EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-2114296645-35-01/F Helsinki, 19 March 2015

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

For sodium hydrogen N-(1-oxododecyl)-L-glutamate, EC No 249-958-3 (CAS No 29923-31-7), 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 registration dossier in accordance with Articles 10(a)(ix) and 12(1)(d) thereof for sodium hydrogen N-(1-oxododecyl)-L-glutamate, EC No 249-958-3 (CAS No 29923-31-7), submitted by [redacted] (Registrant).

- Pre-natal developmental toxicity study (OECD 414) oral: gavage, rabbit, using the analogue substance L-Glutamic acid, N-coco acylderivs., disodium salts (CAS 68187-30-4).

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 15 January 2015, 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 from initiating a compliance check on the registration at a later stage.

ECHA received the registration dossier containing the above-mentioned testing proposal for examination pursuant to Article 40(1) on 25 June 2013.

ECHA held a third party consultation for the testing proposal from 16 May 2014 until 30 June 2014. ECHA did not receive information from third parties.

On 6 August 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. That draft decision was based on submission number [redacted].

On 25 August 2014, ECHA received comments from the Registrant on the draft decision. On 31 October 2014, the Registrant updated his registration dossier with the submission number [redacted].

The ECHA Secretariat considered the Registrant's comments and update. On basis of this information, Section II of the draft decision was amended. The statement of reasons

(Section III) was changed accordingly.

On 15 January 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 test pursuant to Article 40(3)(a) and 13(4) of the REACH Regulation using the indicated test method and the registered substance subject to the present decision:

1. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31/OECD 414) in rats or rabbits, oral route, using the analogue substance L-Glutamic acid, N-coco acylderivs., disodium salts (CAS 68187-30-4).

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 **28 March 2016** 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.

A. Tests required pursuant to Article 40(3)

1. 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 in rabbits according to EU B.31/OECD 414 with the following justification: "*An OECD 414 study is proposed on the read across substance L-Glutamic acid, N-coco acylderivs., disodium salts (CAS 68187-30 -4) in order to investigate the developmental toxicity in the rabbit. […] The read across is considered valid as the target substance is the major component, and the central member of an homologous series of components, of the source substances, possessing identical functional groups and extremely similar structures. It is reasonable to expect that the toxicological properties of the target and source substances will not be markedly different. On this basis, experimental data on the source substances are expected to be directly applicable to the target substance, and can be used to adequately predict its properties.*"

The Registrant's dossier update [redacted], submitted on 31 October 2014, includes a read-across justification document. With respect to the read-across hypothesis, the Registrant states that "*[i]n accordance with the ECHA guidance document, the read across of toxicological or ecotoxicological data from an analogue is justified on the basis of their similar chemical structures, structure activity, patterns of physico-chemical properties, toxicological and ecotoxicological profiles. The read across justification for the target and source substances is therefore based on:*

- *Common functional groups and constituents or chemicals*
- *Likelihood of common breakdown products via biological processes*
- *Common structural alerts or reactivity*
- *Similar physical-chemical, tox and ecotoxicological properties*".

ECHA now considers the Registrant's justification along these same lines:

(i) **Common functional groups and constituents or chemicals:** ECHA notes that the target substance [redacted] (containing [redacted]) is a major constituent of the source substance with a concentration up to [redacted] % (w/w). The composition of the source substance differs from the target substance in that it further contains up to [redacted] % (w/w) [redacted] (containing [redacted]), up to [redacted] % (w/w) [redacted] (containing [redacted]), up to [redacted] % (w/w) [redacted] (containing [redacted]), and up to [redacted] % (w/w) [redacted] (containing [redacted]).

(ii) **Likelihood of common breakdown products via biological processes:** With respect to metabolism, the Registrant explains that

- Substances will not hydrolyse in the presence of water;
- Action by amidases is the first step of metabolism if systemically available;
- Fatty acids are metabolised by via the β-oxidation and tricarboxylic acid cycle pathways;
- Glutamates are metabolised by oxidative deamination or by transamination with pyruvate to yield oxaloacetic acid which then enters the citric acid cycle via formation of alpha-ketoglutarate.

(iii) **Common structural alerts or reactivity:** The Registrant explains that "*given the commonality of the structural alerts and predicted chemical reactivity of the source and target acyl glutamates as per the OECD QSAR tool box (v.3.2) together with the available experimental data, it is unlikely that SLG will exert a different level of toxicity.*" However, the Registrant has not included supporting evidence for ECHA to assess the validity of the prediction for this information requirement.

(iv) **Similar physical-chemical, toxicological and ecotoxicological properties:** The Registrant concludes that target and source substances exert similar physical-chemical properties, similar environmental fate and pathways, similar ecotoxicity, and similar toxicological properties (similarities with respect to toxicokinetics; metabolism; low oral acute toxicity in rats; non-irritating to skin; irritating to eyes; no sensitisation; non-mutagenic; non-clastogenic). Furthermore, "*repeated oral administration of [the source substance] for 112 days in a study with male rats also did not indicate any significant toxicity at the only tested dose of 1,200 mg/kg bw/day (which is greater than the limit dose as per OECD Test guidelines).*"

With respect to impurities, the Registrant states that "*[t]he impurities present in both target and source substances [...] are the fatty chain present as acid or soap depending on pH, the amino acid glutamate and sodium chloride.*" Therefore, ECHA concludes that the impurities do not impair the proposed read-across.

Based on the information provided, ECHA considers that source and target substances are indeed chemically similar and undergo comparable metabolism and displaying similar toxicological profiles. However, ECHA notes that a certain degree of uncertainty remains with respect to the standard information requirement under consideration because the Registrant did not explicitly explain why prediction from the source to the target substance is possible for pre-natal developmental toxicity despite the differences in composition. However, considering the similarity in chemical composition (the target substance is a major constituent of source substance) and identical metabolic pathways, ECHA concludes that the proposed read-across is plausible for the proposed test.

The Registrant proposed testing in rabbits 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) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is requested to carry out the proposed study with the analogue substance L-Glutamic acid, N-coco acylderivs., disodium salts (CAS 68187-30-4): 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 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. 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.

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

Furthermore, 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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