ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-2114293030-61-01/F Helsinki, 16 June 2015

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

For Fatty acids, C16-18 and C18-unsatd., branched and linear, reaction products with diethylenetriamine and tall-oil fatty acids, Me maleates, CAS No 1393571-42-0 (EC No 806-509-1), 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 Fatty acids, C16-18 and C18-unsatd., branched and linear, reaction products with diethylenetriamine and tall-oil fatty acids, Me maleates, CAS No 1393571-42-0 (EC No 806-509-1), submitted by [redacted] (Registrant).

- 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 after 30 October 2014, 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.

The examination of the testing proposal was initiated upon the date when receipt of the complete registration dossier was confirmed on 10 February 2014.

ECHA held a third party consultation for the testing proposal from 5 June 2014 until 21 July 2014. ECHA received information from third parties (see section III below).

On 8 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.

On 15 September 2014 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 30 October 2014 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) 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.

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, 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 **23 June 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 and scientific information submitted by third parties.

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 according to EU B.31/OECD 414.

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 has proposed testing on the registered substance, and ECHA considers this appropriate.

The Registrant did not specify the species to be used for testing and 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.

In his comments to the draft decision, the Registrant proposes a Weight of Evidence approach. ECHA notes that the Registrant claims that the Weight of Evidence approach can be used to demonstrate that the substance does or does not have developmental toxicity properties based on "the outcome of the OECD 422 screening study, toxicokinetic considerations and the results of the risk assessment", which includes risk management measures.

According to Annex XI, 1.2, "*there may be sufficient weight of evidence from several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous property, while the information from each single source alone is regarded insufficient to support this notion*".

1. The Registrant makes reference to an OECD 422 study, as well as to other endpoints. The Registrant claims that the OECD 422 study is considered to be representative for reproductive and developmental toxicity. ECHA notes that the OECD 422 study, and other studies cited, do not provide the information required by Annex IX, Section 8.7.2., because they do not cover key parameters of a pre-natal developmental toxicity study like examinations of foetuses for skeletal and visceral alterations. This key information is not provided in the dossier and cannot be deduced from the available data. This information is an essential part of the key parameters for a pre-natal developmental toxicity study to assume or conclude that a substance has or has not a dangerous property related to developmental toxicity.

2. ECHA notes that an assessment of toxicokinetic properties of the substance has been provided in the CSR and in the comments. Based on this assessment, the Registrant concludes that 10 % absorption of the substance occurs via oral, dermal and inhalation routes. It follows that there is likely systemic absorption of the substance. In any event, a toxicokinetic assessment does not provide information about the intrinsic properties of the substance and therefore, this information does not provide the information required by Annex IX, Section 8.7.2.

3. ECHA notes Annex II of the Registrant's comments, where the Registrant provides an Overview Risk Assessment for workers, which is also provided in the CSR. The exposure estimates and RCRs (0.16-0.8) suggest significant human exposure. The Registrant also argues that risk management measures would sufficiently control reproductive toxicity risk. However, risk assessment does not provide information about the intrinsic properties of the substance and therefore, this information does not provide the information required by Annex IX, Section 8.7.2.

ECHA notes that the Registrant has provided three individual arguments to support his Weight of Evidence approach, each of which is insufficient to meet the information requirement. The Registrant has not provided an explanation for how the independent sources of evidence together may form a sufficient weight of evidence, and therefore there is a failure to provide adequate and reliable documentation for this adaptation. ECHA considers that there is not sufficient Weight of Evidence from several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous property, i.e. the information requirement of Annex IX, 8.7.2.

ECHA further notes that the adaptation also fails to meet the criteria of Annex IX, 8.7, Column 2: "*the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available), it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentrations below detection limit using a sensitive method and absence of the substance and metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure*".

ECHA cannot assess the toxicological activity of the substance, because detailed data has not been provided on the effects observed in the OECD 422 study. However, the toxicokinetic data does not prove that no systemic absorption occurs and the CSR indicate that there is significant human exposure (as discussed above).

Therefore, ECHA concludes that the information provided is not sufficient to adapt the information requirement for pre-natal developmental toxicity based on the Weight of Evidence approach according to Annex XI, 1.2 or based on Annex IX, 8.7, Column 2.

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.

A third party has proposed a weight of evidence approach: "The physicochemical properties of the chemical (insolubility in water, high lipophilicity, molecular weight of the fatty acid amides > 700) imply that the UVCB substance is not bioavailable after oral ingestion. This assessment is consistent with findings of low acute oral toxicity (NOAEL > 2000 mg/kg bw/d) and the absence of systemic or reproductive adverse effects in OECD 422 screening studies with the substance or a structurally related fatty acid amide even at the maximum oral dose of 1000 mg/kg bw/d. Under these circumstances the proposed test is not expected to add toxicologically meaningful information and therefore may be waived in a weight-of-evidence approach which may supported by registration data of the residual starting material methyl hydrogen maleate and 2,2'-iminodi(ethylamine) with low molecular weights".

ECHA acknowledges that the third party has proposed a testing strategy including a weight of evidence approach for the Registrant to consider.

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 weight of evidence as suggested by the third party. If the adaptation can be justified, he should include the adaptation argument with all necessary documentation in the registration dossier. 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 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.

ECHA observes that the third party has proposed a weight of evidence approach based on physicochemical properties implying lack of bioavailability, and studies conducted with structurally similar substances. ECHA considers that the Weight of Evidence adaptation, according to Annex XI, 1.2, does not have adequate and reliable documentation, as it does not set out the basis whereby the information from several independent sources together provide a sufficient weight of evidence leading to the assumption/conclusion that a substance has or has not a particular dangerous property, in this case for the parameters of the pre-natal developmental toxicity study. Moreover, relevant endpoint study records are not provided, and the read-across adaptations that are proposed do not have adequate and reliable documentation of the applied method, according to Annex XI, 1.5. Further ECHA considers that there is not sufficient weight of evidence from several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous property, in this case for the parameters of pre-natal developmental toxicity study. 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: 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 meets 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, 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.

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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