Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

to the Opinion proposing harmonised classification and labelling at Community level of

trichloromethylstannane (MMTC)

ECHA/RAC/CLH-O-0000001538-70-03/A2

Adopted

14 September 2011

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

[ECHA has compiled the comments received via internet that refer to several hazard classes and entered them under each of the relevant categories/headings as comprehensive as possible. Please note that some of the comments might occur under several headings when splitting the given information is not reasonable.]

Substance name: trichloromethylstannane (MMTC)
CAS number: 993-16-8
EC number: 213-608-8

General comments

Date	Country / Person / Organisation / MSCA	Comment	Response	Rapporteur's comments
24/02/2011	UK / MSCA	We support the proposed classification for mutagenicity as previously agreed at TC C&L. We consider the classification for developmental toxicity to be borderline. Please refer to our specific comments below.	Noted	RAC has re-evaluated the data on mutagenicity of MMTC and concluded that the proposed C&L as Muta 2 (GHS) is not warranted
28/02/2011	Germany / Matthias Plog / MSCA	DE supports the proposed classification from the FR-CA. Report page 3 & 5-8 and IUCLID Chapter 1.2 Composition: The substance identity of trichloro(methyl)stannane is not consistent throughout the report and technical dossier. The concentration range is given as >= 50 - <= 90 % w/w (IUC) for the main constituent trichloro(methyl)stannane. This composition does not match the criteria for mono-constituent substances but could be any kind of substance (Mono/multi-constituent substances or UVCB substances). Moreover, there are impurities stated in the composition without any concentration given. DE wonders whether these are hypothetically occurring impurities resulting from production process or whether they are confirmed for substance identity by analysis. However, the substance identity has to be clarified in accordance with RIP3.10 and the documents have to be revised accordingly. Additionally, several SMILES and InChI codes as well as molecular weight, molecular formula and chemical names are not	Noted A registration dossier for MMTC is not available and no further information on purity and impurity profile is available. Inconsistencies have been corrected.	See above. Other comments noted

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		correct or not consistent throughout the report and technical dossier. These points should be taken into account before publishing the document Since the IUCLID5 dossier does not contain Robust Study Summaries DE asks for the inclusion of the toxicological important information (number of animals per sex and dose) in the report. DE wants to add, that a discrepancy between freezing point (~43°C) and physical state (produced as liquid) seems to exist. Since the report only classifies CMR in agreement with article 36 (1) of CLP the physico-chemical properties are of secondary interest but should still be consistent.	The number of animals per sex and per dose were added in the revised CLH report when not already present. SIAR (OECD 2006) reports that MMTC is a colorless liquid or a gray solid. It has been included in the revised CLH report.	
03/03/2011	Sweden / Ing-Marie Olsson / MSCA	In absence of any new data Sweden supports the proposed classification and labelling for Trichloromethylstannane (MMTC) as agreed by the Technical Committee on Classification and Labelling (Directive 67/548/EEC) ('TC C&L').	Noted	See above

Carcinogenicity

Date	Country / Person / Organisation / MSCA	Comment	Response	Rapporteur's comments
		No comments received.		

Mutagenicity

Date	Country/ Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comments
28/02/2011	Germany / Matthias Plog / MSCA	We support the submitter's conclusion	Noted	RAC has re-evaluated the data on mutagenicity of MMTC and concluded that the proposed C&L as Muta 2

Date	Country/ Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comments
				(GHS) is not warranted
03/03/2011	Ireland / Health and Safety Authority	The Irish CA is in agreement with the proposed classification Muta Cat 3; R68 (Muta 2- H341) as previously agreed by the TC C&L in 2006.	Noted	See above

Toxicity to reproduction

Date	Country / Person / Organisation / MSCA	Comment	Response	Rapporteur's comments
24/02/2011	UK / MSCA	We consider the case for classification with Repro Cat 3; R63 to be borderline based on the following observations: In the reproductive/screening study (Appel; 2004), conducted in the Wistar rat, an increase in post-implantation loss (43 %) was observed in the high dose group (measured by subtracting the number of live foetuses from the number of implantation sites; No information on resorptions was provided). In addition, 30 of the 48 pups born alive were reported 'missing' by PND 4 and one was found dead. Given the magnitude of the effects, it appears unlikely that the effect on post-implantation loss/post-natal survival is a chance finding related to the low group sizes employed. However, there are a number of unknowns: • It is not known whether the post-implantation loss was due to increased embryo/foetal death in utero or increased pup death around the time of birth. If pups died and were cannibalised prior to group size determination this will bias the value derived for post-implantation loss • It is not known whether the pups went 'missing' owing to a developmental effect that resulted in their cannibalisation, whether the pups became ill and died through administration of the test substance via the milk or whether the dams cannibalised their pups	In the study by Appel (2004), the test substance has a purity of ca. 84% MMTC and contains ca. 10% of DMTC. The available data on DMTC suggests that DMTC is foetotoxic with a NOAEL of 10 mg/kg in rat (see DMTC CLH report). In the Appel 2004 study, the effects are seen at the highest dose of ca. 50 mg/kg of test substance, which contains around 5 mg/kg of DMTC. The effects can therefore not be attributed to DMTC. No information is available on the developmental toxicity of the other impurities. Their identity and concentration is presented in an additional confidential appendix to the CLH report. No information is therefore available to show that the effect can be attributed to an impurity. We agree that cannibalisation of the pups in Appel 2004 introduces uncertainties in the analyses of the	RAC agrees that the the case for classification with Repro Cat 2 (GHS) of MMTC is borderline. Although the interpretation of the available study has deficits and is difficult to interpret it cannot be ruled out that MMTC induces post implantation losses. RAC concludes therefore that classification with Repro Cat 2 (GHS) is warranted.

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		owing to a neurotoxic effect of the substance on the dams. • The test substance administered was a mixture of 83/ 9% MMTC/DMTC. The composition of the remaining 8 % of the test substance is not clear in the CLH report. It is also not clear if the presence of ~ 9 % DMTC (classified as repr Cat 3; R63 for foetotoxicity) contributed in some way to the effects observed. In addition, no effects on litter size or pup viability were observed in either of the two Moser developmental neurotoxicity studies, conducted in Sprague-Dawley rats at similar dose levels, using a purer form of the test substance (97 % purity). In these studies, the test substance was administered via the drinking water. We can see no reason why this route of administration should produce dramatically different results from dietary administration. We note that in the first Moser study, of the 30 dams selected/group, only 10-12 of them from each group (including the controls) delivered litters, which may reduce confidence in this study. However, in the second Moser study, which employed a higher dose, most of the dams successfully delivered litters. Given the number of uncertainties associated with the screening study and the lack of effects observed in the Moser studies, we do not feel that there is a strong case for classification with Repr cat 3; R 63. However, we appreciate the decision is borderline.	study results, both regarding post-natal effects as well as regarding what was identified as post-implantation loss in the high-dose group. However, cannibalisation was also observed in the other test and control groups although to a much lesser extent (respectively16%,25%, 3% and 62% of missing pups at 0, 30, 150 and 750 ppm). It is therefore difficult to fully explain cannibalisation by the neurotoxicity of the test substance. The magnitude of the effects observed in the high-dose group (43% of post-implantation loss and 65% of pups lost between PND 1 and PND4) raise strong concern on foetotoxicity of MMTC. CLP criteria states that "If deficiencies in the study make the quality of evidence less convincing, Category 2 could be the more appropriate classification". Overall and recognising the uncertainties due to postnatal cannibalisation by the dams, classification in category 2 is therefore considered appropriate. In Moser 2005 that was designed to assess more specifically developmental neurotoxicity, no foetotoxic effect was identified when substance was administered in water. In absence of data on the influence of vehicle (water vs diet) it is not possible to either	

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		In addition, for the Appel study, please express the mg/kg diet values as ppm. At the moment, the tables give the impression that higher doses were achieved than actually were (i.e. the achieved intake in the developmental study at 750 mg/kg diet was only 49/53 mg/kg/day in males/females).	confirm or exclude that it may have impacted the ADME of the substance and its toxicity. The effect seen in the study by Appel cannot be fully dismissed. Mg/kg diet has been changed to ppm in the revised CLH report. Doses in the Appel study have been expressed in ppm in the revised CLH report.	
28/02/2011	Germany / Matthias Plog / MSCA	We support the submitter's conclusion	Noted	Noted
03/03/2011	Ireland / Health and Safety Authority	The Irish CA is in agreement with the proposed classification Repr. Cat 3; R63 (Repr. 2- H361d) as previously agreed by the TC C&L in 2007.	Noted	Noted

Respiratory sensitisation

Date	Country / Person / Organisation / MSCA	Comment	Response	Rapporteur's comments
		No comments received.		

Other hazards and endpoints – Acute toxicity

Date	Country / Person / Organisation / MSCA	Comment	Response	Rapporteur's comments

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPSAL ON TRYCHLOROMETHYLSTANNANE (MMTC)

Date	Country / Person / Organisation / MSCA	Comment	Response	Rapporteur's comments
03/03/2011	Ireland / Health and Safety Authority	The Irish CA notes that the classification agreed by TC C&L in 2006 for acute toxicity (Xn; R22) has not been proposed for harmonisation, even though data justifying classification has been included in the Annex VI dossier.	Acute toxicity data are reported to provide information on the toxicological profile of MMTC but harmonisation is not proposed in agreement with article 36 (1) of CLP.	Noted

Other hazards and endpoints – Repeated dose toxicity

Date	Country / Person / Organisation / MSCA	Comment	Response	Rapporteur's comments
03/03/2011	Ireland / Health and Safety Authority	The Irish CA notes that the classification agreed by TC C&L in 2006 for acute toxicity (Xn; R22) has not been proposed for harmonisation, even though data justifying classification has been included in the Annex VI dossier.	Acute toxicity data are reported to provide information on the toxicological profile of MMTC but harmonisation is not proposed in agreement with article 36 (1) of CLP.	Noted