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Au and PM CN- Working Group Call

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REACH Ready Approved Supplier

ISO 9001 REGISTERED FIRM

ISO 14001 REGISTERED FIRM

GOLD

Test status: N-BET analysis and PSD

- Particle size distribution and N-BET analysis were scheduled to be conducted at Fraunhofer
- A member company has already conducted N-BET analysis for gold powder
- These results are for an equivalent sample to that due to be tested in the bio-elution study, this data can therefore be used
- PSD data is available in the T/D test report from ECTX
- No testing is now required

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Test status: Bio-elution

- Gold powder will be tested in artificial gastric fluid
- Gold sample has been received by CIMM
- Testing due to start w/c 23rd April

Test status: Genotoxicity tests

- A tiered approach to genotoxicity testing was agreed on the last Working Group call
  - » Ames Test (screen & main study)
  - » Micronucleus assay
  - » Mammalian cell gene mutation (if above 2 tests are negative)
- Testing will be conducted at Covance
- Contracts and test protocols are being prepared
- Sample due to be sent end of April
- Testing due to begin early May
- Test programme scheduled for May - September

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Test status: Ecotoxicity tests

- Algae, *Daphnia*, ASRIT for TCA
- Undertaken at Brixham Environmental Laboratories (BEL)
- Practical phase complete for all tests
- Draft reports have been submitted and reviewed
- Final report for ASRIT has been issued
- Awaiting final reports for Algae and *Daphnia*

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Ecotoxicity test results

Test	Endpoint	Calculated based on geomean measured metal conc (mg/L)
Algae	NOEC (yield)	0.90
	EC50 (yield)	2.6
	NOEC (growth rate)	0.90
	EC50 (growth rate)	> 9.0
Daphnia	NOEC	(1.5)
	EC50	(3.6)
ASRIT	NOEC	2
	EC50	28.2

- Based on these results a classification of Chronic Category 2 would be assigned for TCA. Current classification is Chronic Category 3

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PBT assessment of gold balsams

- Gold balsams is a 1-10 tpa substance and may have Annex III derogations. PBT assessment required
- A partition coefficient could not be measured for Gold balsams due to low test item solubility
- In the ITS report it was proposed that a biodegradation study is conducted
- Draft Harlan reports now received
- Partition coefficient could be estimated from solubility data
- Paper circulated outlining proposed approach

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PBT assessment of gold balsams cont.

- Log Kow estimate based on solubility data is -0.17
- Uncertainty in estimates as exact substance composition is unknown
- If the water solubility value determined from measuring the gold concentration is used (likely to considerably overestimate), log Kow is 2.68
- Log Kow >4.5 is considered bioaccumulative
- All estimates are below this threshold
- Recommend Kow estimates used instead of conducting biodegradation study

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Literature search: Au^{1+} and Au^{3+}

- Literature search conducted to identify potential read across data for TCA
- Only 1 relevant article identified and could only be a supporting study
- Options:

  1. Potentially, relevant proprietary data may be held by pharmaceutical companies. This could be difficult to identify

  2. Conduct an OECD 422 Combined repeat dose and reproductive toxicity screening study using TCA

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PM CN-

Test status: Dustiness

- Dustiness testing conducted at DMT for Potassium dicyanoargentate, potassium dicyanoaurate and silver cyanide
- Respiratory tract deposition modelling conducted
- Potassium dicyanoaurate exhibited 35.9% dust generation, other substances far lower
- All substances inhalable as MMAD <100µm, most of inhaled fraction retained in nasopharyngeal (head) region – cleared by ingestion
- Simulated breathing used oronasal augmenter model
- Very little deposition in lower respiratory tract
- Inhalation route unlikely to be relevant

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Test status: Ecotoxicity tests

- Potassium dicyanoaurate and Potassium dicyanoargentate
- *Daphnia*, ASRIT
- Undertaken at Brixham Environmental Laboratories
- Practical phase complete for all tests
- Draft reports have been submitted and reviewed
- Awaiting final reports (due by 4th May 2012)

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Ecotoxicity test results

Substance	Test	Endpoint	Calculated based on geomean measured metal conc (mg/L)	Nominal exposure conc (mg/L)
Potassium dicyanoargentate	Daphnia	NOEC	0.0018	0.0043
		EC50	0.022	0.033
	ASRIT	NOEC		0.64
		EC50		1.85
Potassium dicyanoaurate	Daphnia	NOEC		0.094
		EC50		0.2
	ASRIT	NOEC		60
		EC50		406

- Results indicate a classification of Acute Category 1, Chronic Category 1. No change from current classification

Update on PM CN- toxicity modelling

- Reliable prediction of potassium dicyanoargentate toxicity to Daphnia
- Suggests that prediction of toxicity to algae and fish would also be reliable
- Suggests that prediction of silver cyanide toxicity would also be reliable
- Poor prediction of potassium dicyanoaurate toxicity to *Daphnia*
- Uncertainty over gold cyanide speciation

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Analysis of free cyanide

- Free cyanide measurement was conducted with some success in ecotox tests
- Discussions held with Intertek regarding experiments to determine the dissociation of free cyanide for the mammtox programme
- Proposal received from Intertek and circulated
- Simple dissociation experiments would be conducted in the first instance in order to validate the method
- These would be conducted in solutions of pH 1.5 (simulate pH in stomach) and pH 6.8 (simulate intestinal fluid)
- Depending on results further experiments may be conducted, similar to bio-elution studies

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ITS reports: Way forward for updates

- Updated draft ITS completed end of February
- Proposal that this version of the ITS is finalised, taking into account comments received from PMC
- Any updates to the report after this eg following receipt of results from enabling tests are provided as addenda to the report
- At the end of the project the ITS and all addenda will be compiled and a summary document produced
- A data gap matrix will be produced and updated to show test progress

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