EUROPEAN CHEMICALS AGENCY

Helsinki, 19 July 2018

Addressee: [redacted]

Decision number: TPE-D-2114428712-52-01/F
Substance name: N-[3-(dimethoxymethylsilyl)propyl]ethylenediamine
EC number: 221-336-6
CAS number: 3069-29-2
Registration number: [redacted]
Submission number: [redacted]
Submission date: 30.06.2017
Registered tonnage band: 10-100T

DECISION ON A TESTING PROPOSAL

Based on Article 40 of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), ECHA examined your testing proposal(s) and decided as follows.

While your originally proposed tests for

1. Sub-chronic toxicity study (90-day), oral route (EU B.26./OECD TG 408) in rats using the analogue substance N-[3-(dimethoxymethylsilyl)-2-methylpropyl]ethylenediamine (CAS No 23410-40-4, EC no 245-642-4), and

2. Pre-natal developmental toxicity study (EU B.31./OECD TG 414) in rats, using the analogue substance N-[3-(dimethoxymethylsilyl)-2-methylpropyl]ethylenediamine (CAS No 23410-40-4, EC no 245-642-4)

are rejected, you are requested to perform:

1. **Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26./OECD TG 408) in rats using the registered substance,**

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 proposals submitted by you for the registered substance N-[3-(dimethoxymethylsilyl)propyl]ethylenediamine (CAS no 3069-29-2 , EC no 221-336-6) (hereafter referred to as "target substance"), taking into account the updated dossier.

In relation to the testing proposals subject to the present decision, ECHA notes the following.

The initial draft decision was based on the dossier with the submission number [redacted]. Therein you proposed a testing strategy intending to fulfil the standard information requirements for a

- Sub-chronic toxicity (90-day) (Annex IX, Section 8.6.2.), and a
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.).

In your testing strategy you proposed to test the analogue substance N-[3-(trimethoxysilyl) propyl]ethylenediamine (CAS No 1760-24-3, EC no 217-164-6).

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 endpoints into consideration. Consequently, the testing proposed on the analogue substance was rejected and ECHA requested you to perform a sub-chronic toxicity study (90-day), oral route (Annex IX, 8.6.2; test method: EU B.26/OECD TG 408) and a pre-natal developmental toxicity study, oral route (Annex IX, 8.7.2; test method: EU B.31/OECD TG 414) with the registered substance.

The major reasons for rejecting read-across approach as proposed in the dossier with the submission number [redacted] have been 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 demonstrated:

- how structural differences of the substances may impact their toxicity profiles,
- that the hydrolysis of the target and source substances is both rapid and complete, leading to the formation of the proposed silanol hydrolysis products (N-[3-(dihydroxymethylsilyl)-propyl]ethylenediamine, N-[3-(trihydroxysilyl)propyl]ethylenediamine and methanol), containing the same functional group;
- reduced reactivity of the parent (target) substance due to a methyl group.

Furthermore, due to the lack of data on the target substance you did not provide a necessary comparison of the toxicological profiles of both substances.

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

After receiving the draft decision, you updated your registration dossier with the submission number [redacted] and changed the testing strategy to to address the sub-chronic toxicity (90 day) and pre-natal developmental toxicity for the registered substance.

In your new strategy you propose to generate data on a different analogue substance N-[3-(dimethoxymethylsilyl)-2-methylpropyl]ethylenediamine (CAS No 23410-40-4, EC no 245-642-4), hereafter referred as "source substance".

The results from the structural analogue would then be used to adapt the standard information requirements by using read-across and grouping approach following Annex XI, Section 1.5. of the REACH Regulation. To the extent that all human health related proposed testing relies upon an identical read-across justification, ECHA has considered first the scientific validity of the proposed read-across and grouping approach (preliminary considerations; Section 0, below), before assessing the testing proposed (Sections 1 and 2 below).

0. Grouping of substances and read-across approach

a. Legal Background on ECHA's assessment of the grouping of substances and read-across hypothesis

The evaluation by ECHA of testing proposals submitted by registrants aims at ensuring that generation of information is tailored to real information needs. To this end, it is necessary to consider whether programmes of testing proposed by you are appropriate to fulfil the relevant information requirements and to guarantee the identification of health and environmental hazards of substances. In that respect, the REACH Regulation aims at promoting wherever possible the use of alternative means, where equivalent results to the prescribed test are provided on health and environmental hazards.

Article 13(1) of the REACH Regulation provides that information on intrinsic properties of substances may be generated whenever possible by means other than vertebrate animal tests, including information from structurally related substances (grouping of substances and read-across), "*provided that the conditions set out in Annex XI are met*".

The first Recital and the first Article of the REACH Regulation establish the "*promotion of alternative methods for assessment of hazards of substances*" as an objective pursued by the Regulation. In accordance with that objective, ECHA considers whether a prediction of the relevant properties of the substance subject to the present decision by using the results of the proposed tests is plausible based on the information currently available.

b. Description of the proposed grouping and read-across approach

In your justification document, attached to sections 7.5.1, 7.8.2 and 13.2 of the updated IUCLID dossier and in the updated chemical safety report (section 5.6.3), you present your new read-across hypothesis and justification:

"*The hypothesis is that the toxicology of the target and source substances is similar due to the structural similarity, particularly the presence of the diamine group. The observed effects, or lack of, are expected to be of the same type for all substances. Effect levels (potency) should be the same or relatable to the differences in toxicokinetic profiles caused by differences in physicochemical properties. In the latter case, it is likely that a 'worst-case' approach for selecting substances for read-across would be taken*".

In your read-across justification document, you conclude that:

"There is currently insufficient information to conclude on whether read-across is appropriate and the justification document will need to be updated after the proposed testing is completed. If the results of the proposed testing do not support read-across, testing for all required endpoints will be conducted."

c. Information submitted to support the grouping and read-across approach

You have provided the following read-across documents regarding toxicological endpoints in your updated IUCLID dossier, Section 13,

Read-across justification document [redacted].The document includes the read-across hypothesis and justification, the identification of the source and target substances; comparison of toxicological properties and the available toxicological data on the target and source substances.

1. [redacted]. The document "*outlines the approach*" to mammalian toxicity of aminofunctional alkoxysilanes and silanols. It is explained that individual substances have been grouped for the "*purposes of strategy and read-across approaches*". A summary of mammalian toxicity and data matrix is provided. It is stated that "*where there are data gaps, read-across will be performed from the closest available structurally related substance*". The document does not provide information on the (read-across) approach used for individual substances, but states that "*Details of test proposals and justification of read-across are given in individual Chemical Safety Reports*". A general statement regarding the rapid hydrolysis of the alkoxysilanes is provided. In addition, results of repeated dose, reproductive and developmental toxicity studies conducted with the aminofunctional alkoxysilanes and silanols is provided. ECHA notes that since no data on hydrolysis and no detailed read-across justification of these substances have been provided, ECHA cannot judge the relevance of this data.

Furthermore, you have provided the following studies relevant for the endpoints for testing proposed:

for the target substance:

- An acute oral toxicity study (OECD 423, [redacted] (1999a);
- An acute inhalation toxicity study (OECD 403, [redacted] 1992);
- An acute dermal toxicity study (OECD 402, [redacted] 1982);

for the newly proposed source substance:

- an acute oral toxicity study (OECD 401, [redacted] 1981);
- An acute inhalation toxicity study (OECD 403, [redacted] 1986);
- An acute dermal toxicity study (OECD 402, [redacted] 1981);

You have also provided data on skin and eye irritation, skin sensitisation and mutagenicity for the target and source substances.

d. ECHA analysis of the grouping approach and read-across hypothesis in light of the requirements of Annex XI, 1.5.

ECHA notes that the registrants of aminofunctional alkoxysilanes and silanols have grouped the substances in 'Analogue group', including the substance subject to the current decision, but the category approach is not proposed. Based on the substance specific justification for read-across approach and supporting information provided by you, ECHA understands that no category hypothesis /justification has been included and the proposed prediction is based on the analogue approach using N-[3-(dimethoxymethylsilyl)-2-methylpropyl]ethylenediamine (CAS No 23410-40-4, EC no 245-642-4) as a source substance.

According to ECHA's understanding the proposed read-across hypothesis is based on:

- structural similarity, in particular a common diamine group,
- similar physico-chemical properties, and
- rapid hydrolysis to similar hydrolysis products..

(i) Structural (dis)similarities and their impact on prediction

Structural similarity is a prerequisite for applying the grouping and read-across approach, but ECHA does not accept in general or this specific case that structural similarity *per se* is sufficient to enable the prediction of human health properties of a substance, since structural similarity does not always lead to predictable or similar human health properties. It has to be justified why such prediction is possible in view of the identified structural differences and the provided evidence has to support such explanation. In particular, the structural similarities must be linked to a scientific explanation of how and why a prediction is possible.

In the updated dossier, you have identified the structural similarities between target and source substance as both substances are members of an analogue group of amino substances and dimethoxy(methyl)silanes with a propylethylenediamine containing side-chain. You further explain that the source substance has a methyl group in the propyl chain whereas the target substance has not.
ECHA notes that although you have identified the structural similarities and differences between the target and source substances and their respective hydrolysis products, you have not provided sufficient information on how these structural differences may impact the toxicity of the substances and thus affect the possibility to predict the properties of the registered substance from the data of the source substance. The provided explanation is therefore not sufficient to establish a scientifically credible link between the structural similarity and the prediction.

(ii) Similar properties or regular pattern as a result of structural similarity

Annex XI, Section 1.5. provides that *"substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances"*. One prerequisite for a prediction based on read-across therefore is that the substances involved are structurally similar and are likely to have similar properties. One important aspect in this regard is the analysis of the data matrix to compare the properties of source and target substances and to establish whether indeed they are similar or follow a regular pattern.

Physico-chemical properties and toxicokinetic behaviour

In your updated read-across justification you state that physico-chemical parameters/properties of target and source substances are similar. ECHA observes that the physico-chemical properties of target and source substances are in the same/similar range.

ECHA notes that in the technical dossier you have provided toxicokinetic assessment which is based on the physico-chemical properties of the substances itself and/or its hydrolysis products. ECHA notes that based on the information provided, parent substances are also expected to absorb. However, you have not explained how this may impact the toxicity profiles of the target and source substances.

ECHA observes that your toxicokinetic assessment relies also upon the assumed rapid and complete hydrolysis of the target and source substances to the proposed similar silanol hydrolysis products, N-[3-(dihydroxymethylsilyl)propyl]ethylenediamine and N-[3-(dihydroxymethylsilyl)-2-methylpropyl]ethylenediamine, respectively. However, as pointed out in section "Hydrolysis" below, there is insufficient evidence supporting your assumption regarding the rate and formation of the proposed silanol hydrolysis products.

In addition, ECHA notes that there is no information on whether other metabolic pathways of the parent substances and/or its hydrolysis products would occur and thus play a role in the systemic toxicity of the substances.

ECHA therefore considers that it is not possible to verify whether the target and source substances and their hydrolysis products are likely to have similar toxicity profiles as a result of similar toxicokinetic profiles. In the absence of such information there is not an adequate basis for predicting the properties of the target substance from the data obtained with the source substance.

Hydrolysis

ECHA understands that the hypothesis relies also on the assumption that both target and source substances undergo rapid and complete hydrolysis. In the updated dossier you explain that they form structurally similar silanol hydrolysis products and methanol and that the hydrolysis rate for all substances is < 6 min at pH 4. You also make an assumption that at pH 2 and 37°C (gastric conditions, relevant for oral route of administration), hydrolysis rates are expected to be faster. You further explain that hydrolysis is two-step process (target and source substance) and that exposure to parent substances and intermediate hydrolysis products may occur. In the read-across justification you provide information on potential intermediate/final hydrolysis products. You further recognise that high concentrations and dosing in corn oil or similar vehicle may have impact on hydrolysis rate in the conditions, relevant to oral testing and refer to further testing plan for hydrolysis.

Firstly, ECHA observes that hydrolysis half-life rate at pH2 is based on assumptions which are not substantiated by data. ECHA notes that there is no hydrolysis data available in the registration dossier for pH 2 but that you have postulated that the rate of the hydrolysis reaction is dependent on hydronium ion concentration and that there will be a 100 fold increase in hydrolysis rate on going from pH 4 to pH 2. ECHA accepts that the hydrolysis is catalysed by the hydronium ion, however there is no evidence provided to suggest such a dependence on the hydronium ion concentration and consequently ECHA considers the

assumption of a 100 fold increase in hydrolysis rate on going from pH 4 to pH 2 as not supported by scientific evidence.

Secondly, ECHA considers that the formation of the proposed silanol hydrolysis products is not supported by data. ECHA notes that the formation of these silanol hydrolysis products from the target and source substances would involve several hydrolysis steps. In the hydrolysis data provided in the registration dossier there is no evidence of the formation of the proposed silanol hydrolysis products and therefore it is not possible to verify that ultimate hydrolysis of both target and source substances has indeed occurred within the timeframe of the test.

ECHA acknowledges your intention to conduct further tests to clarify the hydrolysis of alkoxysilanes, as discussed further below

ECHA considers that you have currently not substantiated your assumption of a complete hydrolysis and formation of hydrolysis products. In fact, the hydrolysis process which involves several steps may produce also other substances, which possible presence and effects on your hypothesis you have not addressed.

Condensation

In the updated read-across justification document and the chemical safety report you acknowledge the occurrence of condensation reaction following the hydrolysis of the parent substances. You explain that the silanols "*may undergo condensation reactions in solution to give siloxane dimers, oligomers and polymers*", and that "*the condensation products are not expected to be significant for toxicology*:".

ECHA notes that you have not specified the conditions, neither for the target nor for the source substance, under which the condensation occurs. In particular, substance specific concentration limits, specific pH, temperature and impact of the groups bound to the Si atom relevant for the test conditions are not defined. In consequence, the nature of the condensation products and their rate of formation under conditions relevant to the proposed test(s) are not clear. Thus exposure to condensation products cannot be ruled out following administration of the source and target substances but you have not addressed how and in which manner the condensation products of the source and target substances may affect the systemic toxicity.

You further state that "*Further experimental evidence is being collected about the condensation behaviour of alkoxysilanes*". ECHA acknowledges your intention to provide more data on condensation reactions of alkoxysilanes.

ECHA considers that the information currently available in the registration dossier is not sufficient to conclude on how the condensation products of the source and target substances may affect toxicity.

Toxicological data

With respect to the toxicological data present in the technical dossier relevant to the testing proposed, ECHA observes that both target and source substance are classified as Acute Tox. 4. Target substance is also classified as skin irritant (Cat 2), and both substances are classified as skin sensitizers Cat 1 and are non-genotoxic.

However, no higher tier studies are available for the target substance and a source substance. ECHA considers that acute toxicity data alone is not sufficient to establish the toxicological profile of a substance and support the prediction of the sub-chronic toxicity and prenatal developmental toxicity of the target substance.
ECHA notes that in your read-across justification document, submitted in the updated dossier, you identify and acknowledge the lack of the supporting information and propose further investigations to provide experimental evidence supporting your read-across hypothesis:

"*There are no available measured toxicokinetics data for any of the substances. <...> Further testing is underway to better understand the hydrolysis reactions of alkoxysilanes under conditions relevant for oral exposure in toxicology studies <...>.*

<...> In addition, testing to at least 28-day repeated dose toxicity is planned for the source substances. Consistent properties in the available toxicology studies would indicate that the minimal differences in the hydrolysis rates and physicochemical properties and structures of the hydrolysis products do not impact the read-across."

ECHA agrees with you, as already highlighted in the sections above, that currently submitted read-across justification is deficient and does not allow prediction of the relevant properties of the target substance. Higher tier studies e.g. repeated dose toxicity or screening studies may strengthen the overall read-across approach for the endpoints under consideration, as long as comparison of toxicological profiles between target and source substances is possible. However, the results may or may not confirm your hypothesis. ECHA considers that it is at your discretion to perform any such studies.
Therefore ECHA concludes that based on the presented information it is not possible to confirm that the substances would have similar properties or they would follow a regular pattern in their properties. In the absence of such information there is not an adequate basis for predicting the properties of the target substance from the data obtained with the source substance.

e. Conclusion on the read-across approach

Based on the above considerations ECHA concludes that you have not provided adequate and reliable information to demonstrate that the proposed read-across approach is plausible for the endpoint(s) in consideration.

ECHA therefore concludes that the criteria of Annex XI, Section 1.5, are not met, and consequently the testing proposed on the read-across substance(s) is not appropriate to fulfil the information requirement(s)of the substance subject to the present decision.

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1. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.)

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 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.

In the updated dossier, you have submitted a testing proposal for a sub-chronic toxicity study (90 day) in rats by the oral route according to OECD TG 408 with the analogue substance N-[3-(dimethoxymethylsilyl)-2-methylpropyl]ethylenediamine (CAS No 23410-40-4, EC no 245-642-4.

ECHA has evaluated your proposal to perform the test with the analogue substance N-[3-(dimethoxymethylsilyl)-2-methylpropyl]ethylenediamine ethylenediamine (CAS No 23410-40-4, EC no 245-642-4. As explained in Section 0 "Read-across approach" of this decision, your adaptation of the information requirement cannot be accepted. Hence there is a need to test the registered substance.

In addition to the testing proposal you discuss in your dossier the use of a study performed on another analogue substance for the purpose of an interim hazard and risk assessment for the registered substance. For that purpose in section 7.5.1. of the IUCLID dossier you have submitted a combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test (OECD TG 422, [redacted] 2002) conducted on the previously proposed (and rejected by ECHA) source substance N-(3-(trimethoxysilyl)propyl)ethylenediamine (CAS 1760-24-3, EC No 217-164-6).

In the chemical safety report you further add that *"The key study for this endpoint is an oral OECD TG 422 (Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test). No systemic toxicity was observed in this study and therefore the NOAEL for N-(3-(trimethoxysilyl)propyl)ethylenediamine (CAS 1760-24-3) was concluded to be ≥500 mg/kg bw/day."*

ECHA understands that you intend to use solely the data obtained on the analogue substance N-(3-(trimethoxysilyl)propyl)ethylenediamine (CAS 1760-24-3, EC No 217-164-6) "*in order to perform interim risk characterisation*".

ECHA acknowledges your intention to perform interim risk characterisation for the registered substance. However, due to several deficiencies of your read-across approach, as already explained in the initial draft decision and also summarised at the beginning of the statement of reasons, the requirement of Annex XI, Section 1.5. that toxicological properties may be predicted from data for reference substance(s) within the group, has not been met. Therefore ECHA concludes that the data on the analogue substance N-(3-(trimethoxysilyl)propyl)ethylenediamine (CAS 1760-24-3, EC No 217-164-6) could not be used to fulfil the current information requirement of the registered substance.

Finally, ECHA considers that by submitting the testing proposal on the analogue substance N-[3-(dimethoxymethylsilyl)-2-methylpropyl]ethylenediamine (CAS No 23410-40-4, EC no 245-642) you have deemed it necessary to generate further data for the registered substance for this endpoint. ECHA agrees that the information currently present in the technical dossier is insufficient to fulfil the information requirement of sub-chronic toxicity study (90 day) for the registered substance and it is necessary to provide information on this endpoint.

Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA considers that the oral route - which is the preferred one as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, section R.7.5.4.3 - is the most appropriate route of administration. More specifically, even though the information indicates that human exposure to the registered substance by the inhalation route is likely, there is no concern for severe local effects following inhalation exposure. Furthermore, ECHA points out that no repeated dose toxicity studies by the oral route is available. Hence, the test shall be performed by the oral route using the test method EU B.26./OECD TG 408.

According to the test method EU B.26./OECD TG 408 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

b) Outcome

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, you are requested to carry out the study with the registered substance subject to the present decision: Sub-chronic toxicity study (90-day) in rats, oral route (test method: EU B.26./OECD TG 408).

while your originally proposed test for sub-chronic toxicity study (90-day) in rats, oral route (OECD 408) with the analogue substance N-[3-(dimethoxymethylsilyl)-2-methylpropyl]ethylenediamine (CAS No 23410-40-4, EC no 245-642-4is rejected according to Article 40(3)(d) of the REACH Regulation.

Notes for your consideration

ECHA notes that a revised version of OECD TG 408 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).

2. 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 the updated dossier, you have submitted a testing proposal for a pre-natal developmental toxicity study in rats according to OECD TG 414 with the analogue substance N-[3-(dimethoxymethylsilyl)-2-methylpropyl]ethylenediamine (CAS No 23410-40-4, EC no 245-642-4.

ECHA has evaluated your proposal to perform the test with the analogue substance N-[3-(dimethoxymethylsilyl)-2-methylpropyl]ethylenediamine CAS No 23410-40-4, EC no 245-642-4. As explained in section 0 "Read-across approach" of this decision, your adaptation of the information requirement cannot be accepted. Hence there is a need to test the registered substance.

In addition to the testing proposal you discuss in your dossier the use of a study performed on another analogue substance for the purpose of an interim hazard and risk assessment for the registered substance. For that purpose in sections 7.8.1 and 7.8.2. of the IUCLID dossier you have submitted a pre-natal developmental toxicity study (OECD TG 414, [redacted] 2016) conducted on the previously proposed (and rejected by ECHA) source substance N-(3-(trimethoxysilyl)propyl)ethylenediamine (CAS 1760-24-3, EC No 217-164-6).

ECHA understands that you intend to use solely the data obtained on the analogue substance N-(3-(trimethoxysilyl)propyl)ethylenediamine (CAS 1760-24-3, EC No 217-164-6) "*in order to perform interim risk characterisation*".

ECHA acknowledges your intention to perform interim risk characterisation for the registered substance. However, due to several deficiencies of your read-across approach, as already explained in the initial draft decision and also summarised at the beginning of the statement of reasons, the requirement of Annex XI, Section 1.5. that toxicological properties may be predicted from data for reference substance(s) within the group, has not been met. Therefore ECHA concludes that the data on the analogue substance N-(3-(trimethoxysilyl)propyl)ethylenediamine (CAS 1760-24-3, EC No 217-164-6) could not be used to fulfil the current information requirement of the registered substance.

Finally, ECHA considers that by submitting the testing proposal on the analogue substance N-[3-(dimethoxymethylsilyl)-2-methylpropyl]ethylenediamine (CAS No 23410-40-4, EC no 245-642) you have deemed it necessary to generate further data for the registered substance for this endpoint. ECHA agrees that the information currently present in the technical dossier is insufficient to fulfil the information requirement for a pre-natal developmental toxicity study for the registered substance and it is necessary to provide information on this endpoint.

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 that testing should be performed with the rat or rabbit as a first species.

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 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) Outcome

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, you are requested to carry out the 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 pre-natal developmental toxicity study in rats, (OECD 408) with the analogue substance N-[3-(dimethoxymethylsilyl)-2-methylpropyl]ethylenediamine (CAS No 23410-40-4, EC no 245-642-4 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 6.0, July 2017), Chapter R.7a, section R.7.6.2.3.2.

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).

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Appendix 2: Procedural history

ECHA received your registration containing the testing proposal(s) for examination pursuant to Article 40(1) on 22 March 2013.

ECHA notes that the tonnage band for some member of the joint submission is 100 to 1000 tonnes per year.

ECHA held a third party consultation for the testing proposal(s) from 25 June 2015 until 10 August 2015. ECHA did not receive information from third parties.

ECHA notified you of the draft decision and invited you to provide comments.

You were notified that the draft decision does not take into account any updates after **18 July 2016,** 30 calendar days after the end of the commenting period.

However, following your request and justification provided (including interlinked read-across strategy on several supposedly related registered substances), ECHA has exceptionally granted you additional time until 30 June 2017 for the updated of the IUCLID dossier.

You updated your registration dossier on 30 June 2017 (submission number [redacted]). ECHA took the information in the update of registration of 30 June 2017 into account and modified 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. 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.