicity (hprt / tk)	+ (n=2)		U V C B	U V C B				-				
Other in vitro	+ (n=3)					+	+					
In vivo MN	+	-										

Agreed test substance for in vivo genetox TP

Rh(III) genotox : Further actions

- Agreement to include **TP for in vivo genetox** (comet/MN + TK assay)
  - Proposed assay similar to Pt dossiers
  - TP drafted by Bibra
  - RA from all (moderately) water soluble Rh(III) test data

    → RA justification document being drafted by Secretariat

    Proposal to ask Mark R to review once available
  - Rh sulphate as test compound
  - No inclusion TP in other compounds

- **MISA Workshop**:
  - RA to other compounds once test is performed (no RA TP needed)
  - Two groups with predicted different genetox potential

    → include justification in dossiers that no further testing (in vitro/in vivo) is required!?

    → prioritize chemistry work RhI3 (cfr. next slide)

Rh(III) genotox : Further actions

- **Rh(III) genetox database**

	Rh trichloride hydrate	Rh trinitrate (solid)	Rh trinitrate (liquid)	Rh acetate	Rh sulfate	Triammonium hexachloro rhodate	Dipotassium pentachloro rhodate	Diammonium sodium hexakis(nitrito-N) rhodate	Rh triiodide	Rh trioxide	Rh trihydroxide	Rh tris(2-ethyl-hexanoate)
Water solubility category	WS	WS	WS	WS	WS	WS	WS-MWS	MWS	PWS	PWS	PWS	PWS
Bioelution (gastric) (% dissolution)	101							95	0.014	0.00013	0.54	
Bacterial reverse mutation (Ames)	+ (n=4)	- (n=2)	+	+	+	+	+	-	+*	-	-	-
In vitro MN	+ (n=3)							-				
In vitro mammalian mutagenicity (hprt / tk)	+ (n=2)							-				
Other in vitro	+ (n=3)					+	+					
In vivo MN	+	-										

Chemistry needs further investigation – cfr next slides

Rh(III) genotox : Further actions

- Positive Ames RhI3 attributed to **DMSO as vehicle**?

  → reason to further investigate chemistry

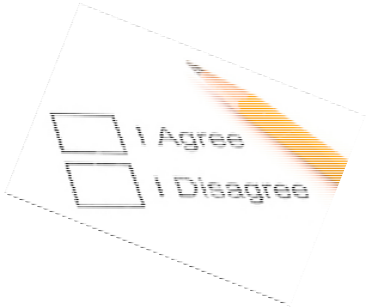
- **Approach**:
  - dissolve RhI3:
    1. in water
    2. in DMSO
    3. in water/DMSO mixtures, eg 0.01%, 0.1%, 1% (equimolar concentrations DMSO and RhI3 at about 1.5% solution), 10%
  - in the positive AMES study, a suspension of 100 mg/mL (=0,207M) was prepared
  - shake the solution/suspension (1-2 h?), centrifuge or filter, and analyse the solution:

    -ICP to measure the Rh concentration in solution

    (-spectral analysis to verify re-speciation?)

Approach OK?

Test by member company?



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7. Ruthenium and compounds

Update ongoing testing

- **Ru(IV) oxide – skin irrit/corr, in vivo skin sensitisation** testing (@LPT), **genotox** testing (AMES, @Covance) (1/2)

  → *data gap filling*

  - **Skin irrit/corr**
    - Applied as solid test item in Epiderm assay
    - 60 min exposure, 42h post treatment

    No irritant properties

  - **In vivo skin sensitization** (OECD442B)
    - ***Results available end of cw 39, draft report available end of cw 40***

    ! Need to develop WoE argumentation ('in vitro testing not appropriate for metals')

Update ongoing testing

- **Ru(IV) oxide – skin irrit/corr, in vivo skin sensitisation** testing, **genotox** testing (2/2)

  → data gap filling

  - **AMES** assay:
    - Suspension in DMF
    - No toxicity observed at 5000 µg/plate
    - No notable and concentration-related increases in revertant numbers were observed, and none that were significantly above the concurrent vehicle control

    No evidence of any Ru(IV) oxide mutagenic activity in this assay

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8. 2019 draft budget

2019 Draft Budget – Pt (1)

7. Pt metal	**21.033 €**	**0,04**
7.1 REACH registration	0 €	
7.2 REACH dossier maintenance	13.000 €	
7.3 REACH evaluation	0 €	
7.4 REACH classification & labelling	0 €	
7.5 REACH authorisation	0 €	
7.6 Internal and external fixed Scientific Managers	6.652 €	
7.7 IUCLID IT hosting system	476 €	
7.8 Knowledge Management tool + hosting	905 €	
8. Chloroplatinates	**271.311 €**	**0,2**
8.1 REACH registration	0 €	
8.2 REACH dossier maintenance	23.000 €	
8.3 REACH evaluation	200.000 €	
8.4 REACH classification & labelling	0 €	
8.5 REACH authorisation	15.000 €	
8.6 Internal and external fixed Scientific Managers	31.930 €	
8.7 IUCLID IT hosting system	476 €	
8.8 Knowledge Management tool + hosting	905 €	

2019 Draft Budget – Pt (2)

9. Karstedt	**851.311 €**	**0,2**
9.1 REACH registration	0 €	
9.2 REACH dossier maintenance	18.000 €	
9.3 REACH evaluation	800.000 €	
9.4 REACH classification & labelling	0 €	
9.5 REACH authorisation	0 €	
9.6 Internal and external fixed Scientific Managers	31.930 €	
9.7 IUCLID IT hosting system	476 €	
9.8 Knowledge Management tool + hosting	905 €	
10. Pt compounds (others)	**433.611 €**	**0,3**
10.1 REACH registration	0 €	
10.2 REACH dossier maintenance	65.000 €	
10.3 REACH evaluation	300.000 €	
10.4 REACH classification & labelling	0 €	
10.5 REACH authorisation	0 €	
10.6 Internal and external fixed Scientific Managers	47.230 €	
10.7 IUCLID IT hosting system	476 €	
10.8 Knowledge Management tool + hosting	905 €	
10.9 Science budget	10.000 €	

2019 Draft budget - Pd

11. Pd metal	**21.033 €**	**0,04**
11.1 REACH registration	**0 €**	
11.2 REACH dossier maintenance	**13.000 €**	
11.3 REACH evaluation	**0 €**	
11.4 REACH classification & labelling	**0 €**	
11.5 REACH authorisation	**0 €**	
11.6 Internal and external fixed Scientific Managers	**6.652 €**	
11.7 IUCLID IT hosting system	**476 €**	
11.8 Knowledge Management tool + hosting	**905 €**	
12. Pd compounds	**306.572 €**	**0,4**
12.1 REACH registration	**0 €**	
12.2 REACH dossier maintenance	**190.000 €**	
12.3 REACH evaluation	**0 €**	
12.4 REACH classification & labelling	**0 €**	
12.5 REACH authorisation	**0 €**	
12.6 Internal and external fixed Scientific Managers	**65.191 €**	
12.7 IUCLID IT hosting system	**476 €**	
12.8 Knowledge Management tool + hosting	**905 €**	
12.10 Science budget	**10.000 €**	

2019 Draft budget – Rh (1)

13. Rh metal	**20.501 €**	**0,04**
13.1 REACH registration	0 €	
13.2 REACH dossier maintenance	13.000 €	
13.3 REACH evaluation	0 €	
13.4 REACH classification & labelling	0 €	
13.5 REACH authorisation	0 €	
13.6 Internal and external fixed Scientific Managers	6.120 €	
13.7 IUCLID IT hosting system	476 €	
13.8 Knowledge Management tool + hosting	905 €	
14. Rh III compounds	**133.611 €**	**0,3**
14.1 REACH registration	0 €	
14.2 REACH dossier maintenance	75.000 €	
14.3 REACH evaluation	0 €	
14.4 REACH classification & labelling	0 €	
14.5 REACH authorisation	0 €	
14.6 Internal and external fixed Scientific Managers	47.230 €	
14.7 IUCLID IT hosting system	476 €	
14.8 Knowledge Management tool + hosting	905 €	
14.9 Science budget	10.000 €	

2019 Draft budget – Rh (2)

15. Rh compounds (others)	178.311 €	0,2
15.1 REACH registration	0 €	
15.2 REACH dossier maintenance	145.000 €	
15.3 REACH evaluation	0 €	
15.4 REACH classification & labelling	0 €	
15.5 REACH authorisation	0 €	
15.6 Internal and external fixed Scientific Managers	31.930 €	
15.7 IUCLID IT hosting system	476 €	
15.8 Knowledge Management tool + hosting	905 €	

2019 Draft budget - Ru

16. Ru metal	20.501 €	0,04
16.1 REACH registration	0 €	
16.2 REACH dossier maintenance	13.000 €	
16.3 REACH evaluation	0 €	
16.4 REACH classification & labelling	0 €	
16.5 REACH authorisation	0 €	
16.6 Internal and external fixed Scientific Managers	6.120 €	
16.7 IUCLID IT hosting system	476 €	
16.8 Knowledge Management tool + hosting	905 €	
17. Ru compounds	60.153 €	0,08
17.1 REACH registration	0 €	
17.2 REACH dossier maintenance	36.000 €	
17.3 REACH evaluation	0 €	
17.4 REACH classification & labelling	0 €	
17.5 REACH authorisation	0 €	
17.6 Internal and external fixed Scientific Managers	12.772 €	
17.7 IUCLID IT hosting system	476 €	
17.8 Knowledge Management tool + hosting	905 €	
17.10 Science budget	10.000 €	

2019 Draft budget - Ir

18. Ir metal	**25.501 €**	**0,04**
18.1 REACH registration	**0 €**	
18.2 REACH dossier maintenance	**18.000 €**	
18.3 REACH evaluation	**0 €**	
18.4 REACH classification & labelling	**0 €**	
18.5 REACH authorisation	**0 €**	
18.6 Internal and external fixed Scientific Managers	**6.120 €**	
18.7 IUCLID IT hosting system	**476 €**	
18.8 Knowledge Management tool + hosting	**905 €**	
19. Ir compounds	**76.501 €**	**0,04**
19.1 REACH registration	**0 €**	
19.2 REACH dossier maintenance	**69.000 €**	
19.3 REACH evaluation	**0 €**	
19.4 REACH classification & labelling	**0 €**	
19.5 REACH authorisation	**0 €**	
19.6 Internal and external fixed Scientific Managers	**6.120 €**	
19.7 IUCLID IT hosting system	**476 €**	
19.8 Knowledge Management tool + hosting	**905 €**	

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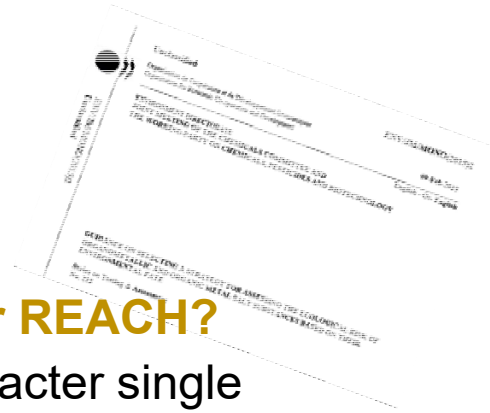
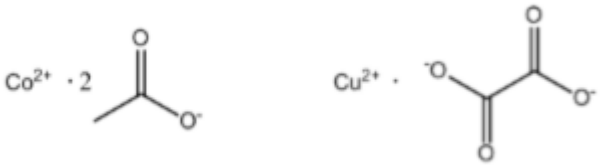
9. AOB. Next meeting(s) and closing remarks

AOB – Organic metal salts vs Organometallics

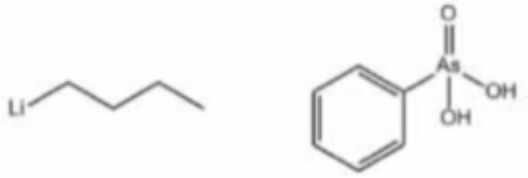


- **EM EHS week: how to cover organic metals salts under REACH?**
  - **Organic metal salt** = metal + organic moiety (ion-character single bond, rapid dissociation)



vs

organometal = metal covalently bound to C



ISSUE: '*For regulatory purposes, OM incl coordination complexes where M has covalent-character bonds with O/N/S/P belonging to organic moiety*'

AOB – Organic metal salts vs Organometallics

- Organometals assessed as organics (ie, bioaccumulation, biomagnification, not exempted from PBT/vPvB etc)
- Need to show (rapid) dissociation in metal + organic moiety (or not)

Identification potential toxicological moieties

Consider/assess relative tox potential of all moieties

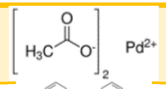
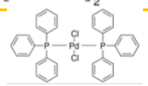
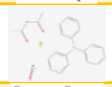
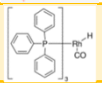
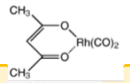
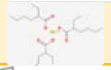
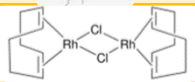
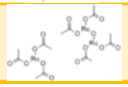
If appropriate, stick to 'current' approach (effects driven by dissolved M^{x+} ion).

Otherwise, assess as OM

HOW? Via OECD TD screening test (max duration of 24h)

AOB – Organic metal salts vs Organometallics

- **Substances to be tested**?

Name	*CAS*		*Water solub (OECD105)*
Palladium(II) acetate	3375-31-3		922 (Harlan 2011)
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)
Hexakis[mu-(acetato-O:O')]-μ3-oxo-triangulo-triruthenium acetate / Ruthenium acetate	55466-76-7		660x10^3 (Gregory 2014)

AOB – Organic metal salts vs Organometallics

- 24h TD screening test (price offer ECTX)

pH 6 (CO2 buffering)	2963.6 €
pH8	2365 €
Total	**5378.6 €** (incl 50€ shipment) for first sample
	3920.9 € for each additional sample

- Total cost (excl test sample) -11 samples à 4055 €/sample:

Pd cmpds	12165 € (n=3)
Rh(III)cmpds	8110 € (n=2)
Rh cmpds (other)	20275 € (n=5)
Ru cmpds	4055 € (n=1)

Nanos

- **Literature review** nanoPGMs ongoing:
  - **Human health**:
    - Bibra contracted (preferred to DHI and WCA)
    - Focus on gold and PGMs and their nanoforms, and HH
    - Review scheduled <end 2018
  - **Environment**:
    - Review by PGM Secretariate
    - Review scheduled <end 2018

! ECHA Newsletter Sept 2018: 'Are the new REACH information requirements for nanos relevant for you?'

[…]When will the new annexes come into force?

The draft Commission Regulation amending the annexes has not yet been formally adopted by the Commission. If adopted, industry will need to comply with the new requirements ***by January 2020****.*

→ ***next steps for nanoPGMs???***

Nanos

- **Way-forward:**
  - Wait outcome HH+ENV lit reviews + send summaries to members once available
  - **Question to companies: are nanoPGMs put on the market? SID? Tonnage?**

    → if no information received <end 2018, assumed to be not relevant!

  - Need for budget in case testing is required, but budget for 2019 is fixed <end 2018

    → use reserves in case testing is required? (proposal to Mgt Cttee)

  - Approach: if registration is required, T is assumed to be low…

    →what to test? all endpoints or a selection ?

    →group (and waive?) based on bioelution / TDp (cfr approach with metallic PGMs)?

    →read-across from metal / metal oxide ?

    To be decided on case-by-case basis if registration is required

Next meeting(s)

- **4-5 December 2018**
  PMC/EPMF GA meeting (Bxl)

- **1 April 2019**
  Spring BtB meeting (Bxl)

- **5-6 June 2019**
  EPMF GA meeting (Bordeaux, France)

- **8-10 October 2019**
  Autumn BtB meeting (Bxl)

Precious Metals Consortium

THANK YOU

www.epmf.be | info@epmf.be

Avenue de Broqueville 12. B-1150 Brussels
+32 (0)2 761 01 00