



Precious Metals
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Precious Metals & Rhenium Consortium

Gold Work Group

19 April 2016 | Brussels, Belgium

11:00 – 12:30



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Welcome and introduction

Competition law and confidentiality

DO	DON'T
<u>Application of competition law</u>	
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.
<u>Consultation in Matters of Competition Law</u>	
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.
<u>Activities in any preliminary phase and at any other stage of operation of the Consortium</u>	
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: <ul style="list-style-type: none"> - 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.

DO	DON'T
<u>Exchange of Confidential Information</u>	
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 : <ul style="list-style-type: none"> - Production capacities; - Productions or sales volumes; - Import volumes; - Market shares; - Price policy; - Distribution and marketing terms; - Marketing strategies; - Information regarding the relationship with suppliers.
<u>Documentation on Cooperation</u>	
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.	



Tour de Table & Apologies

Approval of the draft agenda

1. Welcome and Introduction
2. Phase I: Inventory & Classification
3. Phase II: Data gap analysis & Integrated Testing Strategy
4. Phase III: Testing programme
5. Phase IV: Exposure scenario data collection
6. Phase V: Dossier finalisation
7. Budget
8. AOB, next meetings/calls and closing remarks

Approval of minutes from previous WG meeting

- The previous Au Work Group meeting was held on 13 October 2015
- Draft minutes were distributed on 27 October 2015

→ *Are the minutes of the WG meeting held on 13/10/2015 approved?*

Status of actions

[A]	WHAT	WHO	STATUS
26	Communicate the exclusion of nanogold to the SIEF.	EPMF/ARCHE	Oct '15
27	Review the classification for TCA based on the results of the OECD 422 test. Potential STOT and/or developmental tox. classification based on the NOAELs.	WCA	Done Apr '16
28	The PMC secretariat will prepare a TSCA 8e notification for the developmental toxicity of TCA. This document will be sent to the registrants, as they will complete the notification themselves.	EPMF/ARCHE	On hold, due to validity issues with the OECD 422
29	Inform the WG on the final decision of the management committee on the submission of future TSCA 8e notifications	EPMF/ARCHE	Done
30	A complete list of the non-confidential uses including all the use descriptors will be distributed with the minutes.	EPMF/ARCHE	Oct '15
31	After commenting the draft DNEL report, EBRC will be asked to start the work on exposure scenarios and consider the DNELs as final.	EPMF/ARCHE	On hold, due to validity issues with the OECD 422



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Phase I Inventory & Classification

Inventory and latest classifications

IUPAC Name	Gold	Tetrachloroauric acid	Aurio(1+) 2,6,6-trimethylbicyclo[3.1.1]heptanethiolate	Balsams, copaiba, sulfurized, mixed with turpentine, gold salts
CAS nr	7440-57-5	16903-35-8	68365-87-7	68990-27-2
EINECS nr	231-165-9	240-948-4	269-858-3	273-589-7
REACH category	Mono-constituent	Mono-constituent	Mono-constituent	UVCB
Dossier prepared	Substance	Substance	Substance	Non-SCC Intermediate
Highest tonnage band	10-100 t/a	10-100 t/a	1-10 t/a	1-10 t/a
Registration deadline	2018	2018	2018	2018
Lead Registrant	C. Hafner	Johnson Matthey	Johnson Matthey	Heraeus
Classification	None	Acute tox. 4 (H302: Harmful if swallowed) Skin corr. 1B (H314: Causes severe skin burns and eye damage) Eye dam. 1 (H318: Causes serious eye damage) Aquatic chronic 2 (H411) Met. Corr. 1 (H290: May be corrosive to metals)	Flam. Solid Cat 1 (H228)	Flam. Solid Cat 1 (H228)



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Phase II Data gap analysis & ITS

Data gap analysis TCA hydrate

- TCA hydrate will be registered and TCA solution will be regarded as a mixture

Endpoint	Comments
Melting/freezing point	75°C (Otto <i>et al.</i> , 2014)
Boiling point	Waived, column 2 (Otto <i>et al.</i> , 2014)
Water solubility	Analysis ongoing
Flammability	Waived, expert judgment
Self-ignition temperature	Waived, column 2
Granulometry (particle size distribution)	Analysis ongoing

Otto, K., Oja Acik, I., Krunks, M., Tõnsuaadu, K., & Mere, A. (2014). Thermal decomposition study of H₂AuCl₄·3H₂O and AgNO₃ as precursors for plasmonic metal nanoparticles. *Journal of Thermal Analysis and Calorimetry*, 118(2), 1065–1072.



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Phase III Testing Programme

Test programme – Physicochemical Analyses

Test	Laboratory/ Endpoint	Status	Date
Water solubility (OECD 105)	Siemens/ Annex V	Initiated	January 2016
Development analytical method	Siemens	Initiated	January 2016
Particle Size Distribution (OECD 110)	Siemens/ Annex V	Initiated	January 2016

Test programme – Environment

Test	Laboratory/ Endpoint	Status	Date	Comments
Adsorption/Desorption (OECD 106)	Fraunhofer/ Annex VIII	Final	Jan 2016	Kd = 1105.93 – 4540.71 cm ³ /g

Test programme – Mamtox TCA Skin and Eye tests

Test	Laboratory	Completion date	Result	Comments	Classification
Eye Irritation (in vitro) - BCOP OECD437	Study waived on the basis of corrosivity to skin as a result of low pH				Category 1 (H318) – automatically assigned
Eye Irritation (in vivo) – Rabbit OECD405	Study waived on the basis of corrosivity to skin as a result of low pH				
Skin corrosion test (in vitro) – Episkin OECD431	Berthold (1993)	1993	Positive	Corrosive	Corrosive Category 1b (H314)
Corrositex Assay	BSL BioService	2013	Positive	Corrosive	
Skin Irritation (in vivo) – Rabbit OECD404	Study waived on the basis of corrosivity shown in vitro as a result of low pH				
Skin sensitisation – LLNA OECD429	Study waived on the basis of corrosivity to skin as a result of low pH				No data

Test programme – Mamtox TCA Acute tox tests

Test	Laboratory	Completion date	Result	Comments	Classification
Acute toxicity – oral OECD401	Berthold 1993	1993	LD50 >464 mg/kg	Conducted with a non-neutralised formulation	Category 4 (H302)
Acute toxicity – dermal OECD402	Study waived on the basis of corrosivity to skin as a result of low pH				No data
Acute toxicity – inhalation OECD403	Study waived on the basis of corrosivity to skin and low pH				No data

Test programme – Mamtox TCA Repeat dose toxicity

Test	Laboratory	Completion date	Result	Comments	Classification
MTD oral rat study	Covance	2014	MTD 100 mg/kg/day or 210 mg/kg/day after adjustment for density	Conducted with neutralised formulation. Severe effects on clinical signs, bwt and food cons and renal pathology at 150 mg/kg/day (315 mg/kg/day adjusted)	N/A
Repeated oral dose/Reproductive toxicity screen – OECD422	Covance	2015	Dose levels were 10, 30 and 100 mg/kg/day or 21, 63 and 210 mg/kg/day when adjusted for density. General tox NOAEL = 63 mg/kg/day Fert/Repro NOAEL = 210 mg/kg/day Developmental NOAEL = 21 mg/kg/day?	Conducted with neutralised formulation. Treatment related renal effects were confirmed at the 210 mg/kg/day dose level. Increased incidence of small or missing/cannibalised/dead pups was recorded at 63 and 210 mg/kg/day across a number of litters. This report is still at Draft 2 stage	Category 2 for reproductive effects; STOT RE Not applicable as lowest effect level outside 10-100 mg/kg/day Cat 2 range

Test programme – Mamtox TCA Genetox tests

Test	Laboratory	Completion date	Result	Comments	Classification
Ames test – Bacterial cell mutation OECD471	McGarry 2012	2012	Negative		Not classified
In vitro mammalian cell gene mutation test – OECD476	Study not required as positive in in vitro micronucleus test				
In vitro cytogenicity test in mammalian cells – OECD487	Watters 2013	2013	Positive	Positive response observed in 3+21h and 24+24h cultures - S9. Equivocal response in 3+21h cultures +S9	Potentially aneugenic or clastogenic
In vivo micronucleus assay – OECD474	Covance	2015	Negative	All dose levels (25, 50 and 100 mg/kg/day) below MTD adjusted for density of 210 mg/kg/day	

Test programme – Mamtox TCA Formulation analysis

Test	Laboratory	Completion date	Result	Comments	Classification
Formulation analysis method development	Covance	2015	ICP-MS showed acceptable freedom from interference, linearity, repeatability and sensitivity. Acceptable homogeneity and stability were also confirmed	This report is still at Draft stage. Covance are awaiting confirmation to finalise	N/A
Formulation analysis report OECD474	Covance	2015	Gold recoveries: Day 1: -7.5%, -2.7%, -3.3% Day 2: -8.2%, -10.8%, -5.5%	All assay results were within the $\pm 15.0\%$ acceptance limit	N/A
Formulation analysis report OECD422	Covance	2015	Gold recoveries: Day 1: -0.98%, -15.7%, -27.1% Day 55: +19.3%, -10.2%, -30.3%	The quoted results are those following adjustment of dose levels for density. The original analyses were conducted in October 2014. This report is still at Draft stage	N/A

Covance position on OECD474 study

Test identification	Status	Covance position
OECD474 – in vivo micronucleus assay	<p>Study conducted Aug 2014</p> <p>Report finalised (Feb 2015)</p> <p>Formulation prepared by weight therefore dose levels (25, 50 and 100 mg/g/day) based on unadjusted MTD of 100 mg/kg/day</p> <p>Formulation analysis revealed assays for all groups to be within -11% of nominal</p> <p>All dose levels therefore were below the adjusted MTD of 210 mg/kg/day</p> <p>Analysis of bone marrow smears for gold (Umicore-unreported data) did not detect gold in the target tissue at any dose level</p> <p>Plasma samples from rats on the MTD study (dosed at 168 or 210 mg/kg/day – adjusted for density) are awaiting despatch to Umicore for analysis of gold content in an attempt to demonstrate exposure.</p>	<p>Agreed options:</p> <p>a) Repeat study with control and new high dose level at MTD (at Covance expense)</p> <p>b) Credit note equivalent to (a)</p> <p>c) Reimbursement equivalent to (a)</p> <p>Negotiations currently on hold</p> <p>N.B. any further work on this endpoint will require submission of a testing proposal to ECHA under revised wording of REACH Annex IX</p>

Covance position on OECD422 study

Test identification	Status	Covance position
<p>OECD422 – Repeat-dose toxicity and reproductive toxicity screen</p>	<p>Study conducted Aug-Sept 2014</p> <p>Report at Draft 2 stage (Feb 2016)</p> <p>Formulation prepared by volume as for MTD. Therefore, dose levels selected were 10, 30 and 100 mg/kg/day (21, 63 and 210 mg/kg/day adjusted for density)</p> <p>Formulation analysis revealed the following assay results for Groups 2, 3 and 4: Day 1: -0.98, -15.7 and -27.1% Day 55: +19.3, -10.2 and -30.3% The variability at the low and intermediate dose levels impacts the identification of NOAELs for general toxicity and reproductive toxicity</p> <p>Full comments from PMC on Draft 2 of the report yet to be sent to Covance. However, an updated version (Report amendment 1) of the Formulation analysis report has been received from Covance</p> <p>Protocol Amendment No.2 covering the change of personnel has not been signed by PMC due to GLP statement</p>	<p>Agreed action: Covance to conduct additional formulation analysis in an attempt to add confidence to the actual dose levels used in the main study. This will be done at Covance expense and we are currently awaiting a study plan for approval.</p>



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Phase IV Exposure Scenario Data Collection

PNEC derivations - TCA

PNEC	Value
Freshwater	1,04E-03 mg TCA L ⁻¹
Freshwater sediment	4,5 mg TCA kg ⁻¹ wwt 20,45 mg TCA kg ⁻¹ dwt
Marine water	1,04E-04 mg TCA L ⁻¹
Marine sediment	0,45 mg TCA kg ⁻¹ wwt 2,04 mg TCA kg ⁻¹ dwt
Intermittent releases	0,0104 mg TCA L ⁻¹
Soil	3,65 mg TCA kg ⁻¹ wwt 4,15 mg TCA kg ⁻¹ dwt
STP	0,2 mg TCA L ⁻¹

Draft DNEL derivations

	TCA	Comments
Points of Departure	General toxicity 63 mg/kg/day (45.102 mg/kg/day pure TCA)	Lowest NOAEL from OECD422 study
	Reproductive toxicity 21 mg/kg/day (15.034 mg/kg/day pure TCA)	Lowest NOAEL from OECD422 study
Workers		
Inhalation		
Systemic effects		^a Acute DNELs not derived. Potential for acute effects are protected by long-term DNEL
Long-term exposure	0.171 or 0.029 mg/m ³	
Acute/Short-term exposure	Not derived ^a	
Local effects		^b No route-specific data. Skin and eye corrosive. Potential for local effects protected by long-term DNEL and CLP
Long-term exposure	Not derived ^b	
Acute short-term exposure	Not derived ^b	
Dermal		
Systemic effects		^c Assuming 100% dermal absorption
Long-term exposure	0.05 or 0.008 mg/kg/day ^c	^d No acute dermal exposure data as substance was corrosive. This DNEL is protected by long-term DNELs and CLP
Acute/Short-term exposure	Not derived ^a	
Local effects		
Long-term exposure	Not derived ^d	
Acute short-term exposure	Not derived ^d	
General population		
Inhalation		
Systemic effects		^a Acute DNELs not derived. Potential for acute effects are protected by long-term DNEL
Long-term exposure	0.044 or 0.007 mg/m ³	
Acute/Short-term exposure	Not derived ^a	
Local effects		^b No route-specific data. Skin and eye corrosive. Potential for local effects protected by long-term DNEL and CLP
Long-term exposure	Not derived ^b	
Acute short-term exposure	Not derived ^b	





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Phase V Dossier finalisation

Overview Registration Progress

Dossier	Status
Gold	Registration by Co-registrants in progress
Balsams	Registration by LR in progress
Aurio	Reviewing in progress, Registration by LR in May 2016
Tetrachloroauric acid	Finalisation Q4 2016, depends on the OECD 422



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Budget

Final Budget 2015

	Budget	Real	Delta
Au REACH registration	56.650 €	68.528 €	-11.878 €
Phase 1: Literature search, data gap analysis and recommendations	10.500 €	3.158 €	7.342 €
Phase 2: In-depth data gap analysis and integrated testing strategy	0 €	4.490 €	-4.490 €
Phase 3: Experimental studies (testing programme including cost of samples)	0 €	25.295 €	-25.295 €
Phase 4: Generation of Chemical Safety Reports	38.000 €	24.570 €	13.430 €
Phase 5a: Generation of IUCLID 5 Files and Registration Dossiers	5.000 €	9.013 €	-4.013 €
Phase 5b: IUCLID 5 Hosting System	3.150 €	2.002 €	1.148 €

Budget 2017

	Budget to be spent	Budget to be invoiced
Au-specific costs	45.200 €	45.200 €
Au REACH registration	0 €	0 €
Au REACH dossier maintenance	10.000 €	10.000 €
Phase 4: Generation of Chemical Safety Reports	5.000 €	5.000 €
Phase 5b: IUCLID 5 Hosting System	5.000 €	5.000 €
Au REACH evaluation	0 €	0 €
Au REACH classification & labelling	0 €	0 €
Au internal and external fixed Scientific Manager	35.200	35.200



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Final Remarks

Final Remarks

- A.O.B.
- Actions summary
- Conclusions
- Next meeting/conf call:
 - PMC Plenary meeting: **1-2 June 2016, Wroclaw**
 - Next Au Work Group meeting: **4-6 Octobre 2016, Brussels**
 - + Ad-hoc meetings/conf call



THANK YOU

www.epmf.be | info@epmf.be

Avenue de Broqueville 12, B-1150 Brussels
+32 (0)2 775 63 86