Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling at Community level of

2-ethylhexyl 10-ethyl-4-[[2-[(2-ethylhexyl)oxy]-2-oxoethyl]thio]-4-methyl-7-oxo-8-oxa-3,5-dithia-4-stannatetradecanoate / (MMT(EHMA))

ECHA/RAC/CLH-O-0000001981-71-01/F

Adopted

14 September 2011

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CLH-O-0000001981-71-01/F

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: ***2-ethylhexyl 10-ethyl-4-[[2-[(2-ethylhexyl)oxy]-2-oxoethyl]thio]-4-methyl-7-oxo-8-oxa-3,5-dithia-4-stannatetradecanoate / (MMT(EHMA))***

EC Number: ***260-828-5***

CAS Number: ***57583-34-3***

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		none
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 EHMA 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)		
	2-ethylhexyl 10-ethyl-4-[[2-[(2-ethylhexyl)oxy]-2-oxoethyl]thio]-4-methyl-7-oxo-8-oxa-3,5-dithia-4-stannatetradecanoate; MMT (EHMA)	260-828-5	57583-34-3	Repr. 2	H361d[1]	GHS08 Wng	H361d			

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

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

Index No	International Chemical Identification	EC No	CAS No	Classification	Labelling	Concentration Limits	Notes
	2-ethylhexyl 10-ethyl-4-[[2-[(2-ethylhexyl)oxy]-2-oxoethyl]thio]-4-methyl-7-oxo-8-oxa-3,5-dithia-4-stannatetradecanoate; MMT (EHMA)	260-828-5	57583-34-3	Repr. Cat. 3; R63	Xn R: 63 S: (2)-22-36/37		

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.***

General Comment
The database of MMT(EHMA) is poor. In a gastric simulation study at low pH (0.6-0.7) and at 37°C MMT(EHMA) is rapidly hydrolysed leading to formation of the corresponding alkyltin chloride and release of the ligand EHMA. Assuming first-order kinetics, the half-time of the simulated gastric hydrolysis of MMT(EHMA) was estimated to be 0.27 hours. However, RAC notes that neither the rat nor the human stomach pH is as low so that hydrolysis rates at higher pH 4 values may be lower. The OECD HPV Programme assessed MMT(EHMA) in a group with other monomethyltins. The SIDS Initial Assessment Report for SIAM 23 (2006) states that, despite relatively low water solubilities of the substituted monomethyltins, their labile ligands do hydrolyse in water. The levels of the original organotin stabiliser or the individual hydrolysis products in water cannot be specifically measured. Based on data for other organotins, hydrolysis in water is estimated rapid (within minutes to hours) whereas the alkyltin moiety (MMT) is hydrolytically stable. In water, the chloride ligand on MMTC readily hydrolyses leaving the alkyltin. The alkyltin moiety (MMT) is hydrolytically stable at pH 4, 7 and 9. RAC has concluded therefore that data of MMTC can be read across for classification of MMT (EHMA).

Carcinogenicity
No information available.

Mutagenicity
In vitro:

MMT(EHMA) 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.

MMTC, the hydrolysis product of MMT(EHMA), does not induce mutagenic or genotoxic effects on bacteria in the Ames test, SOS chromotest on *E. coli* and rec-assay on *B. subtilis* in presence and absence of metabolic activation.

In vivo, no data on MMT(EHMA) are available. MMTC induces a weak increase in micronuclei in a guideline study in rats by gavage. The numbers of micronucleated polychromatic erythrocytes (MPE) 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.

Reproductive Toxicity

No data on MMT(EHMA) are available. However, in an 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. The interpretation of the study is not clear due to possible postnatal cannibalisation by the dams. No post-implantation loss or effects on pup viability were identified in two EPA studies, which administered MMTC in the drinking water (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 sizes were normal in all groups. Since 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. Due to the assumed hydrolysis of MMT(EHMA) to MMTC (or rather MMT), the proposed classification of MMTC is extended to MMT(EHMA). RAC notes that no substance specific information is available about hydrolysis extent and rates of MMT(EHMA) to MMT.

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.