Helsinki, 19 July 2018

Addressee: [redacted]

Decision number: TPE-D-2114426294-52-01/F
Substance name: trimethoxy(2,4,4-trimethylpentyl)silane
EC number: 251-995-5
CAS number: 34396-03-7
Registration number: [redacted]
Submission number: [redacted]
Submission date: 22.06.2017
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 and decided as follows.

While your originally proposed test for a 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 analogue substance triethoxy(2,4,4-trimethylpentyl)silane (CAS No 35435-21-3, EC No 252-558-1)

is 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.**

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 January 2020.** You shall also update the chemical safety report, where relevant.

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 trimethoxy(2,4,4-trimethylpentyl)silane (CAS No 34396-03-7, EC No 251-995-5) (hereafter referred to as "target substance") and taking into account the updated dossier with the submission number [redacted].

In relation to the testing proposal subject to the present decision, in your dossier with the submission number [redacted] based on which the initial draft decision was prepared you propose a testing strategy intending to fulfil the standard information requirements for a Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26./OECD TG 408) in rats.

In your testing strategy you propose to test the analogue substance triethoxy(2,4,4-trimethylpentyl)silane (CAS No 35435-21-3, EC No 252-558-1; hereafter referred to as "source substance"). The results from the structural analogues will 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. 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 (Section 1, below).In your comments to the draft decision you did not provide considerations to the specific endpoint, subject to the decision.
After receiving the draft decision you updated your registration with the submission number [redacted] and amended the testing strategy.
ECHA has assessed your amended testing strategy.

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

You have provided the following arguments to justify the read-across approach:
"Read-across hypothesis
Both trimethoxy(2,4,4-trimethylpentyl)silane (CAS 34396-03-7) and triethoxy(2,4,4-trimethylpentyl)silane (CAS 35435-21-3) hydrolyse to the common silanol product (2,4,4-trimethylpentyl)silanetriol. Both substances hydrolyse very rapidly at pH 2 (route of administration), thus hydrolysis is expected to occur during testing and following exposure. The further products of hydrolysis are methanol and ethanol, respectively. It is therefore considered appropriate to read-across the results from triethoxy(2,4,4-trimethylpentyl)silane (CAS 35435-21-3) to the registered substance.The non-silanol hydrolysis products, ethanol and methanol, are not expected to contribute to any adverse effects for systemic or at the relevant dose levels. This is discussed further below.
The predicted half-life oftrimethoxy(2,4,4-trimethylpentyl)silaneat 20-25°C is 5.7 h at pH 7 (see Section 7.5).As the hydrolysis reaction may be acid or base catalysed, the rate of reaction is expected to be slowest at pH 7 and increase as the pH is raised or lowered. At pH 2 and 37.5°C a half-life of 5 and 12 s is predicted fortrimethoxy(2,4,4-trimethylpentyl)silane and triethoxy(2,4,4-trimethylpentyl)silane.
Reaction rate increases with temperature therefore hydrolysis will be faster at physiologically relevant temperatures compared to standard laboratory conditions. Under ideal conditions, hydrolysis rate can be recalculated according to the equation:
DT50(X°C) = DT50(T) x e(0.08.(T-X))
Where T = temperature for which data are available and X = target temperature."

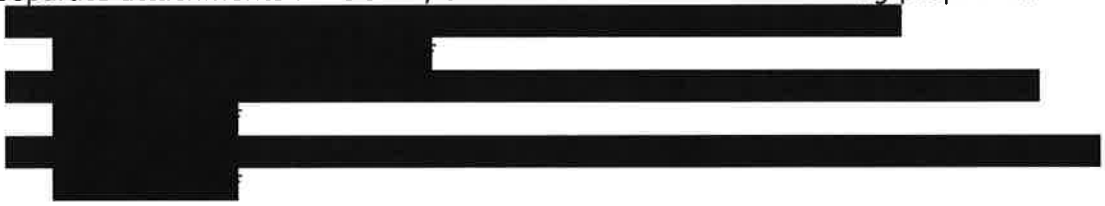
"These substances are part of an analogue group of alkyl alkoxysilanes. "

The basis of the read across is the hydrolytic stability and relevance of the silanetriol hydrolysis products."

"The Registrant proposes to perform the following test for: Triethoxy(2,4,4-trimethylpentyl)silane CAS 35435-21-3 (EC 252-558-1), so as to fulfil the standard information requirement set out in Regulation (EC) No. 1907/2006, Annex IX, 8.6.2:
1. Repeated Dose 90-Day Oral Toxicity Study in Rodents (OECD guideline 408)."

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

In your updated registration you have provided the updated version of several documents as separate attachments in IUCLID, Section 13 relevant to the testing proposed:



Apart from the above general information you have provided the substance specific read-across hypothesis and justification, in the Chemical Safety Report (CSR) in chapter 5.6.3.

This information includes the read-across hypothesis and justification, the identification of the source and target substances; comparison of the structural features, physico-chemical properties, predicted toxicokinetics properties and the available toxicological data of the source and target substances. In the same place you also discuss the repeated systemic toxicity of the non-silanol hydrolysis products and conclude on your read-across approach.

In addition you have provided in the technical dossier of the target substance the following toxicological studies relevant to the testing proposed.
For the target substance:

- acute oral toxicity studies (OECD 423, [redacted] (1998a); OECD 423, [redacted] (2002a));
- an acute inhalation toxicity study (OECD 403, [redacted] (1986a));
- a repeated dose toxicity study via inhalation (OECD 412, [redacted] (1986b));

For the source substance:

- results of a Prenatal Developmental Toxicity Study (OECD 414, [redacted] (2009b))

In the updated dossier you have additionally provided a sub-chronic repeated dose toxicity study via oral route (OECD 408, [redacted] (2015)) performed with the source substance.

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 alkyl alkoxysilanes 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 triethoxy(2,4,4-trimethylpentyl)silane (CAS No 35435-21-3, EC No 252-558-1) as a source substance. According to ECHA's understanding both in your initial and in your updated read-across approach you suggest that based on their structural similarities target and source substances have similar properties:

- target and source substances undergo similar hydrolysis process and as a result the same silanol hydrolysis product is formed;
- due to the similarity of the physico-chemical properties of the parent substances and their silanol hydrolysis products the substances would possess similar toxicokinetic profile;
- and hence the toxicological properties of the substances would be similar.

ECHA also understands that the basis of your hypothesis is the postulation

- that the hydrolysis of the parent substances is both rapid and complete, leading to the formation of the proposed same silanol hydrolysis product (2,4,4-trimethylpentyl)silanetriol);
- and that the formed silanol substance is exclusively relevant in terms of bioavailability and hence would drive the systemic toxicity.

In addition, you claim that the non-silanol hydrolysis products do not contribute to any adverse effects for the systemic toxicity.

In the following, ECHA examines whether the substances have indeed similar properties or that they would follow a regular pattern in their properties, before assessing the scientific validity of your postulation regarding the formation, relevance and exclusivity of the proposed silanol hydrolysis products as the driver for the systemic toxicity of the parent substances.

(i) Substance characterisation of source and target substances

The substance characterisation of the source substance(s) need to be sufficiently detailed in order to assess whether the attempted prediction is not compromised by the composition and/or impurities. In the ECHA practical guide 6 "How to report on Read-Across" it is

recommended to follow the ECHA Guidance for identification and naming of substances under REACH and CLP (version 1.3, February 2014) also for the source substances. This ensures that the identity of the source substance and its impurity profile allows an assessment of the suitability of the substances for read-across purposes.

ECHA notes that the source substance has solely been characterised by its chemical name and CAS No and no information on the composition or impurities has been provided in the technical dossier of the target substance.

No new information has been provided in the updated dossier.

ECHA considers that currently the composition and the impurity profile of the source and target substances cannot be compared using the information provided in the registration dossier. Therefore, ECHA cannot reach conclusion whether the source substance can be used to predict properties for the registered substance.

(ii) 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.

You have described the structural similarities between target and source substances by indicating that *"Both the registration and read-across substances are structurally similar, containing an alkylsilane moiety with three alkoxy (-OX) groups."* ECHA notes that structural difference can be observed in the size of the alkoxy groups. Whereas the source substance contains three ethoxy (-OEt,) groups, the target substance contains three methoxy (-OMe) groups bound to the Si (silicon) atom.

You have clearly identified the structural basis for the prediction, i.e. you postulate that both the source substance and the target substance hydrolyse, forming the same silanol hydrolysis product 2,4,4-trimethylpentyl silanetriol.

However, ECHA notes that you have not provided any information on how the structural differences may impact the toxicity of the substances and thus affect the possibility to predict properties of the target substance from the data obtained with the source substance. ECHA observes that in your updated read-across justification you have not addressed this deficiency.

The provided explanation is therefore not sufficient to establish a scientifically credible link between the structural similarity and the prediction.

(iii) 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.

In your read-across justification you stated that physico-chemical parameters/properties of target and source substances are "*in the same range*". You have proposed that the similar physico-chemical properties of the target and source substances support the structural similarity and enable the read across between the substances. ECHA observes that the physico-chemical properties of target and source substances are in the same range except the water solubility and partition coefficient (log Pow) of the parent substances. Comparison of the water solubility and the partition coefficients of the parent (source and target) compounds reveals that the water solubility of the source substance is approximately 1100 fold higher as that of the target substance; the partition coefficient of the source substance is log Pow=6.5, indicating (bio)accumulation potential of the source substance, whereas the target substance's partition coefficient is log Pow=4, hence the target is potentially not (bio)accumulative.ECHA notes that you have not explained how the presented differences affect the prediction.

ECHA observes that in your updated read-across justification you have not addressed this deficiency.

In your initial read across justification you claimed that "*In the case of repeated dose toxicity relevant properties are structural similarity as well as physical-chemical and basic toxicological parameters in the same range....*"

ECHA notes that in the absence of toxicokinetics studies for the target and source substances, you have provided toxicokinetic predictions/assessments which are based on the physico-chemical properties of the substances itself and/or its hydrolysis products. ECHA observes that your toxicokinetic predictions rely upon the assumed rapid and complete hydrolysis of the target and source substances to the proposed silanol hydrolysis product 2,4,4-trimethylpentyl silanetriol.

However, as will be further elaborated in section (iv) below, there is no evidence supporting your assumption of the formation, presence and stability of the proposed silanol hydrolysis product. Hence the predicted toxicokinetic profile of the target and source substance cannot be considered as valid, as it is based on scientifically unconfirmed assumptions.
ECHA considers that your claim of similar toxicity profiles of the source and target substances as a result of similar toxicokinetic profile is not substantiated and as such does not hold.

ECHA observes that in your updated read-across justification you have not addressed these deficiencies. In particular you have not provided any measured hydrolysis data on the target and source substances to substantiate your claim of fast and complete hydrolysis. Therefore, it is not possible to verify your assumption that only the proposed silanol hydrolysis products are relevant to drive the toxicity profiles of source and target substances.

You further proposed that the results of the acute toxicity data "*indicate that acute systemic toxicity for the oral route is similar for the two silanol hydrolysis products, although there is no specific information on mode of action*". ECHA notes that both the initial and the updated dossier contain an acute oral toxicity studies (OECD 423 [redacted] (1998a); OECD 423, [redacted]

(2002a)); an acute inhalation toxicity study (OECD 403, [redacted] (1986a)) and a repeated dose toxicity study via inhalation (OECD 412, [redacted] (1986b)) with the target substance. For the source substance results of an in vitro mammalian chromosome aberration test (OECD 473, [redacted] (2001a)); results of a micronucleus assay (OECD 474; [redacted] (2001b)) and results of a Prenatal Developmental Toxicity Study (OECD 414, [redacted] (2009b)) are provided in the dossier.

You stated in your initial read-across justification document that the data set available for comparing the toxicity profile of target and source substances is limited: *"Reproductive effects (increased post-implantation loss, prolonged gestation duration and dystocia) only occurred at the 1000 mg/kg bw/day dose level in association with marked maternal toxicity. In the sub-acute oral study with triethoxy(2,4,4-trimethylpentyl)silane a NOAEL of 150 mg/kg bw/day was determined, based on treatment and dose-related histopathological changes in the keratinised gastric mucosa in male rats, the change being present in all dose groups. In the sub-acute inhalation study with trimethoxy(2,4,4-trimethylpentyl)silane the NOAEC was determined to be 2890 mg/m³ (highest dose tested). No specific target organ toxicity was observed."*

ECHA notes that acute toxicity data alone is not sufficient to establish the toxicological profile of a substance with regard to repeated dose toxicity. Furthermore, due to the limited number of common toxicological endpoints in the provided data set and the differences in the route of administration in the presented studies, the comparison of toxicological profiles of the substances is not possible.

In your updated dossier you submitted for the source substance a sub-chronic repeated dose toxicity study via oral route (OECD 408, [redacted] (2015)). However, this study, by itself, does not provide relevant data to support the read-across prediction for the target substance. Hence ECHA considers that there is still no relevant data to allow comparison of the toxicological profiles of the substances.

Therefore ECHA concludes that based on the presented information it is still 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.

(iv) Hypothesis on formation, relevance and "*exclusivity*" of the silanol hydrolysis products, driving the toxicity

ECHA understands that the hypothesis relies on the assumption that both target and source substances undergo rapid and complete hydrolysis at pH 2 (within seconds) and they form the same silanol hydrolysis products 2,4,4-trimethylpentyl silanetriol. You propose that based on the formation and relevance of the similar silanol hydrolysis products, properties of the source substance can be used to predict the properties of the target substance and: *"The basis of the read across is the hydrolytic stability and relevance of the silanetriol hydrolysis products"*.

Firstly, ECHA observes that hydrolysis half-life rate at pH2 is based on assumptions which are not substantiated by data. You postulate that *"The predicted half-life of trimethoxy(2,4,4-trimethylpentyl)silaneat 20-25°C is 5.7 h at pH 7 (see Section 7.5). As the hydrolysis reaction may be acid or base catalysed, the rate of reaction is expected to be slowest at pH 7 and increase as the pH is raised or lowered. At pH 2 and 37.5°C a half-life*

of 5 and 12 s is predicted for trimethoxy(2,4,4-trimethylpentyl)silane and triethoxy(2,4,4-trimethylpentyl)silane.". ECHA notes that there is no hydrolysis data available in the registration dossier for pH 2 (neither for the target nor for the source substance) but instead 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 which are the basis of the hypothesis is not supported by data. Specifically, ECHA notes that the formation of the proposed silanol hydrolysis product from the target and source substances would involve three hydrolysis steps. In the hydrolysis studies/QSAR provided in the registration dossier there is no evidence of the formation of the proposed silanol hydrolysis product so it is not possible to verify that ultimate hydrolysis of both target and source substances has indeed occurred within the timeframe of the test.

Furthermore, you have not substantiated your assumption of a complete hydrolysis. 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.

Thirdly, your assumption that the silanols are exclusively relevant in terms of bioavailability and hence would drive the systemic toxicity is not supported by data. In fact you acknowledge the occurrence of condensation reaction following the hydrolysis of the parent substances but you did not consider the implication of such reaction on the prediction. You explain that the silanol hydrolysis product may undergo condensation reactions leading to the formation of siloxane dimers, oligomers and polymers and state that:
"A highly cross-linked gel may form. The degree of condensation that will occur may vary with:

- *Concentration of the silanol; the greater the initial concentration, the greater the degree of condensation. Significant condensation is not expected at concentrations less than approximately 100 mg/l, but is dependent on specific conditions.*
- *pH;the condensation reaction may be either acid or base catalysed.*
- *Temperature.*
- *Timescale.*
- *The nature of the R-group.*
- *The number of Si-OH groups; silanetriols condense more rapidly than silanediols."*

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 limit, specific pH, temperature and impact of the groups bound to the Si atom 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 would affect the systemic toxicity.

Finally, ECHA notes that you have not addressed adequately how the formation of the non-silanol hydrolysis products influences the prediction. As a result of the hydrolysis reaction non-silanol hydrolysis products are also formed: i.e. methanol from the target substance and ethanol from the source substance. You claim that the non-silanol hydrolysis products

play no significant role in the systemic toxicity of the substances as "The non-silanol hydrolysis products, ethanol and methanol, are not expected to contribute to any adverse effects for systemic or at the relevant dose levels."

ECHA notes that in your read across justification you have not provided information on the "relevant dose levels". In addition, your proposal did not address the possible interactions between the parent substances and their hydrolysis products and you have not taken into consideration the implication of such reaction on the prediction.

In summary, ECHA considers that given the lacking evidence on the formation, and relevance of the proposed silanol hydrolysis products your hypothesis that only the silanols are relevant in terms of bioavailability and hence would drive the systemic toxicity cannot be confirmed.

ECHA notes that in your updated dossier you have not provided any new measured data which would support your assumption. Therefore, the shortcomings observed above are still valid.

Consequently, there is not an adequate basis for predicting the human health 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 in consideration. In the updated dossier you have not provided any information which would allow to change this conclusion. 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 is not appropriate to fulfil the information requirement of the substance subject to the present decision.

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 your initial dossier you have submitted a testing proposal for a sub-chronic toxicity study (90 day) in rats by the oral route according to EU B.26./OECD TG 408 with the analogue substance triethoxy(2,4,4-trimethylpentyl)silane (CAS No 35435-21-3, EC No 252-558-1)

ECHA has evaluated your proposal to perform the test with the analogue substance. As explained in the Section 0 *'Grouping of substances and read-across approach'* of this decision, your adaptation of the information requirement currently cannot be accepted. Hence there is a need to test the registered substance.

In the updated dossier you have also submitted an intention to test the registered substance in a Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test according to OECD TG 422 and to use the results for your read-across testing strategy. You have acknowledged the deficiency of your read-across strategy, as noted by ECHA in the initial draft decision, which is lack of relevant higher tier data to compare relevant toxicological properties of target and source substances.

ECHA acknowledges your intention to perform a Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test, according to OECD TG 422 with the registered substance. Studies conducted according to OECD TG 422 may strengthen the overall read-across approach for the endpoint 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 an OECD TG 422, as mentioned above.

You proposed testing by the oral route. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA agrees that the oral route - which is the preferred one as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.1, October 2015) 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, potential inhalation-specific effects are already addressed by providing a repeated dose toxicity study by the inhalation route (OECD 412, [redacted] (1986b)) and by deriving a long-term DNEL for inhalation. 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.

In addition, ECHA notes that in your CSR document and in the IUCLID dossier under the endpoint 7.5.1 you discuss the use of studies performed on the source substance triethoxy(2,4,4-trimethylpentyl)silane (CAS 35435-21-3) for interim hazard and risk assessment for the registered substance.
For that purpose you have submitted the following data on the source substance:

- a sub-chronic repeated dose toxicity study (90 days), via oral route (OECD 408; BSL Biosevice (2015)) and
- a Prenatal Developmental Toxicity Study (OECD 414, Harlan (2009b)).

ECHA acknowledges your intention to provide interim risk characterisation for the registered substance. However, ECHA observes that your proposed interim read-across approach is based on the read-across and grouping approach as analysed above in Section 0 *'Grouping of substances and read-across approach'*. As already noted therein, there are several shortcomings which result in a conclusion that the requirement of Annex XI, Section 1.5., that human health effects may be predicted from data for reference substance(s) within the group, has not been met. Therefore the data provided on the source substance currently cannot not be used to fulfil the information requirement of sub-chronic repeated dose toxicity study for the registered substance.

To conclude, the information present in the technical dossier is currently insufficient to fulfil the information requirement.

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 a Sub-chronic toxicity study (90-day) in rats, oral route (test method: EU B.26./OECD TG 408) using the analogue substance triethoxy(2,4,4-trimethylpentyl)silane (CAS No 35435-21-3, EC No 252-558-1) is 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).

Appendix 2: Procedural history

ECHA received your registration containing the testing proposal for examination pursuant to Article 40(1) on 13 May 2015.

ECHA held a third party consultation for the testing proposal from 25 June 2015 until 10 August 2015. 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 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.

You updated your registration on 22 June 2017. ECHA took the information in the updated registration into account, and did not amended 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 carrying out the test(s) required by the present decision it is important to ensure that the particular sample of substance tested 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. If the registration of the substance covers different grades, the sample used for the new test(s) must be suitable to assess these. Furthermore, 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.