Decision number: TPE-D-2114306253-63-01/F Helsinki, 27 July 2015

DECISION ON TESTING PROPOSAL SET OUT IN A REGISTRATION PURSUANT TO ARTICLE 40(3) OF REGULATION (EC) NO 1907/2006

For Poly[oxy(methyl-1,2-ethanediyl)], α,α'-(2,2-dimethyl-1,3-propanediyl)bis[ω-hydroxy-], EC No 610-848-9 (CAS No 52479-58-0), registration number: [redacted]

Addressee: [redacted]

The European Chemicals Agency (ECHA) has taken the following decision in accordance with the procedure set out in Articles 50 and 51 of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH Regulation).

I. Procedure

Pursuant to Article 40(1) of the REACH Regulation, ECHA has examined the following testing proposal submitted as part of the egistration dossier in accordance with Articles 10(a)(ix) and 12(1)(e) thereof for Poly[oxy(methyl-1,2-ethanediyl)], α,α'-(2,2-dimethyl-1,3-propanediyl)bis[ω-hydroxy-], EC No 610-848-9 (CAS No 52479-58-0), submitted by [redacted] (Registrant).

- 90-day oral toxicity study (OECD 408) with the registered substance

This decision is based on the registration dossier as submitted with submission number [redacted], for the tonnage band of 100 to 1000 tonnes per year. This decision does not take into account any updates after 17 May 2015, i.e. 30 calendar days after the end of the commenting period.

This decision does not imply that the information provided by the Registrant in his 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.

ECHA received the registration dossier containing the above-mentioned testing proposal for further examination pursuant to Article 40(1) on 8 February 2013.

ECHA held a third party consultation for the testing proposal from 18 September 2014 until 3 November 2014. ECHA received information from third parties (see section III below).

On 11 March 2015 ECHA sent the draft decision to the Registrant and invited him to provide comments within 30 days of the receipt of the draft decision.

On 01 April 2015 ECHA received comments form the Registrant agreeing to ECHA's draft decision.

On 11 June 2015 ECHA notified the Competent Authorities of the Member States of its draft decision and invited them pursuant to Article 51(1) of the REACH Regulation to submit proposals for amendment of the draft decision within 30 days of the receipt of the notification.

As no proposal for amendment was submitted, ECHA took the decision pursuant to Article 51(3) of the REACH Regulation.

II. Testing required

A. Tests required pursuant to Article 40(3)

The Registrant shall carry out the following proposed test pursuant to Article 40(3)(a) of the REACH Regulation using the indicated test method and the registered substance subject to the present decision:

> Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26/OECD 408) in rats.

Note for consideration by the Registrant:

The Registrant 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 to and conforming with the appropriate rules in the respective Annex, and an adequate and reliable documentation.

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

B. Deadline for submitting the required information

Pursuant to Articles 40(4) and 22(2) of the REACH Regulation, the Registrant shall submit to ECHA by **03 February 2017** an update of the registration dossier containing the information required by this decision, including, where relevant, an update of the Chemical Safety Report.

III. Statement of reasons

The decision of ECHA is based on the examination of the testing proposal submitted by the Registrant for the registered substance and scientific information submitted by third parties.

A. Tests required pursuant to Article 40(3)

> Sub-chronic toxicity study (90 day) (Annex IX, Section 8.6.2)

a) Examination of the testing proposal

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

A sub-chronic toxicity study (90 day) is a standard information requirement as laid down in Annex IX, Section 8.6.2. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently, there is an information gap and it is necessary to provide information for this endpoint.

The Registrant has submitted a testing proposal for a sub-chronic toxicity study (90 day) via the oral route (EU B.26/OECD 408).

ECHA considers that the proposed study via the oral route is appropriate to fulfil the information requirement of Annex IX, Section 8.6.2. of the REACH Regulation. The substance is a liquid with low vapour pressure (0.05 Pa at 25°C), and therefore significant human exposure to vapour cannot be anticipated at room temperature. Furthermore, the dossier does not include spray applications, and the substance is not classified as skin or eye irritant, or sensitizer. Due to the fact that human exposure to vapour is unlikely, no concerns for local effects in the respiratory tracts are anticipated. Therefore, the proposed route –oral route - is the most appropriate route of administration having regard to the likely route of human exposure.

The Registrant did not specify the species to be used for testing. According to the test method EU B.26/OECD 408 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

b) Consideration of the information received during third party consultation

ECHA received third party information concerning the testing proposal during the third party consultation. For the reasons explained below the information provided by third parties is not sufficient to fulfil this information requirement.

The third party has proposed the following: "*A NOAEL of 1000 mg/kg bw/d was derived from a 28-day sub-acute study. The registered substance displays a low toxicity profile in acute and local toxicity tests and is not classified for human health effects. A review of more than 40 low toxicity chemicals has shown that the results of the 28-day study are predictive of low toxicity in the 90-day repeated dose toxicity study. A weight of evidence assessment can further be supported by data of three related ethoxylated and propoxylated compounds which mostly exert very low systemic toxicity in oral sub-acute toxicity studies (NOAEL of 1000 mg/kg bw/d). On this background it is unlikely that the proposed test would add significant toxicological information. Waiving the test may therefore be considered.*"

Additionally, a review (ECEAE; Taylor 2013) "*A weight-of-evidence approach for justifying the waiving of the 90-day repeat dose toxicity test under REACH; more data using the ECHA database*" has been attached to the comment.

ECHA acknowledges that the third party has proposed a weight of evidence approach for the Registrant to consider. However, ECHA notes that it is the Registrant's responsibility to consider and justify any adaptation of the information requirements in accordance with the relevant conditions as established in Annex XI, Section 1.2. Therefore, the Registrant should assess whether he can justify an adaptation based on the weight of evidence as suggested by the third party. If the information requirement can be met by way of adaptation, he should include the adaptation argument with all necessary documentation according to Annex XI, Section 1.2 in the registration dossier.[1]

Moreover, ECHA notes that the information provided by the third party is insufficient for demonstrating that the conditions of Annex XI, Section 1.2. of the REACH Regulation are met. The third party comment suggests a waiver for the 90 day studies, based on a NOAEL of 1000 mg/kg bw/d which was derived from a 28-day sub-acute study and on the apparently low toxicity profile of the registered substance.

1 Such update can only be taken into consideration in the decision-making if it is submitted before the draft decision is sent to the Member State Competent Authorities pursuant to Article 51(1) of the REACH Regulation.

However, such studies have not been performed on the registered substance, but on two homologous substances. Furthermore, the Registrant is not proposing a read across or a weight of evidence (WoE) approach for the sub-chronic toxicity study (90-day), but waives the 28-day, the inhalation and the dermal repeated dose studies and proposes a 90-day oral study to fill the data gap.

As no repeated dose study exists on the registered substance, the extrapolation as proposed by the third party is not applicable. Moreover, the third party comment suggests to support the WoE approach with data on three related ethoxylated and propoxylated compounds. Nevertheless, this data has not been attached to the comments. The presented paper (ECEAE; Taylor 2013) describing a predictive weight of evidence approach has shortcomings that prevent its application.

Furthermore, ECHA observes that the third party has proposed a weight of evidence approach based on a database search (ECEAE; Taylor 2013). The third party claims that this general weight of evidence approach can be used to predict the sub-chronic toxic properties of a substance based on observed "low toxicity" in a sub-acute (short-term repeated dose) toxicity study if the substance fulfils certain other criteria described as a "low toxicity profile". However, ECHA notes that this predictive weight of evidence approach has shortcomings that prevent its application.

First of all, ECHA notes that a weight of evidence approach requires substance-specific justification and cannot be addressed with a generic weight of evidence approach which e.g. does not explain whether it is applicable to the registered substance.

Secondly, the proposed approach has a limited predictive power. It is based on eighteen substances with a "low toxicity profile". Out of these eighteen substances, the prediction was incorrect for two substances.

Thirdly, ECHA notes that the proposed general weight of evidence approach that a substance will not have an effect in a sub-chronic toxicity study based on results of a sub-acute toxicity study is not appropriate for the following reasons. The study design of sub-acute toxicity studies and sub-chronic toxicity studies differ in relevant key parameters, which affect the uncertainty and relevance of the information obtained from these studies. For example, the reduced number of animals used in a sub-acute toxicity study (5 animals per sex and dose) compared to the sub-chronic toxicity study (10 animals per sex and dose) results in a lower statistical power of the sub-acute toxicity study to detect effects. Similarly, the duration of exposure in a sub-chronic toxicity study (90 days) covers a prolonged period of the animals' lifespan as compared to the sub-acute toxicity study (28 days). As a consequence of these differences in the study protocols, a sub-chronic toxicity study (90-day) may detect effects which were not observed in a sub-acute toxicity study (28 days). Therefore, the information provided by the third party is not sufficient to adapt the standard information requirement.

c) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is requested to carry out the proposed study with the registered substance subject to the present decision: Sub-chronic toxicity study (90-day) in rats, oral route (test method: EU B.26/OECD 408).

IV. Adequate identification of the composition of the tested material

The process of examination of testing proposals set out in Article 40 of the REACH Regulation aims at ensuring that the new study meet real information needs. Within this context, the Registrant's dossier was sufficient to confirm the identity of the substance to the extent necessary for examination of the testing proposal.

In relation to the proposed test, the sample of substance used for the new study must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is within the specifications of the substance composition that are given by the joint registrants. It is the responsibility of all joint registrants of the same substance to agree to the test proposed (as applicable to their tonnage level) and to document the necessary information on their substance composition.

In addition, it is important to ensure that the particular sample of substance tested in the new study 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 by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new study 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 study to be assessed.

V. Information on right to appeal

An appeal may be brought against this decision to the Board of Appeal of ECHA under Article 51(8) of the REACH Regulation. Such appeal shall be lodged within three months of receiving notification of this decision. Further information on the appeal procedure can be found on the ECHA's internet page at http://www.echa.europa.eu/regulations/appeals. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

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