EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000003631-80-02 Helsinki,

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

**For Amines, N-tallow alkyltrimethylenedi-, propoxylated, CAS No 68603-75-8 (EC No 614-637-2), 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 registration dossier in accordance with Articles 10(a)(ix) and 12(1)(d) thereof for **Amines, N-tallow alkyltrimethylenedi-, propoxylated**, CAS No 68603-75-8 (EC No 614-637-2), by [redacted] (Registrant).

- Viscosity of Liquids (OECD 114);
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- Repeated Dose 90-Day Oral Toxicity in Rodents (OECD 408), test species not specified, with the read across substance 2-Propanol, 1,1'-[[3-[(3-aminopropyl)amino]-propyl]imino]bis-, N-tallow alkyl derivs. (CAS 97592-79-5);
- Pre-natal developmental toxicity study (OECD 414), test species or route not specified with the read across substance 2-Propanol, 1,1'-[[3-[(3-aminopropyl)amino]propyl]imino]-bis-, N-tallow alkyl derivs. (CAS 97592-79-5).

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 20 June 2013, the date upon which ECHA notified its draft decision to the Competent Authorities of the Member States pursuant to Article 51(1) of the REACH Regulation.

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 to initiate a compliance check on the present dossier at a later stage.

On 30 November 2010, pursuant to Article 40(1) of the REACH Regulation, ECHA initiated the examination of the testing proposals set out by the Registrant in the registration dossier for the substance mentioned above.

ECHA held a third party consultation for the testing proposals from 16 August 2011 until 30

September 2011. ECHA did not receive information from third parties.

On 26 September 2012 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 24 October 2012 ECHA received comments from the Registrant agreeing partly to ECHA's draft decision. On 17 December 2012 the Registrant updated his registration dossier. In this update the Registrant removed his original testing proposals Sediment-Water Chironomid Toxicity Using Spiked Sediment (OECD 218), and Earthworm Reproduction Test (Eisenia fetida/Eisenia andrei) (OECD 222).

ECHA considered the Registrant's comments received. The comments are reflected in the Statement of Reasons (Section III) whereas no amendments to the Testing Required (Section II) were made.

On 20 June 2013 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 to amend the draft decision within 30 days of the receipt of the notification.

Subsequently, Competent Authorities of the Member States did not propose amendments to the draft decision and ECHA took the decision pursuant to Article 51(3) of the REACH Regulation.

II. Testing required

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

1. Viscosity (Annex IX, 7.1.7, test method: OECD 114);

The Registrant shall carry out the following additional tests pursuant to Article 40(3)(c) of the REACH Regulation using the indicated test methods and the registered substance subject to the present decision:

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

while the originally proposed tests for a:

- Sub-chronic oral toxicity study to rodents (90-day) (OECD 408)
  and
- Pre-natal developmental toxicity study (OECD 414)

proposed to be carried out using the read across substance 2-Propanol, 1,1'-[[3-[(3-aminopropyl)amino]propyl]imino]-bis-, N-tallow alkyl derivs. (CAS 97592-79-5) are rejected pursuant to Article 40(3)(d) of the REACH Regulation.

The Registrant shall determine the appropriate order of the studies taking into account the possible outcome and considering the possibilities for adaptations of the standard information requirements according to column 1 or 2 provisions of the relevant Annexes of the REACH Regulation.

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by [exact date – 24 months *from the date of the decision*] an update of the registration dossier containing the information required by this decision.
At any time, the Registrant shall take into account that there may be an obligation to make every effort to agree on sharing of information and costs with other Registrants.

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.

## 1. Viscosity

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

A viscosity study is a standard information requirement as laid down in Annex IX, section 7.17. 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.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study: Viscosity (Annex IX, 7.17.; test method: OECD 114) using the registered substance.

## 2. Sub-chronic toxicity study (90-day)

Pursuant to Article 40(3)(d) and (c) of the REACH Regulation, ECHA may reject a proposed test and require the Registrant to carry out other tests in cases of non-compliance of the testing proposal with Annexes IX, X and XI.

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.

2.1. Read-across

Read across is a possible adaptation for the Registrant when the relevant criteria set out in Annex XI, 1.5 are fulfilled. In particular the first paragraph of Annex XI, 1.5 provides that (1) the group/read across concept can be applied to "substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity" and (2) the application of the group concept requires that "physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s) within the group by interpolation to other substances in the group (read-across approach)".

The similarities may be based on:
(1) a common functional group;
(2) the common precursors and/or the likelihood of common breakdown products via physical and biological processes, which result in structurally similar chemicals; or
(3) a constant pattern in the changing of the potency of the properties across the category.
However, this needs in particular to be justified and supported by adequate documentation.

Annex XI, 1.5 further provides that in all cases read-across requires results that should:
— be adequate for the purpose of classification and labelling and/or risk assessment,
— have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3),
— cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter, and
— adequate and reliable documentation of the applied method shall be provided.

In assessing whether a substance meets the conditions for read-across to another substance ECHA first has to examine this latter condition, i.e. whether the Registrant has provided adequate and reliable documentation supporting the read-across approach. Only thereafter ECHA can fully examine whether the criteria of structural predictability of the effects from the reference substance have been fulfilled. Indeed, in cases where the documentation supporting a read-across approach is not adequate or reliable ECHA will not be in a position to evaluate the overall read-across approach and consequently will be unable to verify that there is compliance with the rules of Annex XI, 1.5.

ECHA observes that in the testing proposal on sub-chronic toxicity study (90-day) the Registrant has suggested using the read-across substance "2-Propanol, 1,1'-[[3-[(3-aminopropyl)amino]-propyl]imino]bis-, N-tallow alkyl derivs. (CAS 97592-79-5)" as test material. In his justification document ("Justification in support of cross-reading between a diamine derivative and polyamine derivative" by [redacted] and [redacted] of December 2012) the Registrant concludes: "In conclusion, since diamine derivative and polyamine derivative have comparable physico-chemical properties and the available toxicological data for both substance showed similar profile, it is considered totally justified to read-across the repeated and reproduction toxicity results for polyamine derivative to diamine derivative."

ECHA does not find convincing support for this conclusion in the information and justification presented by the Registrant in the justification document or other parts of the dossier submitted by the Registrant for the registered substance.

ECHA notes in the first place that the similarity in chemical structure between the registered substance ("the target" in read-across terms) and the substance proposed to be tested ("the source" in read-across terms) alone does not justify the read-across, without further substantiation by means of a convincing explanation and supporting information. The Registrant has to point out how similarities and dissimilarities may influence the relevant toxicity of both substances and/or has to substantiate this by means of relevant toxicological data. This is not done by the registrant.

In this respect, ECHA notes that the two substances differ in a number of aspects that may alter the toxicological properties. The read-across entails the comparison of the fully propoxylated diamine (90% of the source) with partly propoxylated comparable compounds. Partial propoxylation introduces markedly different functional groups (mono and secondary non-propoxylated amines) at as yet unknown places of the molecule and in as yet unknown combinations with propoxylated amines. In addition, the justification does not make clear whether the diamine of the source substance is fully propoxylated, which makes it difficult

to compare the diamine in the source with the diamine in the target as regards their possible contribution to the relevant toxicity. ECHA also notes that the Registrant also does not convincingly explain as to why mono-, di-, tri-, and tetra-amino derivatives of the fatty acids are expected, based on their chemical structure, as to have the same toxicological effects, irrespective of the level of propoxylation.

The Registrant points to the similarity in physicochemical properties to further strengthen the read-across proposal. However, ECHA observes that a similarity in physicochemical properties can on its own not substantiate the read-across, without a convincing explanation. Such an explanation is not present in the information submitted by the Registrant. It is stated by the Registrant in the justification document when source and target substance are compared that "their toxicological profile is very much related to their physico-chemical properties and chemical structure". This statement is not further substantiated and can thus not support the proposed read-across.

It is also stated by the Registrant in the justification document: "Similar as with polymers, the hypothesis would be that the toxicity diminishes with increasing numbers of combiners monomers." Whether or not the toxicity of polymers does indeed decrease with increasing numbers of monomers in general is not relevant here. The tallow alkyl groups are supposed to be the same for each of the substances. The differences among the amino-group containing moieties of the molecules cannot be compared to polymers built of different numbers of monomers.

The read-across is further built on a comparison of toxicological data in the justification document. ECHA notes that this comparison does not support the notion that no 90-day repeated-dose toxicity study and pre-natal developmental toxicity study need to be done with the target substance based on other toxicological data obtained with target and/or source substance. For instance, the increase of the exposure duration to 90 days in a repeated-dose toxicity study may result in the observation of effects not observed after 28 days. Also it is not possible to draw conclusions on the pre-natal developmental toxicity of the target substance from the comparison presented in the justification document.

Based on the above, the Registrant has failed to meet the requirements of Annex XI, Section 1.5. governing grouping of substances and read-across approach. ECHA considers therefore that the testing with the read-across substance would be insufficient to meet the information requirement concerning sub-chronic toxicity study (90-day) (Annex IX, 8.6.2) for the registered substance.

2.2. Species and route for testing

The Registrant proposed testing by the oral route. In the light of the physical-chemical properties of the substance and the information provided on the uses and human exposure, ECHA considers that testing by the oral route is appropriate.

The Registrant did not specify the species to be tested. According to the test method EU B.26/OECD 408 the rat is the preferred rodent species. ECHA considers this species as being appropriate.

2.3. Outcome

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, the Registrant is required to carry out the following study: Sub-chronic toxicity study (90-day) in rats, oral route (test method: EU B.26/OECD 408) using the registered substance, while the originally proposed test on the read-across substance 2-Propanol, 1,1'-[[3-[(3-aminopropyl)amino]-

propyl]imino]bis-, N-tallow alkyl derivs. (CAS 97592-79-5) is rejected in accordance with Article 40(3)(d) of the REACH Regulation.

## 3. Pre-natal developmental toxicity study

Pursuant to Article 40(3)(d) and (c) of the REACH Regulation, ECHA may reject a proposed test and require the Registrant to carry out other tests in cases of non-compliance of the testing proposal with Annexes IX, X and XI.

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.

3.1. Read-across

ECHA observes that in the testing proposal on pre-natal developmental toxicity study the Registrant has suggested using the same read-across substance as for subchronic toxicity study with the same statements of justification. For the reasons explained under the point 2.1 above, ECHA considers that the testing with the read-across substance would be insufficient to meet the information requirement concerning pre-natal developmental toxicity study (Annex IX, 8.7.2) for the registered substance.

3.2. Species and route for testing

The Registrant did not specify the species and route to be used for testing. 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 rabbit as a first species to be used.

3.3. Outcome

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, the Registrant is required to carry out the following study: Pre-natal developmental toxicity study in rats or rabbits, oral route (test method: EU B.31/OECD 414) using the registered substance while the originally proposed test on the read-across substance 2-Propanol, 1,1'-[[3-[(3-aminopropyl)amino]-propyl]imino]bis-, N-tallow alkyl derivs. (CAS 97592-79-5) is rejected in accordance with Article 40(3)(d) of the REACH Regulation.

IV. Adequate identification of the composition of the tested material

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 manufactured. If the registration of the substance covers different grades, the sample used for the new studies must be suitable to assess these.

Furthermore, there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the studies to be assessed.

V. General requirements for the generation of information and Good Laboratory Practice

ECHA reminds registrants of the requirements of Article 13(4) of the REACH Regulation that ecotoxicological and toxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice (GLP).

According to Article 13(3) of the REACH Regulation, tests that are required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods laid down in a Commission Regulation or in accordance with other international test methods recognised by the Commission or the European Chemicals Agency as being appropriate. Thus, the Registrant shall refer to Commission Regulation (EC) No 440/2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 as adapted to technical progress or to other international test methods recognised as being appropriate and use the applicable test methods to generate the information on the endpoints indicated above.

VI. 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://echa.europa.eu/appeals/app_procedure_en.asp. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

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