EUROPEAN CHEMICALS AGENCY

Helsinki, 19 July 2018

Addressee: [redacted]

Decision number: TPE-D-2114425320-66-01/F
Substance name: triethoxypropylsilane
EC number: 219-842-7
CAS number: 2550-02-9
Registration number: [redacted]
Submission number: [redacted]
Submission date: 04.04.2013
Registered tonnage band: 100-1000T

DECISION ON A TESTING PROPOSAL

Based on Article 40 of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), ECHA has taken the following decision.

Your testing proposal is accepted and you are requested to carry out:

1. **Sub-chronic toxicity study (90-day), inhalation route (Annex IX, Section 8.6.2.; test method: OECD TG 413) in rats using the registered substance.**

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

2. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a first species (rats or rabbits), oral route using the registered substance.**

You 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 and conforming to the appropriate rules in the respective Annex, and an adequate and reliable documentation.

You are required to submit the requested information in an updated registration dossier by **27 July 2020**. You shall also update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2. Advice and further observations are provided in Appendix 3.

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, shall be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under http://echa.europa.eu/regulations/appeals.

Authorised[1] by Ofelia Bercaru, Head of Unit, Evaluation E3

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix 1: Reasons

The decision of ECHA is based on the examination of the testing proposal(s) submitted by you and scientific information submitted by third parties.

1. 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.

You have submitted a testing proposal for a sub-chronic toxicity study (90 day) in rats by the inhalation route according to OECD TG 413.

In your technical dossier under the repeated dose toxicity endpoint inhalation, you have submitted a 90 day sub-chronic repeated dose inhalation study (OECD TG 413, [redacted], 1992) on the analogue substance triethoxyisobutylsilane (CAS 17980-47-1, EC 402-810-3). In the study summary Rationale for reliability incl. deficiencies you note: "*The study was well documented and meets generally accepted scientific principles, and was conducted in compliance with GLP and is therefore considered to be reliability 1. Read-across of the study itself is considered to be reliability 2. Further information on read-across is given in the endpoint summary.*"

You have indicated that you use the sub-chronic inhalation toxicity study with triethoxyisobutylsilane as an interim measure in risk assessment.

ECHA considers that there is no adequate information present in the technical dossier on the sub-chronic repeated dose toxicity of the registered substance. Consequently there is an information gap and it is necessary to provide information for this endpoint.

ECHA has evaluated the most appropriate route of administration for the study. The information provided in the technical dossier and the chemical safety report on properties of the registered substance (liquid of low vapour pressure), its uses (spray application) and the reported exposure concentrations (up to [redacted] mg/m^3) indicate that human exposure to the registered substance by the inhalation route is likely. Furthermore, there is potential concern for local respiratory tract effects following inhalation exposure because the substance is classified for skin irritation. This concern is not addressed in the registration. Therefore, ECHA considers that the inhalation route is the most appropriate route of administration. Hence, the test shall be performed by the inhalation route using the test method OECD TG 413.

According to the test method OECD TG 413 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

You proposed to extend the sub-chronic toxicity study (90 day) by including additional examinations/parameters: "*These could include but are not limited to "Examination of*

reproductive organs, sperm parameters, and oestrus cycle".. ECHA notes, that it is at your'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, you are reminded that the proposed extension of this study does not fulfil the standard information requirement in the registration dossier for reproductive toxicity set out in Annex X, Section 8.7.3.

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 commented as summarised below:

Third party information 1 (summary): "The provision in Regulation (EC) 1907/2006 applies that testing in vertebrate animals should be carried out as a last resort. At the tonnage level between 10 and 100 t/a (Annex VIII), which is quoted in the disseminated dossier, a 90-day repeated dose toxicity study is only required if available data indicate that the substance may have a dangerous property that cannot be detected in a short-term toxicity study. Such a property cannot be derived from presented data of the substance and the read-across chemical triethoxyisobutylsilane.
Regarding similar physicochemical properties, acute toxicity and local effects of the readacross chemical the registrant may re-consider the suitability of the existing data as key study for the registration of triethoxypropylsilane."

ECHA notes that the total tonnage band published in the related disseminated dossier does not reflect the registered tonnage band(s) and associated information requirement obligations. For the total tonnage band of the disseminated dossier, compiled data is calculated from the non-confidential quantities of a substance manufactured and/or imported by all registrants, excluding any quantity directly used as an intermediate to produce a different chemical.

ECHA acknowledges that the third party has proposed a read-across approach for you to consider.

ECHA notes that it is your responsibility to consider and justify any adaptation of the information requirements in accordance with the relevant conditions as established in Annex XI, Section 1.5. Therefore, you may assess whether you can justify a read-across as suggested by the third party. If the information requirement can be met by way of adaptation, you may include the adaptation argument with all necessary documentation according to Annex XI, Section 1.5. in an updated registration.

ECHA notes that the information provided by the third party is currently insufficient for demonstrating that the conditions of Annex XI, Section 1.5. of the REACH Regulation are met. For example, the third party has not justified why the differences in the structure would lead to an similar toxicity between the source and the target.

Moreover, the third party compares between selected physico-chemical parameters, acute toxicity and skin and eye irritation but there are no repeated dose toxicity studies compared. Already looking at the skin irritation it can be seen that the substances are different in respect to this property. Therefore, the information provided by the third party in itself would not be sufficient to adapt the standard information requirement.

In your comments to the draft decision you agree to perform the requested study.

c) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study with the registered substance subject to the present decision: Sub-chronic toxicity study (90-day) in rats, inhalation route (test method: OECD TG 413).

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species

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.

You have submitted a testing proposal for a pre-natal developmental toxicity study in rats according to EU B.31/OECD TG 414 by the oral route.

In technical your dossier under the developmental toxicity endpoint you have submitted a prenatal developmental toxicity study (OECD TG 414, [redacted] 1991) on the analogue substance triethoxyisobutylsilane (CAS 17980-47-1, EC 402-810-3). In the study summary Rationale for reliability incl. deficiencies you note: "*The study was conducted according to an appropriate OECD test guideline, and in compliance with GLP and is therefore considered to be reliability 1. Read-across of the study itself is considered to be reliability 2. Further information on read-across is given in the endpoint summary.*"

You have indicated that you use the prenatal developmental toxicity study with triethoxyisobutylsilane as an interim measure in risk assessment.

ECHA considers that there is no adequate information present in the technical dossier on the prenatal developmental toxicity of the registered substance. Consequently there is an information gap and it is necessary to provide information for this endpoint.

ECHA considers that the proposed study performed with the registered substance is appropriate to fulfil the information requirement of Annex IX, Section 8.7.2. of the REACH Regulation.

You proposed testing with rats. According to the test method EU B.31/OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the

basis of this default consideration, ECHA considers testing should be performed with rats or rabbits as a first species.

You proposed testing by the oral route.

ECHA agrees that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

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.

Third party information 1 (summary): At the tonnage level between 10 and 100 t/a (Annex VIII), which is quoted in the disseminated dossier, a prenatal developmental toxicity study is only required if evidence for an increased risk to the unborn child is provided. Hence, no teratogenic or embryo-/fetotoxic effects were noted in a reported study with the read-across chemical triethoxyisobutylsilane.

Regarding similar physicochemical properties, acute toxicity and local effects of the readacross chemical the registrant may re-consider the suitability of the existing data as key study for the registration of triethoxypropylsilane (in place of a screening test).

ECHA notes that the total tonnage band published in the related disseminated dossier does not reflect the registered tonnage band(s) and associated information requirement obligations. For the total tonnage band of the disseminated dossier, compiled data is calculated from the non-confidential quantities of a substance manufactured and/or imported by all registrants, excluding any quantity directly used as an intermediate to produce a different chemical.

ECHA acknowledges that the third party has proposed a read across approach for you to consider.

ECHA notes that it is your responsibility to consider and justify any adaptation of the information requirements in accordance with the relevant conditions as established in Annex XI, Section 1.5. Therefore, you may assess whether you can justify a read across as suggested by the third party. If the information requirement can be met by way of adaptation, you may include the adaptation argument with all necessary documentation according to Annex XI, Section 1.5. in an updated registration.

ECHA notes that the information provided by the third party is currently insufficient for demonstrating that the conditions of Annex XI, Section 1.5. of the REACH Regulation are met. For example, the third party has not justified why the differences in the structure would lead to an similar toxicity between the source and the target.

Moreover, the third party compares between selected physico-chemical parameters, acute toxicity and skin and eye irritation but there are no repeated dose, reproductive toxicity or developmental toxicity studies compared. Already looking at the skin irritation it can be seen that the substance are different in respect to this property. Therefore, the information provided by the third party in itself would not be sufficient to adapt the standard information requirement.

In your comments to the draft decision you agree to perform the requested study.

c) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study with the registered substance subject to the present decision: Pre-natal developmental toxicity study in a first species (rats or rabbits), oral route (test method: EU B.31/OECD TG 414).

Notes for your consideration

For the selection of the appropriate species you are advised to consult ECHA *Guidance on information requirements and chemical safety assessment* R.7a, chapter R.7.6.2.3.2 (July 2017).

ECHA notes that a revised version of OECD TG 414 was adopted this year by the OECD. This revised version contains enhancements of certain endocrine disrupting relevant parameters. You should test in accordance with the revised version of the guideline as published on the OECD website for adopted test guidelines (https://www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-4-health-effects_20745788).

Appendix 2: Procedural history

ECHA received your registration containing the testing proposals for examination pursuant to Article 40(1) on 4 April 2013.

ECHA held a third party consultation for the testing proposals from 3 March 2014 unti 17 April 2014 l. ECHA received information from third parties (see Appendix 1).

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation:

ECHA notified you of the draft decision and invited you to provide comments. ECHA took into account your comments and did not amend the request(s).

You were notified that the draft decision does not take into account any updates after 06 July 2016. However, following your request and justification provided (including interlinked read-across testing strategy on several supposedly related registered substances) ECHA has exceptionally granted you additional time until 30 June 2017 for the update for the update of the IUCLID dossier.

You did not update the dossier by the given deadline.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA took the decision according to Article 51(3) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. This decision does not imply that the information provided in your 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.

2. 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.

3. In relation to the information required by the present decision, the sample of the substance used for the new test(s) must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants. It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new test(s) 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 or imported by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new test(s) must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the test(s) to be assessed.