ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-2114306294-57-01/F Helsinki, 27 July 2015

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

For Reaction mass of N,N'-1,6-hexanediylbis[12-hydroxyoctadecanamide], Stearyl hydroxystearyl hexanediamine and bis(Hydroxystearyl) Hydroxystearyl hexanediamine, EC No 434-430-9, 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 Reaction mass of N,N'-1,6-hexanediylbis[12-hydroxyoctadecanamide], Stearyl hydroxystearyl hexanediamine and bis(Hydroxystearyl) Hydroxystearyl hexanediamine, EC No 434-430-9, submitted by [redacted] (Registrant).

- *Daphnia magna* Reproduction Test (OECD Guideline 211);
- 90-day repeat dose toxicity study (OECD 408) including additional reproductive parameters;
- Prenatal developmental toxicity study (OECD 414).

This decision is based on the registration dossier as submitted with submission number [redacted], for the tonnage band of [redacted] tonnes per year. This decision does not take into account any updates 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.

The examination of the testing proposals was initiated upon the date when receipt of the complete registration dossier was confirmed on 27 June 2014.

ECHA held a third party consultation for the testing proposals from 16 October until 1 December 2014. The public consultation was held for the following hazard endpoints: Reproductive toxicity (pre-natal developmental toxicity), Reproductive toxicity (two-generation reproductive toxicity) and Sub-chronic toxicity (90-day): oral. ECHA received two comments from third parties. One comment provided information on the two-generation reproductive toxicity information requirement. After subsequent examination of the scope of the testing proposals it was noted by ECHA that the Registrant did not propose to conduct a two-generation reproductive toxicity study and this requirement is thus not in the scope of the testing proposal examination. The second comment contained only random characters and therefore cannot be considered as a comment. Therefore these comments are not reflected in this decision in the sections II and III.

On 18 December 2014 ECHA sent the draft decision to the Registrant and invited him to provide comments within 45 days of the receipt of the draft decision. Due to the commenting period falling on the Christmas and New Year period, the Registrant was exceptionally granted additional 15 days to the normal 30 days to send comments.

On 6 February 2015 ECHA received comments from the Registrant on the 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 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 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. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: *Daphnia magna* reproduction test, EU C.20/OECD 211).
2. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26/OECD 408) in rats. It is at the Registrant's discretion to perform the intended additional examinations during the testing program.
3. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31/OECD 414) in rats or rabbits, oral route.

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 requests in this decision, or to fulfil otherwise the information requirements 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 August 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.

A. Tests required pursuant to Article 40(3)

1. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)

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.

"Long-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex IX, Section 9.1.5. 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 testing the registered substance for long-term toxicity testing on aquatic invertebrates with the following justification: "*Daphnia magna* reproduction test, EU C.20/OECD 211 with the following justification: "*A Daphnia magna reproduction test, performed to be in accordance with OECD Guideline 211 and EU Method C.20, is proposed to be conducted on the substance. The results of acute toxicity testing showed that clear effects were observed in the daphnia and algal tests with centrifuged WAFs at 100 mg/l loading. No definitive EC50's or NOECs could be derived because the analytical method used in the studies was unable to measure actual concentrations of the three main components of the substance in the test solutions. The EC50value for daphnia and algae was therefore considered to be <0.1 mg/l, being the water solubility limit of the substance. No effects were observed in the acute fish study with filtered WAFs at 100 mg/l loading. The chemical safety assessment indicates some concerns for the effects on aquatic organisms and therefore a long-term toxicity test is considered to be necessary. As the acute toxicity testing showed Daphnia magna to be more sensitive to the test substance than fish, it is considered that long-term testing should be conducted on Daphnia rather than fish. In addition, the results of the Daphnia magna reproduction study will be used to further refine the PBT assessment for the substance, as at present the toxicity (T-) criteria cannot be considered to be conclusively met or not. The results would be evaluated against the 'T-' criteria for long-term NOEC being less than 0.01 mg/l. Based on the acute toxicity testing, it is possible that any effects may be below the limit of detection. However, the long-term study will indicate whether there is chronic toxicity or effects on reproduction at the limit of solubility.*" ECHA considers that the proposed study is appropriate to fulfil the information requirement of Annex IX, Section 9.1.5 of the REACH Regulation.

According to ECHA *Guidance on information requirements and chemical safety assessment* (version 2.0, November 2014), Chapter R7b (Section R.7.8.5 including Figure R.7.8-4), if based on acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially more sensitive, long-term studies may be required on both. There were no indications in the dossier from the short-term toxicity studies on aquatic species that the fish would be substantially more sensitive than aquatic invertebrates.
In such case, according to the integrated testing strategy, the *Daphnia* study is to be conducted first. If based on the results of the long-term *Daphnia* study and the application of a relevant assessment factor no risks are observed (PEC/PNEC<1), no long-term fish

testing may need to be conducted. However, if a risk is indicated, long-term fish testing may need to be conducted.

b) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study using the registered substance subject to the present decision : Long-term toxicity testing on aquatic invertebrates (Annex IX, 9.1.5.; test method: *Daphnia magna* reproduction test, EU C.20/OECD 211).

Notes for consideration by the Registrant

Once results of the proposed test on long-term toxicity to aquatic invertebrates are available, the Registrant shall revise the chemical safety assessment as necessary according to Annex I of the REACH Regulation. If the revised chemical safety assessment indicates the need to investigate further the effects on aquatic organisms, the Registrant shall submit a testing proposal for a long-term toxicity test on fish in order to fulfil the standard information requirement of Annex IX, 9.1.6. If the Registrant comes to the conclusion that no further investigation of effects on aquatic organisms is required, he shall update his technical dossier by clearly stating the reasons for adapting the standard information requirement of Annex IX, 9.1.6.

Due to the low solubility of the substance in water OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA Guidance, Chapter R7b, table R. 7.8-3 summarising aquatic toxicity testing of difficult substances should be consulted by the Registrant for choosing the design of the requested long-term ecotoxicity tests and for calculation and expression of the result of this test.

2. 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) to be performed with the registered substance.

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 because the proposed route is the most appropriate route of administration having regard to the likely route of human exposure due to the following reasons. In light of the physico-chemical properties of the substance (solid with low vapour pressure and not classified as corrosive/irritating to the skin and/or damaging/irritating to the eyes) and the information provided on the uses and human exposure, ECHA considers that testing by the oral route is most appropriate.

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.

The Registrant proposed to extend the sub-chronic toxicity study (90 day) by including additional examinations/parameters (sperm analysis, oestrous cycle, reproductive organ weights and histopathology). ECHA notes, that it is at the Registrant's discretion to perform the intended additional examinations during the testing program and use the results to ensure the safe use of the substance. However, the Registrant is reminded that, if the condition of Annex IX, Section 8.7.3., Column 1 is fulfilled, the proposed extension of the study presently requested does not fulfil the standard information requirement in the registration dossier for reproductive toxicity set out in Annex IX, Section 8.7.3.

The Registrant outlined in the comments to the draft decision how he would address the information requirement by stating that "[redacted] agrees to the importance of this end-point and proposes the use of the existing studies (read-across) to the REACH registration dossier of Reaction products of 12-hydroxyoctadecanoic acid and octadecanoic acid and 1,3-phenylenedimethanamine, with REACH registration number [redacted]. These two substances have very similar chemical structures, and physicochemical and toxicological properties. Complete read across justification will be submitted in a dossier update for the [redacted] registration." However, the Registrant did not submit any further information in the comments. Based on the Registrant's statement of intent in his comments, ECHA's cannot conclude on the plausibility and/or relevance of the intended approach to fulfil the standard information requirement. While the Registrant indicated he would update, no update was received by the deadline of 13 March 2015.

The Registrant is reminded that this decision does not take into account any updates submitted after 13 March 2015. All the new information in the later update(s) of the registration dossier will however be assessed for compliance with the REACH requirements in the follow-up evaluation pursuant to Article 42 of the REACH Regulation.

b) 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). It is at the Registrant's discretion to perform the intended additional examinations during the testing program.

3. 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 with the registered substance subject to

the present decision. 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. He did not specify the route 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 the rabbit as a first species to be used.

The Registrant outlined in the comments to the draft decision how he would address the information requirement by stating that "Similarly to the previous end-point, [redacted] agrees to the importance of this end-point and proposes the use of the existing studies (read-across) from the REACH registration dossier of Reaction products of 12-hydroxyoctadecanoic acid and octadecanoic acid and 1,3-phenylenedimethanamine, with REACH registration number [redacted]. These two substances have very similar chemical structures, and physicochemical and toxicological properties. Complete read across justification will be submitted in a dossier update for the [redacted] registration." However, the Registrant did not submit any further information in the comments. Based on the Registrant's statement of intent in his comments, ECHA's cannot conclude on the plausibility and/or relevance of the intended approach to fulfil the standard information requirement. While the Registrant indicated he would update, no update was received by the deadline of 13 March 2015.

The Registrant is reminded that this decision does not take into account any updates submitted after 13 March 2015. All the new information in the later update(s) of the registration dossier will however be assessed for compliance with the REACH requirements in the follow-up evaluation pursuant to Article 42 of the REACH Regulation.

b) 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 rats or rabbits, 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 has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation.

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

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.

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