ETINSA European Tin Stabilisers Association

The following companies are members of ETINSA:

AKCROS Chemicals	BAERLOCHER	CHEMTURA
GALATA Chemicals	PMC Organometallix	REAGENS

Comments to the ECHA Public Consultation on the identification of SVHC, launched on 1st September 2014

ETINSA comments on DOTE (EC # 239-622-4 ; CAS # 15571-58-1)

Part 1 - proposed SVHC property

Comments on the read-across approach validity:

As the Annex XV dossier pointed out, DOTE will be listed in Table 3.1 (List of harmonized classification and labeling of hazardous substances) of Annex VI, part 3, of Regulation (EC) No 1272/2008 as toxic for reproduction Repr. 1B, H360D (May damage the unborn child).

Therefore, this classification of the substance in Commission Regulation (EC) No 944/2013 shows that the substance meets the criteria for classification in the hazard class: Reproductive toxicity category 1B in accordance with Article 57 (c) of REACH.

As was pointed out in the decision ECHA/RAC/CLH-O-000000243-78-01/F, section "RAC remarks on read-across and category approach to a common metabolite":
*"None of the studies of concern for reproductive toxicity were conducted on the DOT(2-EHMA) (Dioctyltin bis(2-ethyhexyl mercaptoacetate, **DOTE**), which is proposed for classification. The key studies referred to in the proposal used Dioctyltin bis(IOMA) [CAS no. 26401-97-8, **DOTI**]:Octyltin tris(IOMA) [CAS no. 26401-86-5, **MOTI**] mixture (≥80:<20%) (two rat studies, one study in rabbits, one study in mice) and DOTC (Dioctyltin dichloride, EC no. 222-583-2, CAS no. 3542-36-7))(one rat study).*
The Dossier Submitter's view in the original CLH dossier was that DOTC is an appropriate surrogate for the mammalian toxicity of the corresponding thioesters DOT(2-EHMA/(IOMA) due to its 100% hydrolysis in simulated mammalian gastric contents within 30 min, and RAC shares this view.
In conclusion DOTC is considered by RAC as the active moiety causing developmental effects in mammalian species. DOTC is a hydrolysis product of DOT(2-EHMA) and of DOT(IOMA), which are structurally similar and which immediately form DOTC at comparable hydrolysis rates after oral administration. Therefore read-across from DOT(IOMA) and DOTC to DOT(2-EHMA) appears to be justified."

ETINSA wants to refer to a recent study "*in vitro* metabolism study of DOTE" as provided as an attachment to the comment provided by the lead registrant of DOTE Galata Chemicals GmbH. The study was designed to answer a scientific question: is DOTE metabolized via a hydrolytic mechanism at mammalian gastric pH, and if so what is the hydrolytic product using a non-standard in vitro test? The results showed that under the simulated gastric environment (pH 1.2, 40 °C, 0.1 % surfactant) no DOTC was detected by 119Sn-NMR after 72 hours of incubation. The conclusion of the study was that DOTE does not hydrolyze rapidly (within hours) to DOTC.

A discussion of the differences in findings now and before in respect to the hydrolytic pathway has also been provided by Galata Chemicals GmbH in their comment.

This in effect takes away the basis of the decision on the harmonized classification using the read-across method based on the common metabolic pathway. In other words, the DOTC and DOTI studies used to classify DOTE should not be considered valid.

Comments on the new evidence concerning DOTE's developmental toxicity:

During the classification deliberations for DOTE, the registrants maintained that deficiencies in the developmental studies, such as the documented presence of maternal disease, confounded the results, and therefore the read-across from the existing DOTI studies to DOTE based on structural similarity is also questionable. In a recent study conducted outside of Europe for other legislative purposes showed that in two species DOTE did not show adverse effects on the major developmental endpoints (provided as an attachment to Galata Chemicals GmbH's comment). Combined with the facts stated before, it is the commentator's conclusion that the existing harmonized classification based on read-across data has no basis any more. Classification on DOTE's developmental toxicity should not, and need not be based on read-across data any more. The classification decision in 2012 could potentially be wrong and should therefore be reviewed based on the new scientific evidences.

Conclusion

Because the new information challenges the basis for the RAC's decision on DOTE's classification as a Repr. 1B substance and the first direct evidence that DOTE shows no adverse effects on major developmental endpoints, ETINSA believes that there is considerable doubt on the current harmonized classification. Since the listing of DOTE to the candidate list will have detrimental economic effect on the manufacturing industry as well as some downstream users industries, the new evidences deserve a decent chance to be reviewed by a scientific committee first. Combined with the fact that there is currently no process to de-list any substance from the candidate list, it is therefore appropriate to delay the inclusion of DOTE to the candidate list until a thorough scientific review has been performed.

END