Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling at Community level of

trichloromethylstannane (MMTC)

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

Adopted

14 September 2011

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OPINION OF THE COMMITTEE FOR RISK ASSESSMENT ON A DOSSIER PROPOSING HARMONISED CLASSIFICATION AND LABELLING AT COMMUNITY LEVEL

In accordance with Article 37(4) of the Regulation (EC) No 1272/2008 (CLP Regulation), the Committee for Risk Assessment (RAC) has adopted an opinion on the proposal for harmonised classification and labelling of

Substance Name: ***trichloromethylstannane (MMTC)***

EC Number: ***213-608-8***

CAS Number: ***993-16-8***

The proposal was submitted by ***France***
and received by RAC on ***17 January 2011.***

The proposed harmonised classification:

	CLP Regulation (EC) No 1272/2008	Directive 67/548/EEC (criteria)
Current entry in Annex VI CLP Regulation		No entry
Current proposal for consideration by RAC	Muta. 2; H341 Repr. 2; H361d	Muta. Cat. 3; R68 (agreed by TC C&L in October 2006) Repr. Cat. 3; R63 (agreed by TC C&L in September 2007)
Resulting harmonised classification (future entry in Annex VI CLP Regulation)	Muta. 2; H341 Repr. 2; H361d	Muta. Cat. 3; R68 Repr. Cat. 3; R63

PROCESS FOR ADOPTION OF THE OPINION

France has submitted a CLH dossier containing a proposal together with the justification and background information documented in a CLH report. The CLH report was made publicly available in accordance with the requirements of the CLP Regulation at ***http://echa.europa.eu/consultations/harmonised_cl/harmon_cl_prev_cons_en.asp*** on ***17 January 2011***. Parties concerned and MSCAs were invited to submit comments and contributions by ***3 March 2011***.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: ***Helmut Greim***
Co-rapporteur, appointed by RAC: ***Hans-Christian Stolzenberg***

The opinion takes into account the comments of MSCAs and parties concerned provided in accordance with Article 37(4) of the CLP Regulation.

The RAC opinion on the proposed harmonised classification and labelling has been reached on ***14 September 2011,*** in accordance with Article 37(4) of the CLP Regulation, giving parties concerned the opportunity to comment. Comments received are compiled in Annex 2.

The RAC Opinion was adopted by ***consensus.***

OPINION OF RAC

The RAC adopted the opinion that MMTC should be classified and labelled as follows:

Classification & Labelling in accordance with the CLP Regulation

Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors	Notes
				Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
	trichloromethyllstannane (MMTC)	213-608-8	993-16-8	Repro. 2	H361d[1]	GHS08 Wng	H361d			

Classification & Labelling in accordance with Directive 67/548/EEC:

Index No	International Chemical Identification	EC No	CAS No	Classification	Labelling	Concentration Limits	Notes
	trichloromethyllstannane (MMTC)	213-608-8	993-16-8	Repr. Cat. 3; R63	Xn R: 63 S: (2)-22-36/37		

[1] It is the view of RAC that hazard statement H361d is the most appropriate, given the available toxicological profile of MMTC, but RAC recognised that H361 could be applied if the available criteria are applied strictly

SCIENTIFIC GROUNDS FOR THE OPINION

The opinion relates only to those hazard classes that have been reviewed in the proposal for harmonised classification and labelling, as submitted by ***France***.

Carcinogenicity
No data are available.

Mutagenicity
In vitro, MMTC does not induce mutagenic or genotoxic effects on bacteria in Ames test, SOS chromotest on *E. coli* and rec-assay on *B. subtilis* in presence and absence of metabolic activation. MMT, which is hydrolysed to MMTC has been tested in S. typhimurium tests and in *E. coli*. It was negative in *E. coli*. In *S. typhimurium* increases in revertant frequencies to approx.. 1.6- to 2-fold control values were observed in TA 1537 and 1535 strains at a dose of 16.7 ug/plate without S9 under liquid pre-incubation conditions. Since these increases were not dose dependent and revertant frequencies for all other doses and the other 3 strains approximated or were less than control values the slight increases in the two strains were considered spontaneous.

In vivo, MMTC induces a weak and transient increase in micronuclei in a guideline study in rats by gavage. Purity was 98.53% with DMTC 1.32%. Mean number of micronucleated polychromatic erythrocytes (MPE) per 2000 PE in negative control, 37, 111, 333 and 1000 mg/kg MMTC and mitomycin C (1.5 mg/kg) are:
24h-harvest: 1.2±0.4, 3.0±1.2*, 1.8±0.4, 3.0±1.4*, 3.4±1.7*, 26.8±3.3*
48h-harvest: 2.4±1.8, -, -, 1.8±1.1, 1.6±0.9, -
The MPE numbers are slightly elevated about twofold at the lowest concentration tested, whereas the MPE numbers at the three higher concentrations did not further increase. Moreover, the control value at 48 harvest time has been twice that at 24 hrs and the upper and lower bounds of the control value and the values at the different test concentrations at 24 hrs are within the same range. Therefore, MMTC is not considered genotoxic and RAC concludes that the proposed classification (Muta 2; H341 according to the CLP criteria, and Muta. cat. 3; R68 according to the DSD criteria) is not warranted.
RAC notes that in the *in vivo* test, MMTC contains a low proportion of DMTC. The available data suggests that DMTC is not mutagenic *in vivo* (DMTC classification proposal, 2006) and the positive response seen with MMTC can therefore not be attributed to DMTC.

Reproductive Toxicity
In an OECD 421 screening test (Appel, 2004) the dams received 30, 150 and 750 ppm MMTC in their feed. At the highest dose a slight but non-statistically significant reduction of maternal body weight and an increase in post-implantation loss (43%) has been observed. At this dose out of the 48 pups born alive 30 were “missing” and one pup was found dead at PND 4 resulting in a viability index of 35%. However, it remains unclear whether the pups were eaten by the dams at birth before they were counted or whether MMTC caused an increase of post-implantation loss.

By contrast, no post-implantation loss or effects on pup viability were identified in two EPA studies, which administered MMTC in the drinking water up to 245 ppm (Moser, 2006). Since these studies focus on neurodevelopmental effects the number of implantations in the dams was not determined and post-implantation loss was not calculated. However, the litter size were normal in all groups. Since MMTC may have different gastrointestinal absorption

rates from water and from diet the discrepancy in the results and the effects seen in the OECD 421 study cannot be fully dismissed by the Moser studies. Nor significant developmental neurobehavioral neither cognitive deficit in the conditions of the studies have been observed.

Overall, the OCDE 421 study at most indicates an adverse effect of MMTC on development (decreased viability and post-implantation loss) in the absence of maternal toxicity. Since the interpretation of the study is not clear due to possible postnatal cannibalisation by the dams and the EPA studies are inappropriate to rule out a reprotoxic potential of MMTC a classification Repr. 2 – H361d according to the CLP criteria, and Repro. Cat. 3 – R63 according to the DSD criteria is proposed. RAC supports this proposal.

Additional information

The Background Document, attached as Annex 1, gives the detailed scientific grounds for the Opinion.

ANNEXES:

Annex 1	Background Document (BD)[1]
Annex 2	Comments received on the CLH report, response to comments provided by the dossier submitter and rapporteurs' comments (excl. confidential information)

[1] The Background Document (BD) supporting the opinion contains scientific justifications for the CLH proposal. The BD is based on the CLH report prepared by a dossier submitter.