Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at Community level of

hexabromocyclododecane (HBCDD)

ECHA/RAC/CLH-O-0000001050-94-03/F

Adopted

8 December 2010

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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 ("the CLP Regulation"), the Committee for Risk Assessment (RAC) has adopted an opinion on the proposal for harmonised classification and labelling of

Substance Name: **hexabromocyclododecane (HBCDD)**

EC Number: **247-148-4 and 221-695-9**

CAS Number: **25637-99-4 and 3194-55-6**

The proposal was submitted by ***Sweden***
and received by RAC on ***07 October 2009***

	CLP Regulation (EC) No 1272/2008	Directive 67/548/EEC (criteria)
Current entry in Annex VI CLP Regulation	No entry (Table 3.1)	No entry (Table 3.2)
Current proposal for consideration by RAC	Repr. 2 - H361fd Lact. - H362	Repr. Cat 3; R62-R63 R64
Resulting harmonised classification (proposed future entry in Annex VI CLP Regulation)	Repr. 2 - H361fd Lact. - H362	Repr. Cat 3; R62-R63 R64

PROCESS FOR ADOPTION OF THE OPINION

Sweden 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/doc/consultations/cl/clh_axvrep_sweden_CD001435-70.pdf on ***4 November 2009***. MSCAs and parties concerned were invited to submit comments and contributions by ***19 December 2009***.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: ***Boguslaw Baranski***
Co-rapporteur, appointed by RAC: ***Katalin Gruiz***

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 ***8 December 2010,*** 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 **hexabromocyclododecane (HBCDD)** should be classified and labelled as follows[1]:

Classification & Labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

Classification: Repr. 2 - H361 (Suspected of damaging fertility or the unborn child.)

Lact. - H362 (May cause harm to breast-fed children)

Specific concentration limits: none

M-factors: none

Notes:

Labelling: GHS08, Wng, H361, H362

Classification & labelling in accordance with Directive 67/548/EEC

Classification:

Repr. Cat 3;

R63 (Possible risk of harm to the unborn child)

R64 (May cause harm to breastfed babies)

Specific concentration limits: **none**

Notes:

Labelling: Xn; R 63 - 64; S36/37-53

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 Sweden.

[1] Note that not all hazard classes have been evaluated

Reproductive toxicity

Effects of HBCDD on sexual function, fertility and development were assessed based on the results of six studies: a two-generation study (Ema *et al.* 2008), a one-generation study (van der Ven e*t al*. 2009), a one-generation developmental study (Saegusa *et al*. 2009), the study of neurobehavioral development by Lilienthal *et al.* (2009), the studies of Murai *et al.* (1985) and of Stump (1999) reported in EU Risk Assessment Report (May 2008) and studies on humans providing supplementary evidence reviewed in the background document (Annex 1).

Comparison with criteria:

As described in the background document, there were observations of increased postnatal mortality, delayed physical development, and alterations in the weight of internal organs in offspring in one- and two-generation studies (Ema et al. 2008; van der Ven et al. 2009, Saegusa et al. 2009) at dose levels inducing mild maternal toxicity. The contribution of prenatal developmental alterations to these postnatally manifested effects cannot be excluded based on the available data.

The observations from the study of Ema et al. (2008) suggesting potential effects of HBCDD on fertility such as reduction of primordial follicles in ovaries of F1 generation females in the medium and high dose exposure levels was not alone sufficient as a basis for classification for adverse effects on fertility. This is because of the unknown significance of this observation (due to lack of clarity of the methodological procedure) and the fact that the reduced number of follicles were within a range of values observed in animals of historical control groups evaluated in the same laboratory.

CLP Regulation:
It is the opinion of RAC that HBCDD should be classified into category Repr. 2, because there is some evidence of an adverse effect on development from experimental studies on animals. The evidence for an adverse effect on fertility is not sufficient for classification. In accordance with the available guidance, this hazard profile merits labelling with the hazard statement
H361 without specifying fertility or developmental toxicity.

Dangerous Substances Directive:
It is the opinion of RAC that HBCDD should be classified in category 3 for reproductive toxicity given the evidence in animal studies for a possible effect on development (Repr Cat 3; R63 - Possible risk of harm to the unborn child). Regarding fertility, the available evidence for this effect alone is not sufficient for any further classification and labelling.

Summing up the above considerations the following classifications is proposed:

CLP Regulation: Repr. 2 - H361 (Suspected of damaging fertility or the unborn child.) DSD; Repr. Cat 3; Xn, R63 (Possible risk of harm to the unborn child).

Adverse effects on or via lactation

HBCDD due to its high bioaccumulation properties (EU Risk Assessment Report, May 2008) may cumulate in mammary glands, from which it may be transferred to milk. It is known from animal studies, that a lengthy exposure of animals (months) is required to reach steady-state.

The detected concentrations in human milk were in a range of 0.13 – 5.4 ng HBCDD /g of milk lipids (Polder *et al.*, 2008a, Thomsen *et al.*, 2003; Fängström *et al.*, 2008; Colles *et al.*,

2008; Lignell *et al*., 2003, Polder *et al.*, 2008b; Kakimoto *et al.*, 2008; López *et al.*, 2004) up to 188 ng HBCDD/g of milk lipids (Eljarrat *et al* (2009). A calculation in the EU Risk Assessment Report (May 2008) of HBCDD intake by breast-feed babies gives the following estimates (based on 3.2 ng of HBCDD/g of fat in breast milk): 0.015 µg/kg bw/day for 0-3 months old and 0.0056 µg/kg bw/day for 3-12 months old. Using a recent Spanish breast milk study (Eljarrat *et al*, 2009) a calculated median daily intake for 1 month-old Spanish infants amounted to 0,175 µg HBCDD/kg bw/day, much higher than in a previous estimation. However, at present the potential of HBCDD to affect child development at the observed levels is unknown.

The evidence to demonstrate that HBCDD may cause adverse effects on or via lactation comes from animal studies. The increased pup mortality during lactation, particularly increased between postnatal day 4 (PND 4) and PND 21, in the F2 generation in a 2-generation study on rats, indicates that HBCDD may act on or *via* lactation on pup development (Ema *et al*., 2008). In order for this increased pup mortality to occur during the lactation period a rather long exposure before pregnancy is required. This may have been the reason that the effect on or via lactation was not observed in F1 generation in Ema *et al*. study (2008) following shorter exposure before pregnancy of F0 dams or in the offspring of the one generation studies (Saegusa *et a*l. 2009 and van der Ven *et al*. 2009).
However, since cross-fostering was not done in any of these studies, it is not possible to distinguish between developmental effects induced *in utero* and those induced during lactation. In addition, those effects were observed in offspring of mothers showing mild signs of maternal toxicity (hypothyroidism).

Comparison with criteria

The above data fulfil the classification criteria for the additional category for effects on or via lactation (CLP Regulation) as they provide some evidence of the adverse effect on or via lactation from experimental animal studies.

Taking into account the above considerations RAC is of the opinion that the following classification applies to HBCDD:
CLP Regulation: **Lact. - H362** (CLP Regulation) (May cause harm to breast-fed children)

DSD - **R64** (May cause harm to breastfed babies)

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

ANNEXES:

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

[2] The Background Document (BD) supporting the opinion contains scientific justifications for the CLH proposal.