EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-2114309057-56-01/F Helsinki, 28 September 2015

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

For Reaction product of 3-aminomethyl-3,5,5-trimethylcyclohexanamine with oligomerisation products of 4,4'-propane-2,2-diyldiphenol with 2-(chloromethyl)oxirane, CAS RN 38294-64-3 (EC No 500-101-4), 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 proposals submitted as part of the jointly submitted registration dossier in accordance with Articles 10(a)(ix) and 12(1)(d) thereof for Reaction product of 3-aminomethyl-3,5,5-trimethylcyclohexanamine with oligomerisation products of 4,4'-propane-2,2-diyldiphenol with 2-(chloromethyl)oxirane, CAS RN 38294-64-3 (EC No 500-101-4), submitted by [redacted] (Registrant):

- Repeated dose toxicity: oral (OECD 408) in rats;
- Developmental toxicity / teratogenicity study (OECD 414).

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 submitted after the deadline for updating (13 March 2015) communicated to the Registrant by ECHA on 4 February 2015.

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 proposals for further examination pursuant to Article 40(1) on 28 November 2013.

ECHA held a third party consultation for the testing proposals from 15 April 2014 until 30 May 2014. ECHA received information from third parties (see section III below).

On 14 November 2014, 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 17 December 2014, ECHA received comments from the Registrant agreeing to ECHA's draft decision.

The ECHA Secretariat considered the Registrant's comments. The information is reflected in the Statement of Reasons (Section III) whereas no amendments to the Information Required (Section II) were made.

On 23 July 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 tests pursuant to Article 40(3)(a) and 13(4) of the REACH Regulation using the indicated test methods and the registered substance subject to the present decision:

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26/ OECD 408) in rats;
2. Pre-natal developmental toxicity study, oral route (Annex IX, Section 8.7.2.; test method: EU B.31/ OECD 414) in rats or rabbits.

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(s) in this decision, or to fulfil otherwise the information requirement(s) with a valid and documented adaptation, shall 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 **5 October 2017** an update of the registration dossier containing the information required by this decision, including, where relevant, an update of the Chemical Safety Report. The timeline has been set to allow for sequential testing as appropriate.

III. Statement of reasons

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

A. Tests required pursuant to Article 40(3)

1. Repeated dose toxicity study (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) in rats via the oral route (EU B.26/OECD 408) with the following justification: *"experimental study planned".*

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. After considering the arguments related to the properties of the substance, namely the high irritancy potency (liquid with low vapour pressure classified as corrosive to the skin and/or damaging to the eyes, water soluble) and the information provided on the uses and human exposure (no uses with spray application), ECHA considers that testing by the oral route is most appropriate.

The Registrant proposed testing in rats. 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 further below the information provided by third parties is not sufficient to fulfil this information requirement.

The third party has indicated that "*the main constituents of the UVCB substance are high molecular weight polymers which are predicted to be not bioavailable, and a bioavailable component with a molecular weight of 170. It is recommended to refer to these data for the registration of the UVCB substance in a read-across approach.*
Further the third party proposed an approach to read across to 3-aminomethyl-3,5,5-trimethylcyclohexylamine: " *As a reference polymer constituent (with a MW at the lower limit of all polymer constituents) is predicted to be likely not absorbed from the gastrointestinal tract, classification and risk assessment for the UVCB chemical may rely on the bioavailable non-polymer constituent. This substance, 3-aminomethyl-3,5,5-trimethylcyclohexylamine (EC No. 220-666-8), has been registered with an oral 90-day repeated dose toxicity study which may be used in a read-across approach. The substance, also named isophorone diamine, was administered in drinking water to rats at actual dose levels of 21.5, 59 and 150 mg/kg bw/d for males, and 22.6, 62 and 147 mg/kg bw/d for females, respectively. At the high dose level morphological alterations of the kidneys were noted in both sexes (tubular basophilia, tubular casts and lymphoid foci indicative of tubular nephrosis).*"

The third party bases their comment on existing data for another substance, which is one of the constituent of the registered substance (and which is also registered as a substance on its own) for which the leading effects are on the kidney, and proposed an adaptation argument relying on a read across approach for the Registrant to consider.
ECHA notes that it is the Registrant's responsibility to consider and to justify any adaptation of the information requirements in accordance with the relevant conditions as established in

Annex XI, Section 1.5.. Therefore, the Registrant should assess whether they can justify a read-across as suggested by the third party. If the information requirement can be met by way of adaptation, they should include the adaptation argument with all necessary documentation according to Annex XI, Section 1.5. in the registration dossier[1].

ECHA notes that the information provided by the third party is currently insufficient for demonstrating that the conditions of Annex XI, Section 1.5. of the REACH Regulation are met. For example, the data on which it relies has not been made available to ECHA or to the Registrant.

It is noteworthy that the Registrant should access the robust study summary in order to assess whether the possible adaptation holds. Therefore, the information provided by the third party in itself would not be sufficient to adapt the standard information requirement.

In conclusion, the information provided by the third party is not sufficient to adapt the standard information requirement since it has not demonstrated that the conditions of Annex XI of the REACH Regulation are met.

ECHA notes that the Registant has considered the third party comments, suggesting "*read across to 3-aminomethyl-3,5,5-trimethylcyclohexylamine (isophorone diamine, IPD, EC 220-666-8, CAS 2855-13-2)*". The lead registrant has considered this suggestion and concluded that "*it will not be possible to read across to IPD for this substance because the 28-d toxicity studies for the two substances show significantly different findings. The differential response suggests that components of the substance differ from that of IPD and therefore read across for the requested endpoints is not justified. We therefore plan to conduct the 90day Toxicity Study and Prenatal Developmental Toxicity Studies in rats based upon ECHA's decision.*"

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).

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

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 pre-natal developmental toxicity study for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. 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 pre-natal developmental toxicity study according to EU B.31/OECD 414 to be performed on 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.

ECHA considers that the proposed study is appropriate to fulfil the information requirement of Annex IX, Section 8.7.2. of the REACH Regulation.

The Registrant did not specify the species to be used for testing. The Registrant proposed testing by the oral route. According to the test method EU B.31/OECD 414, the rat is the preferred rodent species, the rabbit the preferred non-rodent species and the test substance is usually administered orally. ECHA considers these default parameters appropriate and testing should be performed by the oral route with the rat or the rabbit as a first species to be used.

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 further below the information provided by third parties is not sufficient to fulfil this information requirement.

The third party has indicated that: "*the main constituents of the UVCB substance are high molecular weight polymers which are predicted to be not bioavailable, and a bioavailable component with a molecular weight of 170. It is recommended to refer to these data for the registration of the UVCB substance in a read-across approach. Two main constituents of the UVCB substance have been identified by the registrant, as 3-aminomethyl-3,5,5-trimethyl-cyclohexylamine (EC No. 220-666-8) with a molecular weight of 170, and poly(bisphenol A-co-epichlorohydrin-co-isophoronediamine) with MW ranges between 680 and 700, or > 700, respectively. A polymer with a molecular weight of 681 which is specified as a reference compound by means of the chemical structure is predicted by Lipinski rule OASIS (OECD Toolbox 3.2) to be not bioavailable. In contrast, the low molecular weight constituent 3-aminomethyl-3,5,5- trimethylcyclohexylamine is expected to be bioavailable.*
As a reference polymer constituent (with a MW at the lower limit of all polymer constituents) is predicted to be likely not absorbed from the gastrointestinal tract, classification and risk assessment for the UVCB chemical may rely on the bioavailable non-polymer constituent. This substance, 3-aminomethyl-3,5,5-trimethylcyclohexylamine (EC No. 220-666-8), has been registered with an oral prenatal developmental toxicity study which may be used in a readacross approach. Dose levels up to 250 mg/kg bw/d were administered by oral gavage in an OECD Guideline 414 compliant study. No teratogenic or embryo-/fetotoxic effects were seen. Reduced food consumption and body weight gain of the dams at the maximum dose level indicated that maternal toxicity was associated with the treatment."

The third party bases their comment on existing data for an another substance, which is one of the constituent of the registered substance (and which is also registered as a substance on its own) for which the developmental parameters were not affected.

ECHA acknowledges that the third party has proposed an adaptation argument relying on a read across approach for the Registrant to consider, as the dossier of the constituent 3-aminomethyl-3,5,5-trimethylcyclohexylamine contains a prenatal developmental toxicity study.

ECHA notes that it is the Registrant's responsibility to consider and to justify any adaptation of the information requirements in accordance with the relevant conditions as established in Annex XI, Section 1.5.. Therefore, the Registrant should assess whether they can justify a read-across as suggested by the third party. If the information requirement can be met by

way of adaptation, the Registrant should include the adaptation argument with all necessary documentation according to Annex XI, Section 1.5. in the registration dossier[2].

ECHA notes that the information provided by the third party is currently insufficient for demonstrating that the conditions of Annex XI, Section 1.5. of the REACH Regulation are met. For example, the data on which it relies has not been made available to ECHA or to the Registrant. It is noteworthy that the Registrant should access the robust study summary in order to assess whether the possible adaptation holds. Therefore, the information provided by the third party in itself would not be sufficient to adapt the standard information requirement.

In conclusion, the information provided by the third party is not sufficient to adapt the standard information requirement since it has not demonstrated that the conditions of Annex XI of the REACH Regulation are met.

ECHA notes that the Registant has considered the third party comments, suggesting "*read across to 3-aminomethyl-3,5,5-trimethylcyclohexylamine (isophorone diamine, IPD, EC 220-666-8, CAS 2855-13-2)*". The lead registrant has considered this suggestion and concluded that "*it will not be possible to read across to IPD for this substance because the 28-d toxicity studies for the two substances show significantly different findings. The differential response suggests that components of the substance differ from that of IPD and therefore read across for the requested endpoints is not justified. We therefore plan to conduct the 90day Toxicity Study and Prenatal Developmental Toxicity Studies in rats based upon ECHA's decision.*"

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: Pre-natal developmental toxicity study in rabbits or rats, by oral route (test method: EU B.31/OECD 414).

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 studies 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. The Registrant must note, however, that this information, or the information submitted by other registrants of the same substance, has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation.

In relation to the proposed tests, the sample of substance used for the new studies 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 tests 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 studies 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

[2] 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.

manufactured by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new studies 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 studies 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.

Authorised[3] by Ofelia Bercaru, Head of Unit, Evaluation E3

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