LITERATURE SEARCHES FOR POTENTIAL READ ACROSS INFORMATION FOR TETRACHLOROAURIC ACID

1. Background

Tetrachloroauric acid is being registered as a 10 – 100 tpa substance and therefore requires Annex VII and Annex VIII endpoints to be filled. A number of Annex VIII endpoints can be waived on the basis that TCA has exhibited corrosive properties in an *in vivo* rabbit skin irritation study (proprietary report, Klimisch 1). A genotoxicity testing programme has been initiated following agreement from the PMC on 30 January 2012. This leaves the following endpoints as data gaps:

- Subacute toxicity
- Reproductive toxicity screen

An updated interim position paper was issued by wca on 12 January 2012. This included the recommendation that a limited literature search should be conducted to identify the scope of relevant published information on the animal toxicity of gold(I) or gold(III) ions if relevant proprietary data were not available. The potential data holder, Evonik, confirmed that they do not have any relevant data and therefore the literature search was conducted. This paper outlines the search strategy that was used, a summary of the results and recommendations for next steps following this.

2. Search strategy

Searches were conducted in February and March 2012 in order to obtain any data that may be available for gold(I) or gold(III) substances that could potentially be read across to tetrachloroauric acid. Searches were conducted using the following databases:

- Toxline[1]
- Thomson innovation[2]
- OECD eChemportal[3]

The search terms that were used and the number of hits obtained are presented in Table 1. CAS numbers are not recognised when searching Thomson Innovation therefore they were not used in these searches.

[1] http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?TOXLINE
[2] https://www.thomsoninnovation.com/login
[3] http://www.echemportal.org/echemportal/page.action?pageID=9

Table 1 Search terms used and number of hits returned

Search term	Number of hits		
	Thomson Innovation	Toxline	OECD eChemportal
Sodium tetrachloroaurate OR 15189-51-2	21	7	2
Gold trichloride OR 13453-07-1	17	116	2
Gold triiodide OR 13453-24-2	0	0	1
Gold tribromide OR 10294-28-7	2	0	1
Gold trinitrate OR 13464-77-2	0	0	1
Gold ion	178	1503	0
Univalent gold	11	2	0
Trivalent gold	12	21	0

3. Search Results

Search results were compiled into a spreadsheet (Gold_Phase III_TCA literature search_All data_210312) and screened for relevance by reviewing the title in the first instance. If the title appeared to be potentially relevant, the abstract was reviewed. Following this screening process only one article was considered to be potentially relevant, and only as supporting evidence:

Suwalsky M., Zambenedetti P., Carpen E., Ibnlkayat M., Wittkowski W., Messori L., Zatta P., (2004) Effects of chronic treatment with sodium tetrachloroaurate(III) in mice and membrane models, Journal of Inorganic Biochemistry, Dec 98 (12):2080-6.

This study looked at the *in vivo* chronic exposure of sodium tetrachloroaurate in mice on neurotoxicity. The route of administration is not specified in the abstract and only limited parameters were assessed for the chronic toxicity of the test substance. This study could only be used as supporting evidence for repeat dose toxicity for the purposes of REACH.

4. Next steps

Following the literature search we can conclude that there is very likely to be insufficient data in the published literature to fill the required endpoints. There are therefore two options going forward.

- Gold (I) and gold(III) compounds are known to be used in pharmaceuticals. Data may therefore be available, but are likely to be proprietary. It may be possible to identify pharmaceutical companies that supply gold (I) and gold (III) substances and approach them in order to determine whether they have any relevant data available. A brief internet search was conducted but we were unable to locate any potentially relevant

companies. Therefore even though there may potentially be proprietary data held by pharmaceutical companies that could be relevant for REACH registration, it could be very difficult to identify and obtain these data unless any member of the PMC is able to assist.

- The second option is to conduct testing for these endpoints. An OECD 422 test would be proposed to fill the subacute toxicity and reproductive toxicity endpoints. The very low pH of the test item (pH 1) would limit the amount that could be administered orally to test animals; hence this may potentially restrict identification of a suitable NOAEL. There are two potential options for testing a substance with extreme pH, either to dilute the material substantially or to neutralize it with e.g. NaOH before testing. wca has made preliminary enquiries with a test laboratory about the likelihood of the latter approach being accepted considering the risk assessment for humans and it would appear that neutralisation would be an option, but this would need to be considered in more detail before any testing could commence.

Minako Takamiya-Allen
Becky Marks

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