

# Integrated Testing Strategy for gold and gold substances

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## Annex III exemptions

- 1-10 tpa substances:
  - Aurio(1+)2,6,6-trimethylbicyclo[3.1.1]heptanethiolate
  - Balsams, copaiba, sulfurized, mixed with turpentine, gold salts
- PBT assessments:
  - Aurio(1+)2,6,6-trimethylbicyclo[3.1.1]heptanethiolate currently considered P but not B (QSAR data). To be reviewed following partition coefficient test results
  - Balsams, copaiba, sulfurized, mixed with turpentine, gold salts cannot be assessed until further composition details become available

## Annex III exemptions

- Not considered CMR on the basis of available data
- Confirmation received that there are no dispersive or diffuse uses
- Assume Annex III exemption applies until further information becomes available

## Read across Strategy

- Reduce overall testing requirement
- Test key substances and read-across to other substances where appropriate
- Approach taken depends on endpoint
- Physico-chemical endpoints generally not read-across
  - May be valuable in supporting read-across strategies for other end-points

## Read across - Environment

- Gold metal and tetrachloroauric acid require adsorption / desorption and ecotoxicity data
- T/D test with gold powder determined no gold dissolution above the limit of detection (LOD)
- Two approaches for filling ecotoxicological endpoints for gold metal:
  - Test using the solutions from a T/D test
  - Read across from a soluble gold salt

## Read across - Environment

- A possible strategy for filling the ecotoxicological endpoints is to test using solutions prepared from the T/D tests
- This approach would not be able to explicitly derive a PNEC value, only demonstrate no toxicity at the levels of gold that are dissolved
- It is likely a threshold would be set equal to 0.01 times the limit of water solubility
- On the basis that a PNEC could not be explicitly derived this approach is not recommended

## Read across - Environment

- Read across required from a soluble gold substance for gold metal to fulfil Annex VIII endpoints
- It is not clearly defined which oxidation state any soluble fraction of gold metal will be in the environment ( $\text{Au}^+$ ,  $\text{Au}^{3+}$ , or potentially colloidal  $\text{Au}^0$ )
- Speciation analysis is not practical as there was so little dissolution demonstrated in the T/D test, and the analysis may not be practically possible

- There are two potential read across substances in the scope of the project:

Substance	Oxidation state of gold	Testing required
Aurio(1+)2,6,6-trimethylbicyclo[3.1.1]heptanethiolate	1+	No testing if Annex III exemption confirmed
Tetrachloroauric acid	3+	Annex VIII dataset required

- Aurio(1+)2,6,6-trimethylbicyclo[3.1.1]heptanethiolate does not currently require any ecotoxicological testing on the basis of an Annex III exemption, and it is also not recommended to read across from an organometallic substance such as this
- Tetrachloroauric acid requires testing for Annex VIII endpoints as part of its REACH registration, and a pragmatic approach would be to read across from this substance

- In principle, testing both tetrachloroauric acid (Au 3+) and a substance with gold in the +1 oxidation state (e.g. gold[I] chloride) would allow comparison between the toxicity of the two oxidation states
- The more stringent of the two results could then be applied to the soluble component of metallic gold (without confirming its applicability)
- Overall, read across from tetrachloroauric acid is recommended as a pragmatic approach, with results compared to the dissolution of gold metal determined from the T/D test

## Classification of Gold Metal

- Ecotoxicity Reference Value (ERV) for  $\text{Au}^{3+}$  from tetrachloroauric acid
  - Lowest EC50 (acute) or EC10 (chronic)
- Solubility of metallic gold from Transformation/Dissolution test
  - $<0.3 \mu\text{g l}^{-1}$  (limit of detection)

## Classification of Gold Metal

- If solubility (in TD test) is greater than ERV for  $\text{Au}^{3+}$  then aquatic hazard classification will be required
- Current indications (fish only) are that  $\text{Au}^{3+}$  is of limited toxicity to salmonid fish
- Invertebrates or algae would need to be much more sensitive for classification to be required

## PNEC for Soluble Gold

- PNEC for soluble gold derived from dissolution of metallic gold
- Adopted directly from Au<sup>3+</sup> data (tests on tetrachloroauric acid)
- Gold (metal) is unlikely to be sufficiently soluble for the dissolved concentration to approach the PNEC

## Read across – Human health

- Read across is not required for gold metal as data are available or studies can be waived
- Read across may be appropriate for tetrachloroauric acid from an out of scope substance (sodium tetrachloroaurate). This requires further investigation

## PHYSICO-CHEMICAL ENDPOINTS

### Physico-chemical Properties

- Annex VII dataset required for all substances
- Testing carried out for CLP for some endpoints
- For balsams, copaiba, sulfurised, mixed with turpentine, gold salts it is recommended that the tests required under CLP are carried out alongside the REACH physico-chemical tests

## Physico-chemical endpoints

- Gold: Existing data available for all endpoints
- Tetrachloroauric acid - Testing proposed:
  - Freezing point
  - Boiling point
  - Vapour pressure

## Physico-chemical endpoints

- Aurio (1+) 2,6,6-trimethylbicyclo[3.1.1]heptanethiolate - Testing proposed:
  - Boiling point
  - Density
  - Water solubility
  - Vapour pressure
  - Partition coefficient

## Physico-chemical endpoints

- Balsams – Testing proposed:
  - Melting point
  - Boiling point
  - Density
  - Water solubility
  - Vapour pressure
  - Flammability
  - Self-ignition temperature
  - Granulometry
- Further composition details are required to confirm some waivers

## ENVIRONMENTAL FATE AND ECOTOXICOLOGY ENDPOINTS

## T/D testing

- Draft report has just been received for the T/D tests carried out with gold powder
- The 24-hour screening test showed no dissolution above the limit of detection (LOD) of  $0.1 \mu\text{g L}^{-1}$  at a loading rate of  $100 \text{ mg L}^{-1}$
- The full test carried out at pH 6 showed no dissolution above the LOD of  $0.3 \mu\text{g L}^{-1}$  at loading rates of 1, 10 or  $100 \text{ mg L}^{-1}$

## Environmental fate endpoints

- Biodegradation and hydrolysis waived for inorganics (gold, tetrachloroauric acid)
- Adsorption / desorption: Testing proposed for tetrachloroauric acid and read across to gold. A waiver may be appropriate as the standard HPLC screening study is not suitable for metals

## Ecotoxicology

- Annex VIII dataset now required for tetrachloroauric acid following tonnage increase (Algae, aquatic invertebrates, fish, microorganisms)
- Published data available for acute fish study
- Testing proposed for *Daphnia*, algae and microorganisms
- To avoid pH effects, neutralisation of tetrachloroauric acid may be required (eg by NaOH) prior to testing
- Recommend results read across to gold

## TOXICOLOGICAL ENDPOINTS

## Gold

- Default approach for assessing the hazards of metals in the zero valency state is to evaluate the hazards of salt(s) of the metal and read across
- No testing proposed at this point for other gold substances
- Some proprietary data available for skin sensitisation and in vivo gene mutation on bacteria
- Zero valent gold is considered inert and there would be a lack of transformation / dissolution into soluble forms within the mammalian body

- Particle size screening of gold powder indicated only 4.9% below 100  $\mu\text{m}$  therefore inhalation is not considered a relevant route of exposure
- Gold is used in jewellery, dental alloys and as a food additive
- Chemically inert properties of gold and lack of bioavailability via oral administration are frequently cited in the literature

## Bioaccessability testing

- We recommend development of a weight of evidence argument based around bioaccessability (published or test data)
- Limited published data have been identified for release of gold metal in artificial sweat
- Bioaccessability testing proposed using artificial gastric fluid

## Tetrachloroauric acid

- Tonnage increase to 10-100 tpa, Annex VIII dataset now required
- Published data available for Skin irritation / corrosion and Acute toxicity (oral)
- Due to very low pH / corrosivity Eye irritation, Skin sensitisation and Acute toxicity (dermal and inhalation) can be waived

- .Data gaps:
  - *In vitro* gene mutation study in bacteria (Ames test): A rec assay in *Bacillus subtilis* is available as a supporting study. Mouse lymphoma assay recommended for metals instead
  - *In vitro* cytogenicity study in mammalian cells
  - *In vitro* gene mutation assay in mammalian cells (mouse lymphoma assay)
  - Repeated dose toxicity (28-day oral or dermal toxicity in rats)
  - Reproductive toxicity (screening for reproductive / developmental toxicity)

- Hazard likely to result from its low pH, the  $[\text{Cl}_4\text{Au}]^-$  ion and gold[1] complexes
- Testing strategy requires further investigation
- Extreme low pH could adversely impact mutagenicity studies
- Possible strategy to neutralise the acid eg with NaOH
- Sodium tetrachloroaurate was pre-registered under REACH. Available hazard data would be relevant for tetrachloroauric acid
- Consider bioaccessability testing in order to consider dissociation products under gastric conditions