EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000002689-60-05/F Helsinki, 7 June 2013

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

For triethoxy(2,4,4-trimethylpentyl)silane, CAS No 35435-21-3 (EC No 252-558-1), 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 proposals submitted as part of the registration dossier in accordance with Articles 10(a)(ix) and 12 (1)(e) thereof for triethoxy(2,4,4-trimethylpentyl)silane, CAS No 35435-21-3 (EC No 252-558-1), by [redacted] (Registrant):

- 90-day oral toxicity study (OECD 408) in rats, with additional examinations for reproductive endpoints, proposed to fulfil the information requirement for both a sub-chronic toxicity study (Annex IX, 8.6.2), and reproductive toxicity (Annex X, 8.7.3)

The present decision relates to the examination of the testing proposals for repeated dose 90-day oral toxicity study for the purposes of fulfilling the information requirement for a sub-chronic toxicity study (Annex IX, 8.6.2). The testing proposal for fulfilling the information requirement for a reproductive toxicity study (Annex X, 8.7.3) is addressed in a separate decision although all these 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 2 November 2012, 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.

On 29 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 29 April 2011 until 14 June 2011. ECHA did receive information from third parties (see section III below).

On 28 August 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.

By 27 September 2012 the Registrant did not provide any comments on the draft decision to ECHA.

On 2 November 2012 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 5 December 2012 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 17 December 2012 ECHA referred the draft decision to the Member State Committee.

On 3 January 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 to fulfil the information requirements for reproductive toxicity (Annex X, 8.7.3) and one relating to the testing proposal to fulfil the information requirements for a sub-chronic toxicity study (90-day) 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 was reached on 21 January 2013 in a written procedure launched on 11 January 2013. ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Testing required

The Registrant shall carry out the following proposed test 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. 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.

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **7 December 2014** 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 and scientific information submitted by third parties.

1. Sub-chronic toxicity study (90-day)

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 generate the data for this endpoint.

The Registrant proposed testing by the oral route. 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. Specifically, the physico-chemical properties of the substance support the use of the oral route of exposure, as the substance is a liquid with a low vapour pressure (0.22 Pa at 25 °C). While the identified uses do include some processes such as industrial and non-industrial spraying where exposure to aerosols may occur, the Chemical Safety Report does not indicate high exposure via the inhalation route.

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.

The Registrant proposed to extend the sub-chronic toxicity study (90 day) by including additional examinations for reproductive endpoints. 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.

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.

The third party submitted the following comments for consideration for the 90 day study:

1. Evaluate the need to conduct a sub-chronic toxicity study (OECD Guideline 408) in light of the results of the existing oral 28-Day Repeated Dose Toxicity Studies (OECD Guideline 407) and data on the analogues triethoxyoctylsilane, trimethoxy(methyl) silane, and 3-aminopropyltriethoxysilane

2. Exposure considerations: use the TTC for repeated dose and reproduction toxicityend points

ECHA concludes as follows:

Comment 1:

A third Party has proposed a weight-of evidence approach for ECHA to take into account before further tests on vertebrate animals are required. As part of this approach, the third party provided results from a sub-chronic inhalation toxicity study (OECD Guideline 413) by using the read-across substance trimethoxy(methyl)silane, and an oral sub-chronic toxicity study (OECD Guideline 408) using the read-across substance 3-aminopropyltriethoxysilane.

ECHA has taken the information provided into account and concludes that it is insufficient for demonstrating that the conditions of Annex XI, Section 1.2 and 1.5 of the REACH Regulation are met. More specifically, the proposed weight-of-evidence approach is not sufficient to assume that the substance has or has not a particular dangerous property after sub-chronic administration of the substance and that the standard information requirement for a sub-chronic toxicity study could be adapted. Furthermore, the proposed read-across approach as an element of the weight of evidence justification did not demonstrate the human health effects of the registered substance may be predicted from data on the reference substance.

Although ECHA recognises that the information as provided by the third party might be scientifically valid, it does not fulfil Annex XI requirements and is therefore not sufficient to allow ECHA to reject the testing proposal. Nevertheless, ECHA acknowledges that the Registrant may himself supplement under its own responsibility the argumentation and information provided by the third party in order to make use of adaptation possibilities. This would require that the Registrant documents, using several independent sources of information, that there is a sufficient weight of evidence leading to the assumption/conclusion that a substance has or has not particular dangerous properties, according to the criteria laid down in Annex XI of the REACH Regulation.

Comment 2: Exposure considerations:

The third party states that since testing can be exempted based on the negligible exposure, exposure should be thoroughly analysed before conducting the test. In addition, they suggest that the Threshold of Toxicological Concern (TTC) concept should be adopted and cut-off values (human exposure values below which there is no significant risk to human health) of :

- for oral repeated dose toxicity 1.5/9/30 µg/kg bw/day for chemicals with higher/medium/lower toxic potential exposure should be used.
- For developmental toxicity 1.0 µg/kg bw/day for oral and 0.5 µg/kg bw/day for inhalation
- For fertility: 1,5 µg/kg bw/day for oral and 1.0 µg/kg bw/day for inhalation exposure

According to Annex XI, Section 3 of the REACH Regulation, the testing can be omitted if it can be demonstrated that there is no or no significant exposure. The Registrant did not use substance-tailored exposure-driven testing according to Annex XI, Section 3 but indicated that opportunity for exposure arises in batch and other processes. Therefore, ECHA concludes that the testing cannot be omitted based on negligible exposure.

c) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study: Sub-chronic toxicity study (90-day) in rats, oral route (test method: EU B.26/OECD 408) using the registered substance.

d) Deadline for submitting the information

In the draft decision communicated to the Registrant the time indicated to provide the requested information was 30 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 18 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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