



Precious Metals & Rhenium Consortium
Brussels, 08 October 2014, 12:30 - 14:00

Will start 12:40
Enjoy lunch

Precious Metals & Rhenium Consortium

Gold Working Group



1. Welcome & Introduction

1. Welcome and introduction

2. Phase I
3. Phase II: Data gap analysis and ITS
4. Phase III: Testing programme
5. Phase IV: Use, exposure, and emission data collection
6. Phase V: Dossier finalisation
7. AOB, next meetings/calls and closing remarks

Steven Verberckmoes



Welcome & Introduction

- Reminder on Confidentiality and Competition Law
- Tour de table and apologies
- Agenda approval
 - Next slide



Agenda approval

Gold Working Group Members were emailed the draft agenda on October 1st, 2014

1. Welcome and introduction
2. Phase I
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Status of actions

Legend:

Done

Ongoing

Not started

#	What?	Who?	When?	Status
	Draft text explaining why the PBT calculation approach is acceptable based on the structure of the Gold balsams, so it can be attached to the IUCLID file		Jul 2012	Done
	Finalise REACH Annex III assessment for Gold balsams		Jul 2012	Done
	Discuss and clarify how TCA can be neutralised before administration to test animals in OECD 422 study		Jul 2012	Done
	Cancel Aug 2012 planned HPRT/MLA study, share tentative MoGA and proposal to proceed with FISH/associated timescale study with Covance for discussion		Jul 2012	Done
	Launch FISH study		Jul 2012	Done, test completed
	Contact David Kirkland to arrange timeslot for discussions when FISH timescale is known		Jul 2012	Done
	Consider need for <i>ad hoc</i> literature search on Au I and Au III genotoxicity		Jul 2012	Done
	Prepare summary of TCA dataset and read-across reference substance status and present to David Kirkland for assessment/advice		Jul 2012	Done
	Decide on best <i>in vivo</i> assessment avenue/path		Jul 2012	Done, updated ITS
	Re-evaluate read-across strategy from TCA to other Au compounds, from Au III to Au I more particularly		Jul 2012	Done
	Confirm realistic (versus optimistic) registration submission windows for GOLD project	R. Nicolay	Dec 2014	Work plan updated, CON approval to do
	Confirm scope of Au registration dossier: nano in or out? (Consult WGC if needed)	R. Nicolay	Q3 2015	Survey deadline: Oct 10 2014
	Prepare 2015-2020 budget projection for GOLD	R. Nicolay	Dec 2014	Not started
	Document decision-making re genotoxicity testing of TCA	R. Nicolay	Q3 2014	Pending Members' approval: today



2. Phase I

1. Welcome and introduction

2. Phase I

- a. Inventory and latest classifications
- b. Outcome of literature searches

3. Phase II: Data gap analysis and ITS

4. Phase III: Testing programme

5. Phase IV: Use, exposure, and emission data collection

6. Phase V: Dossier finalisation

7. AOB, next meetings/calls and closing remarks

Renaud Nicolay
& WCA



Inventory & Classification

IUPAC Name	Gold	Tetrachloroauric acid (in aq. solution)	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 (t/a)	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)	Flam. Solid Cat 1 (H228)	Flam. Solid Cat 1 (H228)
		Skin corr. 1B (H314: Causes severe skin burns and eye damage)		
		Eye dam. 1 (H318: Causes serious eye damage)		
		Aquatic chronic 3 (H412: Harmful to aquatic life with long lasting effects)		
		Met. Corr. 1 (H290: May be corrosive to metals)		

Literature search - strategy



- Searches conducted individually for each substance name and CAS number. Search strings were used for gold.
- Databases searched:
 - *Toxline*: <http://toxnet.nlm.nih.gov>
 - *Thomson Innovation*: <http://info.thomsoninnovation.com>
 - *US-EPA ECOTOX Database*: <http://cfpub.epa.gov/ecotox/>

Date of search	Period covered
November 2012	Jan 2009 – Oct2012
November 2013	Nov 2012 – Nov 2013

Reliability and relevance assessment



- All results were combined and any duplicate records were removed
- Data screened based on title and abstract
- Results from the 2013 search – screened also for data on nanogold.
- Copies of each potentially relevant study – subject to detailed assessment (Klimisch et al. 1997, ToxRTool, specific criteria for studies with nanoparticles)

Output of searches and next steps



Search date	Number of results	Number of potentially relevant results	Number of relevant studies
November 2012	13,345	25	11
November 2013	4,120	32 (incl. studies on NPs)	11

- 22 studies considered sufficiently reliable for inclusion in the REACH dossiers
- 3 additional studies identified by PMC
- Searches of the published literature are scheduled to take place every year.
- Next searches – to be conducted in November 2014



3. Phase II: Data Gap Analysis & Integrated Testing Strategy

1. Welcome and introduction
2. Phase I
- 3. Phase II: Data gap analysis and ITS**
4. Phase III: Testing programme
5. Phase IV: Use, exposure, and emission data collection
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Renaud Nicolay



Data Gap Analysis & Integrated Testing Strategy

- In order to provide a comprehensive and compliant registration dossier, the data gap analysis is pointing out at endpoints that can only be generated through a testing programme once these have been considered
 - Klimisch 1 & 2 existing studies (literature search)
 - Waiver/Exemptions (typically for substances where the endpoint is not applicable)
 - Read-across from other substance(s)
- The status on dossier completion is further discussed under
 - item 2 “Phase I: Outcome of literature searches”
 - item 5 “Phase V: Dossier finalisation”



4. Phase III: Testing Programme

1. Welcome and introduction
2. Phase I
3. Phase II: Data gap analysis and ITS
- 4. Phase III: Testing programme**
 - a. Current status, bottlenecks and next steps
 - b. Status and timing of PNEC and DNEL derivation
5. Phase IV: Use, exposure, and emission data collection
6. Phase V: Dossier finalisation
7. AOB, next meetings/calls and closing remarks

WCA

Testing status at last WG meeting: Toxicology



- Enabling tests conducted for gold metal

Test	Laboratory	Draft Report	Status	Comments
N-BET analysis + PSD	Fraunhofer	N/A	Not required	N-BET already provided by member company PSD in T/D test report from ECTX
Bio-elution test (gastric fluid)	CIMM	Nov 2012	Term	No release of gold to the synthetic gastric medium above detection limit of 1µg/L

- Other endpoints for gold waived or filled with existing data
- Some data available for TCA, and further testing in progress
- No toxicology data required for other gold substances (Annex III exempt)

Current testing status: Toxicology (TCA)



■ Genetic toxicology studies

- » A tiered approach to genotoxicity testing was agreed by the Working Group
 - *Ames Test (screen & main study)*
 - *In vitro Micronucleus assay*
 - *In vitro Mammalian cell gene mutation (not conducted due to +ve result in vitro micronucleus test)*
 - *In vivo Micronucleus assay (conducted under Annex VIII requirement)*
- » Testing has been conducted at Covance, UK

Current testing status: Toxicology (TCA)



■ Genetic toxicology studies

Test	Laboratory/ Endpoint	Draft /Final Report	Status	Comments
AMES Screen	Covance UK	Oct 2012	Term	Toxic to Salmonella strains (not pH related)
AMES GLP (OECD ₄₇₁)	Covance UK/ Annex VII	Oct 2012	Term	-ve result upto toxic concentrations (not pH related)
<i>In vitro</i> Micronucleus test (OECD ₄₈₇)	Covance UK/ Annex VIII	Jan 2013	Term	+ve response (-S ₉) and equivocal response (+S ₉)
<i>In vivo</i> Micronucleus test (OECD ₄₇₄)	Covance UK/ Annex VIII	Sep 2014	Term	Dose levels set at 25, 50 and 100 mg/kg/day; Clear -ve has been indicated

no TP

Current testing status: Toxicology (TCA)



- General toxicology studies
 - » MTD/DRF Rat study
 - *Required due to the absence of sufficient information to predict suitable dose levels for repeat-dose administration*
 - » OECD422 Repeat-dose/Reproductive screen Rat study
 - » Formulation analysis
 - *Assessment of gold content in formulations administered in OECD422 and OECD474 GLP studies*

Current testing status: Toxicology (TCA)



■ General toxicology studies

Test	Laboratory/ Endpoint	Draft/Final Report	Status	Comments
MTD/DRF Rat study	Covance UK	Mar 2014	Term	MTD for repeat dosing set at 100 mg/kg/day
Repeat-dose/Repro screen Rat study (OECD ₄₂₂)	Covance UK/ Annex VIII	Nov 2014	Ongoing	Dose levels set at 10, 30 and 100 mg/kg/day; neutralised formulation
Formulation analysis	Covance UK	Nov 2014	Ongoing	ICP-MS methodology; initial problems with positive analytical bias

Implications of results from toxicology studies



■ Classification/Further testing - TCA

Classification as of Feb 2014	Source	Further testing	Potential classification change?
Acute tox. 4 (H302)	Berthold (1993a) LD ₅₀ >464 m/k	None required	No change
Skin corr. 1B (H314)	Berthold (1993b)	Limier (2013) CDS >3 – 60min	No change
Eye dam. 1 (H318)	Expected – based on pH	None required	No change

Status and timing of DNEL derivation



- To be assessed
 - » Insufficient data until completion of repeat-dose toxicology studies
- Timing
 - » Data will be available by the end of Q1 2015

Testing status at last WG meeting: Environment



- Acute ecotoxicity testing complete for TCA
- Ecotoxicity endpoints waived for gold metal (no dissolution in T/D test)
- Ecotoxicity tests not required for other gold substances (Annex III exemption)

Testing status at last WG meeting: Ecotoxicology



■ Acute ecotoxicity test results for TCA

Test	Final Report	Result (mg TCA / L)	
Algae	May 2012	NOEC (growth rate and yield)	0.90
		EC ₅₀ (growth rate)	> 9.0
Daphnia	May 2012	EC ₅₀	4.8
ASRIT	Feb 2012	NOEC	2
		EC ₅₀	27.9

Current testing status: Environment



- Sediment and terrestrial data not required for TCA (<100 tonnes)
- Sediment and terrestrial PNECs for TCA to be derived based on equilibrium partitioning
- Adsorption / desorption information required – literature data not available

Current testing status: Adsorption / desorption



- Test proposed – modified OECD 106 method (OECD 121 HPLC method specified in regulation not suitable for metals)
- Conduct preliminary stages of the test only to determine a partition coefficient
- Quotes received and Fraunhofer chosen as test laboratory
- Proposal signed (09/09/2014)
- Test item received at Fraunhofer (sent 25 Sep)

Implications of ecotoxicity results



- No further ecotoxicity testing currently being conducted for gold substances
 - » No anticipated classification changes at present
- Adsorption / desorption test results will be used to derive sediment and terrestrial PNECs. No impact on classification

Substance	Environmental classification (Feb 2014)	Classification change proposed?
Gold	Not classified	No change
TCA	Aquatic chronic 2	No change
Balsams, copaiba, sulfurized, mixed with turpentine, gold salts	Not classified	No change
Aurio(1+) 2,6,6-trimethylbicyclo[3.1.1]heptanethiolate	Not classified	No change

Status and timing of PNEC derivation



- Aquatic PNECs for TCA derived based on ecotoxicity data for the substance itself
- TCA terrestrial and sediment PNECs will be derived using equilibrium partitioning following results from adsorption / desorption study
 - » PNEC freshwater: 0.0048 mg TCA/L
 - » PNEC marine water: 0.00048 mg TCA/L
 - » PNEC intermittent releases: 0.048 mg TCA/L
 - » PNEC STP: 0.2 mg TCA/L
- PNECs not required for gold metal (waived)
- Other gold substances <10 tpa – no PNECs required



5. Phase IV: Use, exposure, and emission data collection

1. Welcome and introduction
2. Phase I
3. Phase II: Data gap analysis and ITS
4. Phase III: Testing programme
- 5. Phase IV: Use, exposure, and emission data collection**
 - a. Use data collection and confirmation on use of nanoforms
 - b. Exposure and emission data collection
 - c. Potential monitoring needs
6. Phase V: Dossier finalisation
7. AOB, next meetings/calls and closing remarks

Renaud Nicolay
& WCA



Use of Gold nanoforms

- Definition of “nanomaterial” recommended by the European Commission:

“Nanomaterial means a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm - 100 nm. In specific cases and where warranted by concerns for the environment, health, safety or competitiveness the number size distribution threshold of 50 % may be replaced by a threshold between 1 and 50 %.”

“Particle” means a minute piece of matter with defined physical boundaries;

“Agglomerate” means a collection of weakly bound particles or aggregates where the resulting external surface area is similar to the sum of the surface areas of the individual components;

“Aggregate” means a particle comprising of strongly bound or fused particles.

- PMC internal survey issued on 12 Sep 2014 with deadline on 10 Oct 2014
- Survey partial results, 3 days from deadline:

Producing:	Nanogold	Other gold nanocompounds
% answers on Oct 7	50 %	50 %
Result: “Yes production”	0 %	0 %
Result: “No production”	100 %	100 %



- Members having already answered to the survey are invited to double-check that they have indeed no nanogold: PMC may not generate any specific registration dossier or data if this is confirmed
- So-called “nanogold” has announced applications in cosmetics, electronics, medicine, ...

Use data collection



- Questionnaire has been circulated
- To be completed for Manufacture and all downstream uses of Gold substances
- Select type of use at the top of the spreadsheet (Manufacture, Formulation, Industrial, Professional, Consumer, Article service life)
- Incompatible use descriptors are unable to be selected
- Selected use descriptors are compatible with those that can be selected

Environmental emissions data collection



- Emissions data will be used to develop the Generic Exposure Scenario (GES) in the CSR
- Site-specific exposure assessments will be conducted for each manufacturing site to demonstrate safe use if $RCR < 1$
- Completing the questionnaire as fully as possible ensures the GES is representative and that safe use can be demonstrated for the site (site-specific data rather than EUSES defaults are most likely to achieve this)

Environmental emissions data collection



- Questionnaires circulated to collect environmental emissions data. Exposure assessment required for TCA only
- Questionnaire to be completed once per site
- Covers
 - » Tonnages of TCA and other gold substances used at site
 - » Environmental emissions of gold to air and water
 - » Any RMMs used on-site
 - » Information on the municipal STP and the final receiving water (flow rates are important)

Environmental emissions data collection



- If STP and receiving water information already completed for PGMs project this can be used - please indicate
- If potassium dicyanoaurate also produced on site, the PM CN- questionnaire can be completed. This questionnaire collects data on gold emissions to assess the emissions of gold from potassium dicyanoaurate
 - » Gold emissions data will be collected from the gold tab

Potential monitoring needs



- Site-specific monitoring programme launched for PGMs (aquatic and sediment) to refine environmental exposure assessment
- Recommended for sites with RCRs >0.5
- Until initial exposure assessment for TCA is run we cannot determine which sites may have RCRs >0.5 and therefore require monitoring or further refinement of exposure assessment
- For companies involved in the PGMs programme it may be worth adding gold analysis (minimal cost) to the monitoring programme

Occupational exposure scenarios (occ. ES)

- Occ. ES are required for hazardous substances manufactured and/or imported at or above 10 tonnes per year
- According to ECHA guidance*, the scope of the exp. assessment has to be determined (please also see provided discussion paper)
- ECHA's official "Chemical Safety Assessment and Reporting tool" Chesar can be used for the development of (occ.) ES, also providing information on the scope of exposure assessment
- Information received that occ. ES are required for
 - tetrachloroauric acid
 - potassium dicyanoargentate
 - silver cyanide
 - potassium dicyanoaurate→ Development of occ. exp. questionnaire for manufacturers

Occupational exposure questionnaire

- Use of activity classes (ACs), defining a set of conducted activities, differentiation between:
 - process-driven emission potential (spraying, drying, transport operations etc.)
 - emission potential of handled material (dusty solids vs. solutions)
 - temperature-driven emission potential (ambient temperature vs. substantially elevated temperature)
- Introduction and detailed glossary provided for print-out
 - Provided for your own comfort – please read thoroughly
- Information to be provided per substance
- Different ACs can be nominated per substance
- Please also provide information on availability of monitoring data (tailored submission form will follow in case of availability)

Tailored occ. exposure assessment

- Complexity of exposure assessment depends on:
 - Hazard potential of the substance (level of DNEL)
 - Emission potential
 - Identified uses (generic vs. specific assessments)
- Modelled vs. measured exposure data depends on:
 - Availability of monitoring data
 - Personal measurements
 - Inhalable fraction?
 - Substance-specific, e.g. analysed for Au
 - Contextual information complete?
 - Conservative model estimates may result in high RCRs
 - Other reasons for monitoring:
 - national legislation
 - product stewardship, etc.



... 5 min coffee break ...





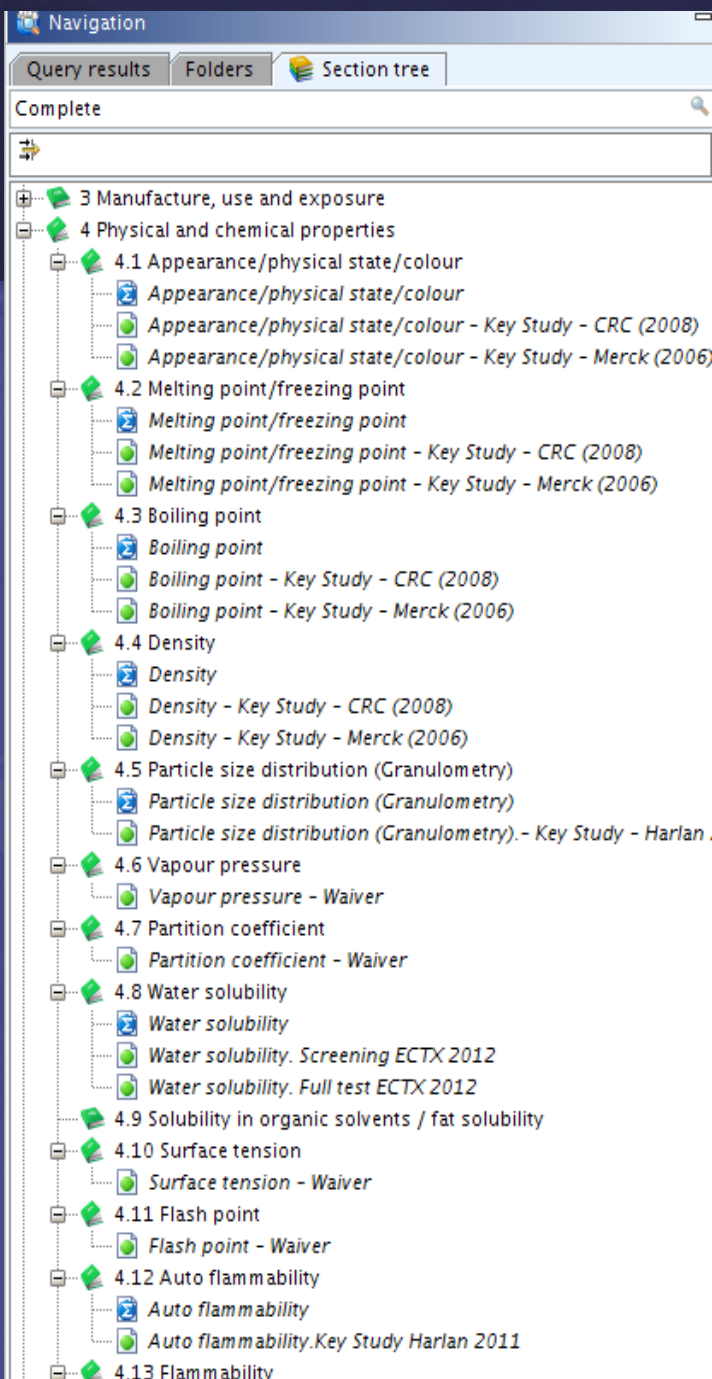
6. Phase V: Use, exposure, and emission data collection

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& WCA

6. Phase V: Dossier finalisation

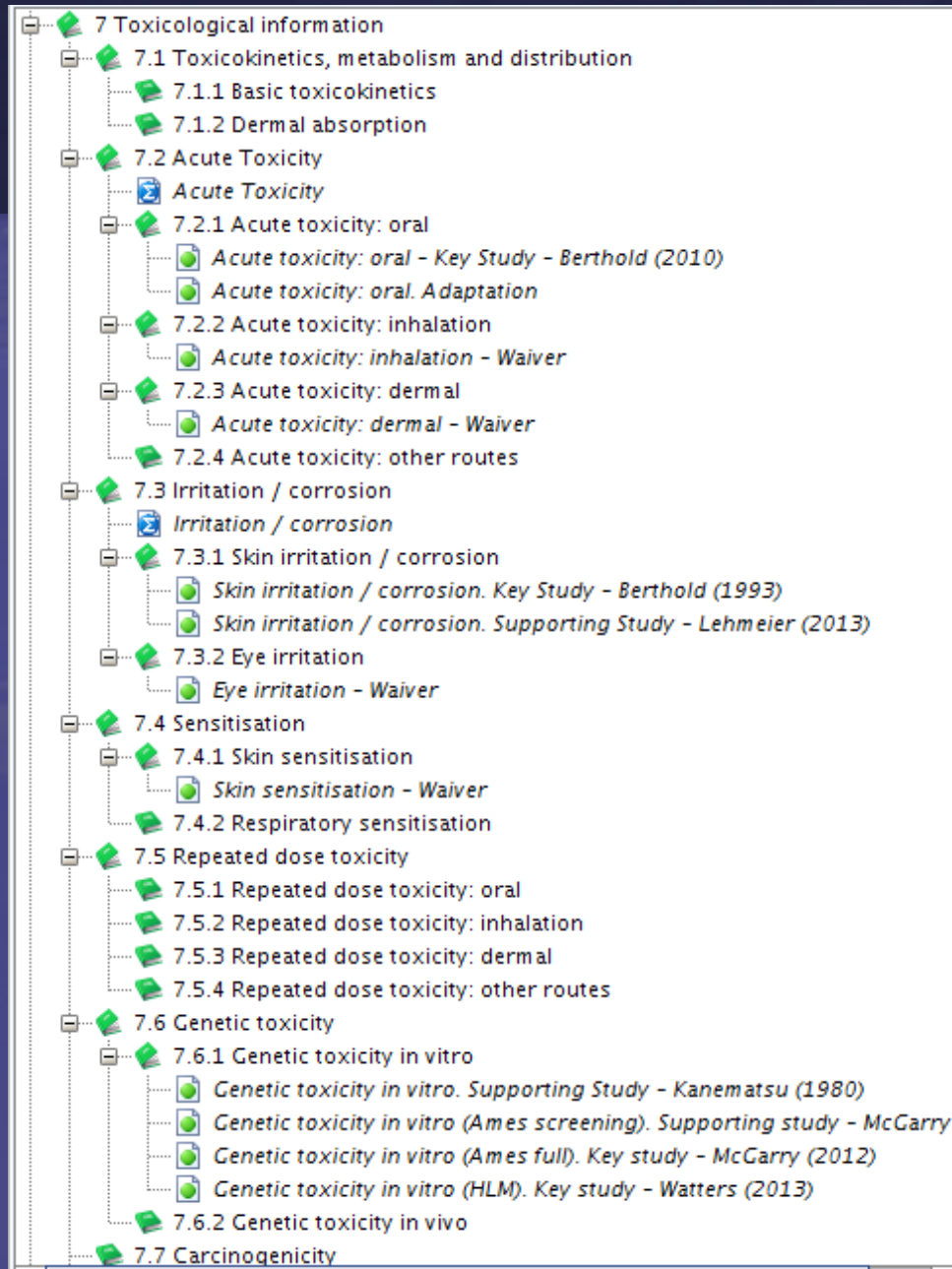
- a. IUCLID dossier constitution
 - b. Registration target and project full overview
7. AOB, next meetings/calls and closing remarks



Gold



- Phys-chem: Complete
- Environmental fate and ecotox: Exact wording of waivers still to be agreed
- Mamtox: Exact wording of waivers still to be agreed



- Phys-chem: Wording of waivers to be agreed (aqueous solution)
- Environmental fate and ecotox: Studies entered where available. PNECs to be added once finalised
- Mamtox: Studies entered where available

IUCLID 5 - PMC - Au - Aurio(1+) 2,6,6-trimethylbicyclo[3.1.1]heptanethiolate / aurio(1+)

File Edit Go Window Help Plugins

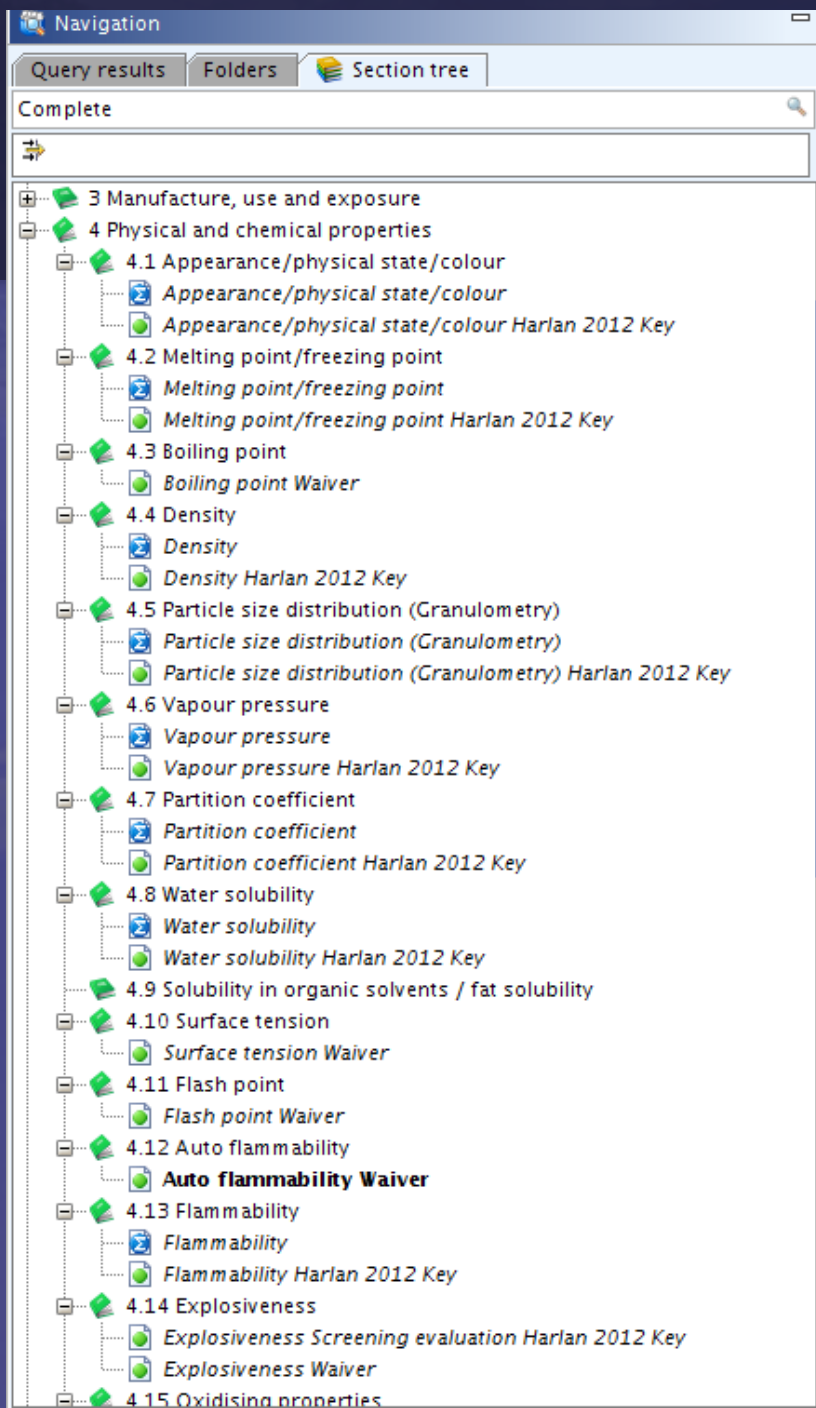
Navigation

Query results Folders Section tree

Complete

- 0 Related information
- 1 General information
- 2 Classification & Labelling and PBT assessment
- 3 Manufacture, use and exposure
- 4 Physical and chemical properties
 - 4.1 Appearance/physical state/colour
 - Appearance/physical state/colour
 - Appearance/physical state/colour Key study Harlan 2011
 - 4.2 Melting point/freezing point
 - Melting point/freezing point
 - Melting point/freezing point.Key Study Harlan 2011
 - 4.3 Boiling point
 - Boiling point Waiver
 - 4.4 Density
 - Density
 - Density Key study Harlan 2012
 - 4.5 Particle size distribution (Granulometry)
 - Particle size distribution (Granulometry)
 - Particle size distribution (Granulometry).- Key Study - Harlan 2011
 - 4.6 Vapour pressure
 - Vapour pressure
 - Vapour pressure Key study Harlan 2012
 - 4.7 Partition coefficient
 - Partition coefficient
 - Partition coefficient Key study Harlan 2012
 - 4.8 Water solubility
 - Water solubility
 - Water solubility Key study Harlan 2012
 - 4.9 Solubility in organic solvents / fat solubility
 - 4.10 Surface tension
 - Surface tension - Waiver
 - 4.11 Flash point
 - Flash point Waiver
 - 4.12 Auto flammability
 - Auto flammability
 - Auto flammability.Key Study Harlan 2011
 - 4.13 Flammability
 - Flammability
 - Flammability Key Study Harlan Laboratory 2011

- Phys-chem: Complete
- Environmental fate and ecotox: Annex III exemption statement to be attached
- Mamtox: Annex III exemption statement to be attached



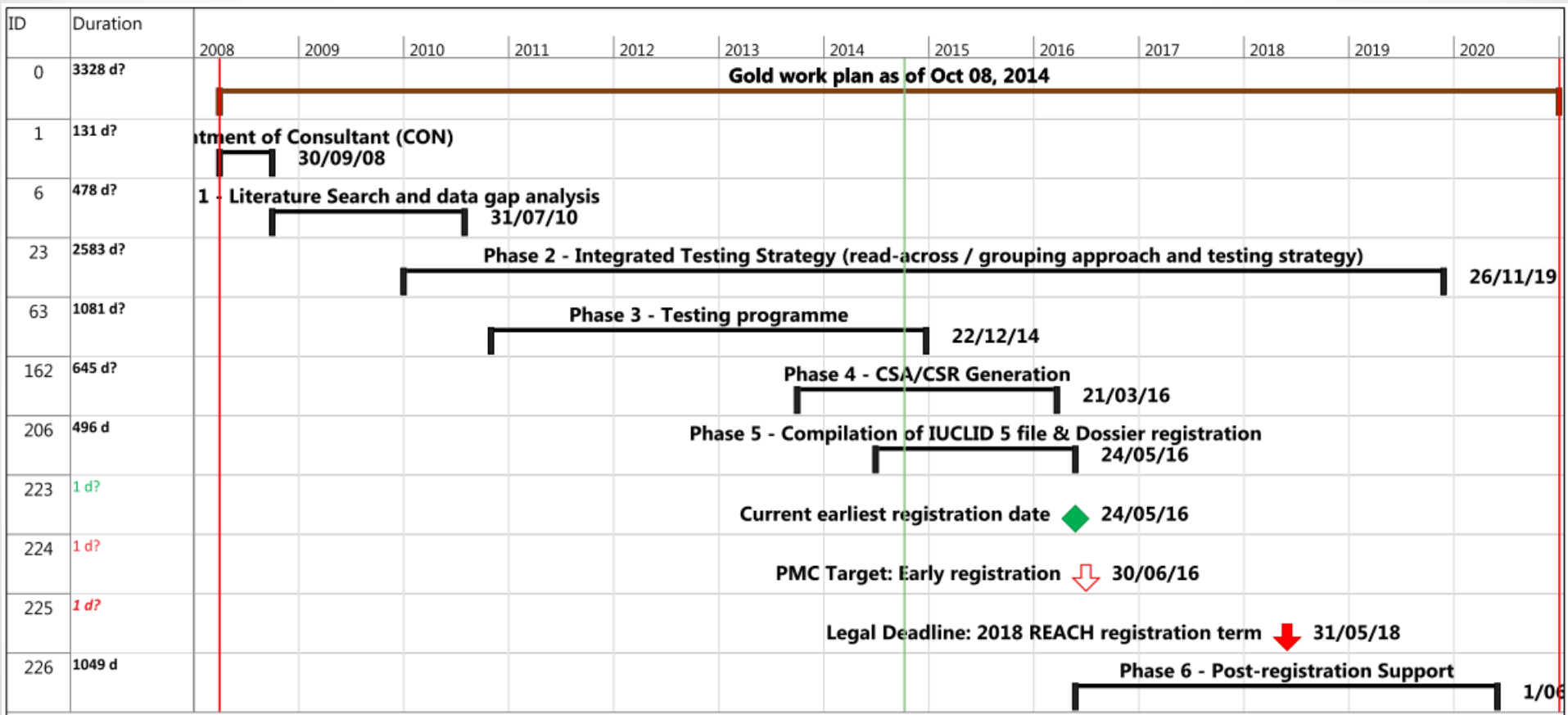
Gold balsams



- Phys-chem: Complete
- Environmental fate and ecotox: Annex III exemption statement to be attached
- Mamtox: Annex III exemption statement to be attached



Project Work Plan 2008-2020





Project Work Plan 2013-2018

ID	Duration	Q4	2014	Q1	Q2	Q3	Q4	2015	Q1	Q2	Q3	Q4	2016	Q1	Q2	Q3	Q4	2017	Q1	Q2	Q3	Q4	2018	Q1	Q2	Q3	Q4
0	3328 d?	Gold work plan as of Oct 08, 2014																									
1	131 d?																										
6	478 d?																										
23	2583 d?	egrated Testing Strategy (read-across / grouping approach and testing strategy)																									
63	1081 d?	programme																									
162	645 d?	Phase 4 - CSA/CSR Generation																									
206	496 d	Phase 5 - Compilation of IUCLID 5 file & Dossier registration																									
223	1 d?	Current earliest registration date ◆ 24/05/16																									
224	1 d?	PMC Target: Early registration ↓ 30/06/16																									
225	1 d?	Legal Deadline: 2018 REACH registration term ↓ 31/05/18																									
226	1049 d	Phase 6 - Post-registration Support																									



7. AOB, next meetings/calls & closing remarks

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AOB, next meetings/calls and closing remarks

- AOB
 - 4 Borates on the Final 6th Recommendation List for REACH Annex XIV;
 - Public consultations (ECHA & COM) period running until Nov 30, 2014
 - PMC Secretariat communication will follow to better scope out the extent of the challenge for the PM sector
 - Response to public consultation left at each company's discretion
 - Secretariat will support by transmitting any information received from EBA and answering general questions on the Public Consultation process
 - Other business ... ?
- Appropriate time for next meeting or call:
 - Tier-1 ES discussion (?): meeting, timing to be confirmed (Q2 2015?)
 - ...
- Closing remarks



Thank you
for your
attention
and
participation!