EUROPEAN CHEMICALS AGENCY

Helsinki, 29 May 2017

Addressee: [redacted]

Decision number: TPE-D-2114361205-57-01/F
Substance name: 2-ethylhexyl 10-ethyl-4-[[2-[(2-ethylhexyl)oxy]-2-oxoethyl]thio]-4-octyl-7-oxo-8-oxa-3,5-dithia-4-stannatetradecanoate
EC number: 248-227-6
CAS number: 27107-89-7
Registration number: [redacted]
Submission number: [redacted]
Submission date: 18 January 2016
Registered tonnage band: 1000 tonnes or more

DECISION ON A TESTING PROPOSAL

Based on Article 40 of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), ECHA has taken the following decision.

Your testing proposal is accepted and you are requested to carry out:

1. ***In vivo* mammalian alkaline comet assay (Annex IX/X, Section 8.4., column 2; test method: OECD TG 489) in rats, oral, on the following tissues: liver, glandular stomach and duodenum using the registered substance.**

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI of the REACH Regulation. In order to ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective Annex, and an adequate and reliable documentation.

You are required to submit the requested information in an updated registration dossier by **5 June 2018**. You shall also update the chemical safety report, where relevant.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2. Advice and further observations are provided in Appendix 3.

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, shall be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under http://echa.europa.eu/regulations/appeals.

Authorised[1] by Claudio Carlon, Head of Unit, Evaluation E2

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix 1: Reasons

1. ***In vivo* mammalian alkaline comet assay (Annex IX/X, Section 8.4.)**

The decision of ECHA is based on the examination of the testing proposal submitted by you. Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require you to carry out the proposed test.

"Mutagenicity" is an information requirement as laid down in Annex VIII, Section 8.4. of the REACH Regulation. Column 2 of Annex X, Section 8.4. provides that "If there is a positive result in any of the *in vitro* genotoxicity studies in Annexes VII or VIII, a second *in vivo* somatic cell test may be necessary, depending on the quality and relevance of all the available data."

The technical dossier contains an *in vitro* study "[redacted], 2010, In vitro Mammalian Cell Gene Mutation Test" performed according to OECD Guideline 476 with the registered substance that shows positive results. There was a positive result in the in vitro mammalian mutagenicty test without metabolic activation. The result was ambiguous with metabolic activation. The positive results indicate that the substance is inducing gene mutations under the conditions of the tests. Clastogenic mechanism could not be ruled out since the number of both small and large colonies was increased.

You have adequately followed up for the clastogenicity by performing an *in vivo* micronucleus study which was negative. An appropriate second *in vivo* genotoxicity study to follow up the concern on gene mutations is not available for the registered substance but may be necessary to meet the information requirements. Consequently there is an information gap and you proposed to generate information for this endpoint by submitting a testing proposal for the comet assay.

ECHA further notes that according to the ECHA *Guidance on information requirements and chemical safety assessment* R.7a, chapter R.7.7.6.3 (July 2015), the *in vivo* mammalian alkaline comet assay ("comet assay", OECD TG 489) is suitable to follow up positive *in vitro* result for gene mutation. Hence, ECHA considers that this test is appropriate to address the concern.

You did not specify the route of administration, target organ or the species to be used for testing. According to the test method OECD TG 489, the test shall be performed by analysing tissues from liver as primary site of xenobiotic metabolism, glandular stomach and duodenum as sites of contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the substance, and probable different local absorption rates of the substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to sample both tissues to ensure a sufficient evaluation of the potential for genotoxicity at the site of contact in the gastro-intestinal tract.

Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study with the registered substance subject to the present decision: *In vivo* mammalian alkaline comet assay (test method: OECD TG 489) in rats, oral route, on the following tissues: liver, glandular stomach and duodenum."

Appendix 2: Procedural history

ECHA received the registration of the previous lead Registrant containing the testing proposal(s) for examination pursuant to Article 40(1) on 8 July 2015.

ECHA held a third party consultation for the testing proposal(s) from 30 November 2015 until 14 January 2016. ECHA did not receive information from third parties.

This decision is addressed to you because you have taken over the role of the joint submission's lead registrant from ARKEMA B.V on 18 January 2016.

This decision does not take into account any updates after **4 April 2016**, 30 calendar days after the end of the commenting period.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation:

ECHA notified you of the draft decision and invited you to provide comments. ECHA did not receive any comments by the end of the commenting period.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

ECHA received proposal for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendment(s).

ECHA referred the draft decision to the Member State Committee.

You did not provide any comments on the proposed amendment(s).

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-53 written procedure and ECHA took the decision according to Article 51(6) of the REACH Regulation.

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Appendix 3: Further information, observations and technical guidance

1. This decision does not imply that the information provided in your registration dossier is in compliance with the REACH requirements. The decision does not prevent ECHA from initiating a compliance check on the registration at a later stage.

2. Failure to comply with the request(s) in this decision, or to fulfil otherwise the information requirement(s) with a valid and documented adaptation, will result in a notification to the Enforcement Authorities of the Member States.

3. In relation to the information required by the present decision, the sample of the substance used for the new test(s) must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants. It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new test(s) is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new test(s) must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the test(s) to be assessed.