EUROPEAN CHEMICALS AGENCY

Helsinki, 19 July 2018

Addressee: [redacted]

Decision number: TPE-D-2114425277-49-01/F
Substance name: trichloro(propyl)silane
EC number: 205-489-6
CAS number: 141-57-1
Registration number: [redacted]
Submission number: [redacted]
Submission date: 24.02.2017
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 examined your testing proposal(s) and decided as follows.

While your proposed test for a 28-day repeated dose toxicity study in rats, via oral route, using the registered substance

is rejected, you are requested to perform:

1. **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 **26 July 2019**. 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 submitted by you for the registered substance trichloro(propyl)silane (CAS No 141-57-1, EC No 205-489-6), taking into account the updated dossier.

In relation to the testing proposal subject to the present decision, ECHA notes that the initial draft decision was based on the dossier with the submission number [redacted]. Therein you proposed a testing strategy of conducting a pre-natal developmental toxicity study on the analogue substance triethoxy(propyl)silane (CAS No 2550-02-9, EC No 219-842-7) in order to fulfil the standard information requirement for a pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) of the registered substance. ECHA has considered the scientific validity of the proposed read-across and grouping approach, assessed the testing proposed and concluded that you did not provide adequate and reliable information to demonstrate that the proposed read-across approach is plausible for the endpoint in consideration. Consequently the testing proposed on the read-across substance(s) was rejected and ECHA requested you to perform the pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a first species (rat or rabbit), oral route with the registered substance.

The major reasons for rejecting read-across approach as proposed in the dossier with the submission number [redacted] have been thoroughly addressed in the initial draft decision and are briefly summarised below. Based on the provided data, the read-across hypothesis and justification, ECHA concluded that you did not sufficiently demonstrate,

- that structural similarity as well as physical-chemical and basic toxicological parameters are in the same range;
- that the hydrolysis of the target and source substances is both rapid and complete, leading to the formation of the proposed silanol hydrolysis product (propylsilanetriol) which is the same for both source and target substances; and
- that the formed silanol substance is exclusively relevant in terms of bioavailability and hence would drive the systemic toxicity.

In your comments to the draft decision you did not provide considerations to the specific endpoint, subject to the current decision.

After receiving the draft decision you updated your registration with the submission number [redacted] and changed the testing strategy *i.e.* you plan to conduct a 28-days repeated dose toxicity study with the registered substance. ECHA notes that although you have unticked the IUCLID tick box 'experimental study planned' you still have an intention to generate data on the registered substance in order to fulfil the standard information requirement for a pre-natal developmental toxicity study. Therefore the decision-making process of the testing proposal continues and ECHA has assessed your changed strategy.

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

Pursuant to Article 40(3)(d) and (c) of the REACH Regulation, ECHA may reject a proposed test and require the Registrant to carry out other tests in cases of non-compliance of the testing proposal with Annexes IX, X or XI.

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.

In your updated dossier you have submitted the following information in Section 7.8.2 "Developmental toxicity / teratogenicity": *"A 28-day DRF study (oral; rats) will be conducted to demonstrate that in order to avoid corrosive effects in laboratory animals, trichloro(propyl)silane can only be administered at low doses at which no systemic toxicity would be expected."*

In the justification document of the proposed testing strategy attached to this endpoint in the technical dossier you explain that *"The study on dichloro(3-chloropropyl)methylsilane ([redacted] 1997) shows that a practical and humane dose range for subsequent longer term studies is likely to be below the limit of technical practicality and toxicological significance. [...] Overall, based on the available studies, it is evident that local corrosive effects of chlorosilanes in the gastrointestinal tract do occur and supports the conclusion that testing of chlorosilanes in developmental toxicity studies via the oral route is unethical and scientifically unjustified."*

In the following ECHA examines the scientific validity of your proposed testing strategy.

Firstly, ECHA notes that the experimental data on dichloro(3-chloropropyl)methylsilane (CAS 7787-93-1) ([redacted] 1997) and triacetoxy(ethyl)silane (CAS 17689-77-9) ([redacted] 2004) referred to in your dossier to support your claim that *"local corrosive effects of chlorosilanes in the gastrointestinal tract do occur"* and that *"testing of chlorosilanes in repeated dose toxicity studies via the oral route is unethical and scientifically unjustified"* was generated by testing substances unchanged, without vehicles. ECHA is of the opinion that these testing conditions may have contributed to the development of local lesions in the gastro-intestinal tract in these studies.

Additionally you have provided the acute dose toxicity study via oral route on the registered substance ([redacted] 2002), however you acknowledge the absence of macroscopic examinations and clinical observations which you consider as essential. Consequently you conclude that based on this study *"it is not possible to conclude with confidence that there were no signs of corrosion in the gastrointestinal tract"*. ECHA considers that based on the available data/information provided it cannot be concluded whether or not the registered substance causes local toxicity in the gastrointestinal tract after acute and/or repeated oral administration.

Secondly, ECHA notes that corrosivity is not an adaptation option for reproductive toxicity studies. ECHA considers that even for corrosive substances there are provisions that require testing and allow conditions that are adequate to achieve results. In accordance with the ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) when testing corrosive or highly irritating substances in reproductive toxicity studies *"The vehicle should be chosen to minimise gastrointestinal irritation."*
In addition the guidance document also explains that *"For some substances dietary administration may allow adequate dosing without irritation compared with oral gavage dosing. In certain cases, testing of neutral salts of alkaline or acidic substances may be appropriate and allows investigation of intrinsic properties at adequate dose levels"*

ECHA notes that your dossier does not contain records of a testing approach which would allow to investigate the hazardous properties of this substance at adequate dose levels. Hence, ECHA concludes that you have not demonstrated that the registered substance could

not be successfully tested with the application of an appropriate testing approach as described above.

With respect to the proposed 28 days repeated dose toxicity study to be performed with the registered substance ECHA notes that it is not adequate to fulfil the information requirement of Annex IX, Section 8.7.2. of the REACH Regulation. A 28 days dose range finding study does not provide the information required by Annex IX, Section 8.7.2. because it does not cover key parameters of a pre-natal developmental toxicity study such as examinations of foetuses for skeletal and visceral alterations.

In summary, ECHA concludes that your new arguments do not provide any valid information to fulfil or waive the information requirement of Annex IX, Section 8.7.2. of the REACH Regulation. ECHA considers that a pre-natal developmental study performed with the registered substance is necessary and appropriate to fulfil the information requirement of Annex IX, Section 8.7.2. of the REACH Regulation. ECHA considers 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 4.1, October 2015) 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.

Outcome

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, you are requested to carry out the additional 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) while your originally proposed test for a 28 days repeated dose toxicity study in rats, via oral route, using the registered substance is rejected according to Article 40(3)(d) of the REACH Regulation.

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* (version 4.1, October 2015), Chapter R.7a, section R.7.6.2.3.2.

ECHA notes that due to the chemical nature of the substance, exposure to HCl cannot be excluded. The technical recommendations for testing corrosive or highly irritating substances presented in ECHA's *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) should be taken into account when deciding on the study design of the requested pre-natal developmental toxicity study. A dose range finding study may assist you to identify the maximum tolerated dose of the registered substance which may be used in the requested pre-natal developmental toxicity study.

ECHA notes also 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 proposal(s) for examination pursuant to Article 40(1) on 7 March 2013.

ECHA held a third party consultation for the testing proposal(s) from 4 April 2014 until 19 May 2014. ECHA did not receive information from third parties.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

ECHA notified you of the draft decision and invited you to provide comments. In your comments to the draft decision you did not provide specific considerations to the endpoint subject to the current decision.

You were notified that the draft decision does not take into account any updates after 6 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.

You updated your registration on 24 February 2017. ECHA took the information in the updated registration into account, and did not amend the draft decision.

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.

4. 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.