EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000002410-89-05/F Helsinki, 18 September 2013

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

For Alkenes, C13-14, hydroformylation products, distn. residues, CAS No 90622-29-0 (EC No 292-429-7), 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 proposals submitted as part of the jointly submitted registration dossier in accordance with Articles 10(a)(ix) and 12 (1)(e) thereof for Alkenes, C13-14, hydroformylation products, distn. residues, CAS No 90622-29-0 (EC No 292-429-7), by [redacted] (Registrant).

- 90-day oral toxicity study (OECD 408), including an additional histopathological assessment of reproductive organs, using the analogue substance Alkenes, C11-12, hydroformylation products, distn. residues;
- Developmental toxicity / teratogenicity study (OECD Guideline 414), using the analogue substance Alkenes, C11-12, hydroformylation products, distn. residues; and
- Annex X, 8.7.3. Two-generation reproduction toxicity study. Reproductive toxicity would be assessed by conducting a 90-day oral toxicity study (OECD 408), including an additional histopathological assessment of reproductive organs, using the analogue substance Alkenes, C11-12, hydroformylation products, distn. residues.

The present decision relates solely to the examination of the testing proposal for a 90-day toxicity study and a prenatal developmental toxicity study. The testing proposal for the two-generation reproductive toxicity study is addressed in a separate decision although all testing proposals were initially addressed together in the same draft decision.

This decision is based on the registration dossier as submitted with submission number [redacted], for the tonnage band of 1000 tonnes or more per year. This decision does not take into account any updates after 18 January 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.

On 2 December 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 15 September 2011 until 31 October 2011. ECHA did not receive information from third parties.

On 28 March 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 26 April 2012 ECHA received comments from the Registrant.

ECHA considered the Registrant's comments received and reflected its view in the statement of reasons (see section III, below). However, these comments did not affect the outcome of the draft decision (see section II, below).

On 18 January 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 submitted proposals for amendment to the draft decision.

On 21 February 2013 ECHA notified the Registrant of proposals for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on those proposals for amendment within 30 days of the receipt of the notification.

ECHA reviewed the proposals for amendment received and decided not to amend the draft decision.

On 4 March 2013 ECHA referred the draft decision to the Member State Committee.

On 25 March 2013 the Registrant provided comments on the proposed amendments. The Member State Committee took the comments of the Registrant into account.

The draft decision was split into two draft decision documents: one relating to the testing proposal for a two-generation reproduction toxicity study (Annex X, 8.7.3), and one relating to the testing proposals for a 90-day oral toxicity and the pre-natal developmental toxicity study.

A unanimous agreement of the Member State Committee on the draft decision relating to the testing proposal for a repeated dose 90-day oral toxicity study and the pre-natal developmental toxicity study was reached on 8 April 2013 in a written procedure launched on 27 March 2013. ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Testing required

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:

1. Sub-chronic toxicity study (90-day) in rats, oral route (Annex IX, 8.6.2; test method: EU B.26/OECD 408).
   It is at the Registrant's discretion to perform the intended additional examinations during the testing program
2. Pre-natal developmental toxicity study in rats or rabbits, oral route (Annex IX, 8.7.2; test method: EU B.31/OECD 414).

while the originally proposed tests to be carried out using the analogue substance Alkenes, C11-12, hydroformylation products, distn. residues 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 the column 2 provisions of the respective Annex and those contained in Annex XI of the REACH Regulation.

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **18 September 2015** 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.

Data from a second pre-natal developmental toxicity study on another species is a standard information requirement according to Annex X, 8.7.2. of the REACH Regulation, subject to the Annex IX, 8.7.2 column 2 requirements. If the Registrant considers that testing is necessary to fulfil this information requirement taking into account the outcome of the pre-natal developmental toxicity study on a first species and all other relevant and available data, he should include in the update of his dossier a testing proposal for a pre-natal developmental toxicity study on a second species.

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.

1. Sub-chronic toxicity (90-day)

a) Examination of the testing proposal

Pursuant to Article 40(3)(c) of the REACH Regulation, ECHA may require the Registrant to carry out one or more additional tests in case of non-compliance of the testing proposal with Annexes IX, X or XI of the REACH Regulation.

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 generate the data for this endpoint.

In the light of the physico-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.

According to the test method EU B.26/OECD 408 the rat is the preferred rodent species. ECHA considers this species as being appropriate.

In addition to the standard assay parameters of the guideline, the Registrant proposed to perform an additional histopathological assessment of reproductive organs.

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 the proposed extension of this study does not fulfil the standard information requirements in the registration dossier for reproductive toxicity set out in Annex X, 8.7.3 unless Annex X, 8.7 column 2 adaptation is applied.

ECHA further observes that in his testing proposal the Registrant has proposed to use Alkenes, C11-12, hydroformylation products, distn. residues, CAS No 90622-27-8 (EC No 292-427-6) as test material instead of the registered substance. If the Registrant proposes to carry out the tests required by Annex X with a substance other than the registered substance, Article 13(1) and Annex X, third introductory paragraph, require the Registrant to clearly state reasons for adapting the standard information according to the rules in Annex XI.

Annex XI, Section 1.5. governing the "Grouping of substances and read-across approach" provides that substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity may be considered as a group, or 'category' of substances. Application of the group approach requires that physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s) by interpolation to other substances in the group (read-across approach). It is further required by Annex XI, Section 1.5. that "-adequate and reliable documentation of the applied method shall be provided."

The following is stated by the Registrant: "Available information supports the prediction that [redacted] [the read-across substance] and [redacted] [the registered substance] can be considered analogue substances and provides evidence that these substances exhibit similar physicochemical, toxicological and ecotoxicological properties such that information presented within the dossier for [redacted] can be used as robust representation for specific [redacted] results."

On the basis of information submitted in the registration dossier, ECHA notes however that the Registrant fails to explain how the similarities in composition and the information in the dossier on the physicochemical properties allows for the prediction of the endpoint under consideration for the registered substance from the still to be performed test with the proposed test material. Specifically, ECHA did not find in the registration dossier submitted by the Registrant evidence that these substances exhibit similar toxicological properties and also other toxicological data for the registered substance are lacking. This means that a reasoned prediction of the endpoint under consideration for the registered substance cannot be supported by a comparison of test material and registered substance as regards their effects on other toxicological endpoints.

Within its comments to the draft decision, in accordance with Article 50(1) of the REACH Regulation, the Registrant provided further argumentation to support his read-across strategy that it was not present in the original read-across justification in the registration dossier. The Registrant argues that only the constituents with lower molecular weight (alcohols monomers C11-C16 and diols C13-C16) should be considered because of the low bioavailability of the constituents with higher molecular weight. Further, the Registrant mentions that "many of these groups of chemicals [lower molecular weight constituents] are already formally defined and accepted by regulators as categories for the purpose of REACH and other regulatory programs".

ECHA notes that, while the Registrant's arguments might be scientifically plausible, the Registrant has not provided, in the comments, any scientific data to support these claims. Further, neither this new argumentation nor data to support it is present in the read-across justification provided in the registration dossier.

Annex XI, Section 1.5 of the REACH Regulation requires the Registrant to provide "adequate and reliable documentation of the applied method" in the form of a scientifically credible explanation as to how the prediction can be made. ECHA considers that the Registrant has not provided all the necessary information to meet these conditions and support his arguments. Therefore, ECHA concludes that the read-across proposal cannot be accepted.

b) 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 Alkenes, C13-14, hydroformylation products, distn. residues, CAS No 90622-29-0 (EC No 292-429-7), while pursuant to Article 40(3)(d) of the REACH Regulation the originally proposed sub-chronic toxicity study (90-day) (OECD 408) using the read-across substance Alkenes, C11-12, hydroformylation products, distn. residues, CAS No 90622-27-8 (EC No 292-427-6) is rejected.

2. Pre-natal developmental toxicity

a) Examination of the testing proposal

Pursuant to Article 40(3)(c) of the REACH Regulation, ECHA may require the Registrant to carry out one or more additional tests in case of non-compliance of the testing proposal with Annexes IX, X or XI of the REACH Regulation.

Pre-natal developmental toxicity studies are part of the standard information requirements as laid down in Annexes IX and X, 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 generate the data for this endpoint.

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 the rabbit as a first species to be used.

ECHA further observes that in his testing proposal the Registrant has proposed to use Alkenes, C11-12, hydroformylation products, distn. residues, CAS No 90622-27-8 (EC No 292-427-6) as test material instead of the registered substance. ECHA notes however, as explained in detail in section III (1)(a) above, that the Registrant fails to explain how the similarities in composition and the information in the dossier on the physicochemical properties allows for the prediction of the endpoint under consideration for the registered substance from the still to be performed test with the proposed test material. Specifically, ECHA did not find in the registration dossier submitted by the Registrant evidence that these substances exhibit similar toxicological properties and also other toxicological data for the registered substance are lacking. This means that a reasoned prediction of the endpoint

under consideration for the registered substance cannot be supported by a comparison of test material and registered substance as regards their effects on other toxicological endpoints.

The "adequate and reliable documentation of the applied method" in the form of a scientifically credible explanation as to how the prediction can be made is lacking in the dossier ECHA therefore concludes that as adequate justification for the proposed read-across is not provided by the Registrant according to the requirements of Annex XI, Section 1.5 of the REACH Regulation, the read-across proposal cannot be accepted.

b) 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 Alkenes, C13-14, hydroformylation products, distn. residues, CAS No 90622-29-0 (EC No 292-429-7), while pursuant to Article 40(3)(d) of the REACH Regulation the originally proposed Pre-natal developmental toxicity study in rats, oral route (test method: EU B.31/OECD 414) using the read-across substance Alkenes, C11-12, hydroformylation products, distn. residues, CAS No 90622-27-8 (EC No 292-427-6) is rejected.

3. Deadline for submitting the information

In the draft decision communicated to the Registrant the time indicated to provide the requested information was 36 months from the date of adoption of the decision. This period of time took into account the fact that the draft decision also requested a reproductive toxicity study according to the standard information requirement of Annex X, 8.7.3 of the REACH Regulation. As the testing proposal for this study is not addressed in the present draft decision, ECHA considers that a reasonable time period for providing the required information in the form of an updated IUCLID5 dossier is 24 months from the date of the adoption of the decision. The decision was therefore modified accordingly.

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

ECHA always 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). National authorities monitoring GLP maintain lists of test facilities indicating the relevant areas of expertise of each facility.

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.

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://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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