Helsinki, 19 July 2018

Addressee: [redacted]

Decision number: TPE-D-2114428710-56-01/F
Substance name: N-(dimethylvinylsilyl)-1,1-dimethyl-1-vinylsilylamine
EC number: 231-701-1
CAS number: 7691-02-3
Registration number: [redacted]
Submission number: [redacted]
Submission date: 27.06.2017
Registered tonnage band: 100-1000T

DECISION ON A TESTING PROPOSAL

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

While your originally proposed tests for:

- Sub-chronic toxicity study (90-day), inhalation route (OECD TG 413) in rats using the analogue substance hexamethyldisilazane (HMDZ, CAS No 999-97-3, EC No 213-668-5), and
- Pre-natal developmental toxicity study (EU B.31./OECD TG 414) in rats or rabbits, oral route using the analogue substance trimethylsilanol CAS No 1066-40-60 (EC No 213-914-1)

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-(dimethylvinylsilyl)-1,1-dimethyl-1-vinylsilylamine, CAS No 7691-02-3 (EC no 231-701-1) (hereafter referred to as target substance) the submitted third party comments and taking into account the updated dossier.

In your dossier with submission number [redacted], based on which the initial draft decision was prepared, you proposed a testing strategy intending to fulfil the standard information requirements for a

- Sub-chronic toxicity (90-day) study (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 hexamethyldisilazane (HMDZ) CAS No 999-97-3 (EC No 213-668-5); (hereafter referred to as source substance 1) for sub-chronic toxicity (90-day) study, and trimethylsilanol CAS No 1066-40-60 (EC No 213-914-1) a hydrolysis product of HMDZ (hereafter referred to as source substance 2) for the pre-natal developmental toxicity study. 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 (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

You have provided the following arguments to justify the read-across approach:

- Target and source substances and their hydrolysis products have similar chemical structures;

- Target and source substances possess similar physicochemical properties;
- Target and source substances have similar toxicological effects.

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

You have provided the following documents to support your read-across approach in Section 13 of the IUCLID, relevant for the testing proposed:

[redacted]

[redacted] The document "*outlines the approach*" to mammalian toxicity of alkyl 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*". Study results of the source substance 2, trimethylsilanol, have been provided.

In addition to the general information above you have provided the substance specific read-across hypothesis and justification, in the technical dossier under the endpoint study summary for repeated dose toxicity, in Section 7.5 and in the Chemical Safety Report (CSR) in section 5.6.3.

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

for the target substance:
- Acute oral toxicity (equivalent of similar to OECD 401),

for the source substance 1 (HMDZ):
- Acute inhalation toxicity (OECD 403),
- Acute dermal toxicity (equivalent of similar to OECD 402),
- Combined repeated dose toxicity study with the reproduction / developmental toxicity screening test via inhalation (OECD 422).

After receipt of the draft decision you have updated your technical dossier (submission number [redacted]) and provided an updated read-across justification document [redacted]; You attached this document also in the technical dossier under the endpoint study summary for repeated dose toxicity and pre-natal developmental toxicity, in Sections 7.5.2 and 7.8.2 and in section 5.6.3. of the Chemical Safety Report (CSR) .

You have also provided the additional toxicological studies:

for the source substance 1 (HMDZ):
- Supporting acute oral toxicity study (non GLP, equivalent of similar to OECD 401, [redacted] 1980),
- Supporting combined repeated dose toxicity study with the reproduction / developmental toxicity screening test via inhalation (GLP, OECD 422, [redacted] 2008),

- Key sub-chronic repeated dose toxicity study (90 day) via inhalation (GLP, OECD 413, [redacted] 2014).

For the source substance 2 (trimethylsilanol):

- Supporting sub-acute repeated dose toxicity study (28 day) via oral route (GLP, OECD 407, [redacted] 1986),
- Supporting sub-acute repeated dose toxicity study via inhalation route (GLP, OECD 412, [redacted] 2007),
- Supporting combined repeated dose toxicity study with the reproduction / developmental toxicity screening test via inhalation (GLP, OECD 422, [redacted] 2008),
- Key pre-natal developmental toxicity study via oral route (GLP, OECD 414, [redacted] 2014).

You have also provided data available on supporting substances 1,1,3,3-tetramethyl-1,3-divinyldisiloxane (referred to also as 'Vi2-L2') (EC No 220-099-6, CAS No 2627-95-4) and hexamethyldisiloxane (referred to also as 'L2')(EC No 203-492-7) to justify your claim that "*replacement of a vinyl group at silicon with a methyl group does not impact the toxicological properties*."

For Vi2-L2

- Supporting repeated dose 14-day inhalation toxicity study (deviating from OECD 412, GLP, [redacted] 1993);
- Supporting Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test (OECD 422, GLP, [redacted] (2011a);

For L2:

- Supporting study, toxicokinetics *in vivo* (OECD 417, GLP, [redacted] (2006);
- Supporting study, toxicokinetics *in vivo* (OECD 417, GLP, [redacted] (2008);
- Supporting dermal absorption study ex vivo/*in vitro (no guideline, GLP,* [redacted] 2000);
- Supporting sub-acute oral toxicity study (OECD 407, GLP, [redacted] (1994);
- Supporting repeated dose 14-day inhalation Toxicity Study (following OECD 412, GLP, [redacted] 1992);
- Supporting sub-acute inhalation study (OECD TG 412, GLP, [redacted] 1997);
- Supporting sub-chronic 90-day inhalation study (OECD TG 413, GLP, [redacted] 1998);
- Supporting sub-chronic inhalation study with recovery period (OECD TG 413, GLP, [redacted] 1997);
- Supporting 2-year inhalation study (OECD TG 453, GLP, [redacted] 2005);
- Supporting two-generation reproductive toxicity study, inhalation route (OECD 416, GLP, [redacted] 2006).

ECHA notes that all of the above studies (for source 1, source 2, Vi2-L2 and L2) are existing data i.e. they have been conducted before the decision making process has started.

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 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 hexamethyldisilazane (HMDZ) CAS No 999-97-3 (EC No 213-668-5) (source substance 1) for sub-chronic toxicity (90-day) study, and trimethylsilanol (CAS No 1066-40-60, EC No 213-914-1) (source substance 2) for pre-natal developmental toxicity study, as source substances.

Based on the information provided, ECHA understands that the proposed read-across hypothesis is based on structural similarity, similar physico-chemical and toxicokinetic properties, rapid hydrolysis, and similar properties of the silanol 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.

You have described the structural similarities between target and source substances by explaining that both the target and source substance 1 are disilazanes with a functional group –Si-N-Si-, which hydrolyses rapidly. You have further explained the differences in the structures: two methyl groups and one vinyl group on each silicon in the target substance and three methyl groups on each silicon in the source substance 1.

ECHA observes that you have provided information to demonstrate the structural similarities and differences between the target and source substance 1. ECHA notes that due to these differences the non-common hydrolysis products formed from the parent substances are different: dimethylvinylsilanol and trimethylsilanol from the target and source substance 1, respectively. ECHA observes that the source substance 2, trimethylsilanol, is the hydrolysis product of the source substance 1.

You claim that the hydrolysis products have similar properties. ECHA observes that you have not provided any information to support your claim, *i.e.* explanation or data on how the structural differences in the parent substances, and consequently in the hydrolysis products, may impact the toxicity of the substances, and thus affect the possibility to predict the properties of the target substance from the data of the source substance 1 for sub-chronic toxicity (90-day) and from the data of the source substance 2 for pre-natal developmental toxicity (as discussed in section (ii) below).

ECHA notes that you have not provided sufficient information on how the structural differences in the parent substances and consequently in the silanol hydrolysis products 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 1 and the source substance 2. The provided explanation is therefore not sufficient to establish a scientifically credible link between the structural similarity and the prediction.

In your updated read-across justification document you have also provided a list of potential metabolites of the target and source substances predicted with OECD QSAR Toolbox. You explain that the metabolites formed from the target and source substances are structurally similar, and some differences in structures are not considered significant. ECHA considers that this claim is not confirmed by experimental data as explained in section (ii) below.

(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.

You claim that both target and source substances have very similar physicochemical properties.

ECHA observes that the physico-chemical properties of target substance and source substance 1 and their hydrolysis products are similar, and consequently their toxicokinetic properties can be assumed to be similar. In addition, based on the data provided, hydrolysis of the substances is rapid and complete.

ECHA notes that the fact that physico-chemical parameters are similar, that the hydrolysis is rapid and complete, and toxicokinetic behaviour may be similar, may support similar toxicity profile of the substances. However, ECHA considers that these facts alone are not a sufficient basis for predicting the human health properties of the target substance from the data obtained with the source substances.

Additionally you have proposed that the target and source substances have similar toxicological profiles and therefore the properties of the target substance can be predicted from the data obtained from the source substances.

Firstly, ECHA observes that both the target substance and source substance 1 are classified as Acute Tox. 4. ECHA notes that no higher tier studies are available for the target substance. ECHA notes that acute toxicity data alone is not sufficient to establish the toxicological profiles of the substances and support the prediction of repeated dose toxicity of the target substance from the source substance 1.

Secondly, for the source substance 2, results of an acute oral toxicity, skin irritation and screening studies have been provided in the document ([redacted]). ECHA observes that no experimental studies are available for dimethylvinylsilanol (the hydrolysis product of the target substance). ECHA therefore notes that your claim that *"silanol hydrolysis products have similar properties"* cannot be verified. In addition, ECHA notes that acute toxicity data alone is not sufficient to establish the toxicological profiles of the substances and support the prediction of pre-natal developmental toxicity of the target substance from the source substance 2.

In the updated dossier you have additionally provided a combined repeated dose/reproductive toxicity screening study (OECD TG 422) and a sub-chronic toxicity (90-day) study conducted with the source substance 1 and a combined repeated dose/reproductive toxicity screening study (OECD TG 422) and a pre-natal developmental

toxicity study conducted with trimethylsilanol, source substance 2. However, as you have not provided any higher tier studies for the target substance, the comparison of the toxicological profiles still cannot be made.

ECHA further notes that you refer to the supporting, existing data submitted for two siloxane substances Vi2-L2 and L2 but you emphasise that "*these supporting data are not read across due to differing physicochemical properties of the parent substances, but provide evidence that replacement of a vinyl group at silicon with a methyl group does not impact the toxicological properties.*" For that purpose you claim that "*The metabolites of Vi2-L2 and L2 are shown not to result in different toxicity profiles in existing higher tier toxicity tests available, which showed that these two substances have comparable systemic effects".*

ECHA has analysed your claim that these two substances have comparable systemic effects and concludes that your assumption is not confirmed by provided data set on supporting substances Vi2-L2 and L2. ECHA observed dissimilar effects which indicates that these two substances do not have a comparable systemic effects. Please see below for further analysis.

Specifically, in the oral OECD 422 study Vi2-L2 showed the following effects in males that had not been observed with L2: relative and absolute decreased brain and adrenal weight, adrenal cortical atrophy and vacuolation of pituitary. ECHA notes the effects of the supporting substance Vi2-L2 on the pituitary cannot be considered non-adverse based on the information provided in the endpoint study record that shows a dose-response relationship (0/0, 4/10, 6/10, 8/10 for control, 50, 150 and 600 mg/kg bw/day, respectively). ECHA further notes that it cannot be excluded that the effects on adrenal cortex are adverse as a dose-response, although lower than for pituitary effects, were observed (0/10, 1/10, 2/10, 6/10 for control, 50, 150 and 600 mg/kg bw/day, respectively). Similarly, ECHA considers that decreased post-natal survival observed in the OECD 422 study with Vi2-L2 indicates different toxicological profile of the substances. Therefore your assumption that "*replacement of a vinyl group at silicon with a methyl group does not impact the toxicological properties.*" is not confirmed.

In conclusion, the existing studies you provided in the updated dossier do not contribute to the read-across assessment and deficiencies. Thus the concerns highlighted in the initial draft decision, still remain. Specifically, the absence of repeated dose toxicity data on the target substance prevents establishing and comparing the toxicological profiles of the target and source substances. In addition, dissimilar toxicological profiles of the supporting source substances do not support your claim that structural dissimilarities do not impact the toxicological profiles.

Therefore ECHA concludes that based on the presented information it is not possible to confirm that the target and source 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 substances.

e. Conclusion on the read-across approach

Based on the above considerations ECHA concludes that there is not an adequate basis for predicting the repeated-dose toxicity and the pre-natal developmental toxicity properties of the target substance from the source substances because comparison of toxicological profiles of the target substance and source substances regarding repeated dose toxicity and

pre-natal developmental toxicity cannot be established due to lack of repeated dose/screening studies on the target substance.

Thus, the information provided does not provide sufficient evidence to conclude that the structural differences between the source and target substances do not impact the toxicity profiles of the target and source substances.

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 endpoints in consideration.

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

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

a) Examination of the testing proposal

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 dossier with the submission number [redacted], based on which the initial draft decision was prepared you have submitted a testing proposal for a sub-chronic toxicity study (90 day) by the inhalation route according to OECD TG 413 with the analogue substance hexamethyldisilazane (HMDZ, CAS No 999-97-3, EC No 213-668-5).

ECHA has evaluated your proposal to perform the test with the analogue substance hexamethyldisilazane (HMDZ, CAS No 999-97-3, EC No 213-668-5). As explained in the section 0 '*Read-across approach*' of this decision, your adaptation of the information requirement cannot be accepted and information submitted in the updated dossier does not change this conclusion. Hence there is a need to test the registered substance.

In your comments to the draft decision you did not provide considerations to the specific endpoint, subject to the current draft decision.
Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA notes 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, the exposure concentrations reported in the chemical safety report for the inhalation route is low (maximum [redacted] mg/m^3). 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) 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 proposed to use existing information to fulfil the information requirement: "*We refer to an overview of existing information on the registered substance and the readacross candidate. The similarities in structural, physicochemical and toxicological characteristics may support the read-across justification to be provided by the registrant. Results of the proposed sub-chronic inhalation toxicity study conducted with the read-across compound are already available. No toxicological findings considered to be relevant to humans were noted (NOAEC ≥ 400 ppm)*".

ECHA acknowledges that the third party has proposed a testing strategy including a read across approach for you to consider. The third party informs that the proposed study with HMDZ has already been carried out and suggests that it could be used to fulfil the information requirement for sub-chronic toxicity (90-day) endpoint.

ECHA notes that the information provided by the third party is insufficient for demonstrating that the conditions of Annex XI, Section 1.5. of the REACH Regulation are met, for the reasons explained in Section 0. above. Therefore, the information provided by the third party is not sufficient to adapt the standard information requirement.

c) 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 (90-day) (OECD 413) with the analogue substance hexamethyldisilazane (HMDZ, CAS No 999-97-3, EC No 213-668-5) 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).

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)(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 dossier with the submission number [redacted] based on which the draft decision was prepared you have submitted a testing proposal for a pre-natal developmental toxicity study according to EU B.31./OECD TG 414 with the analogue substance trimethylsilanol CAS No 1066-40-60 (EC No 213-914-1).

ECHA has evaluated your proposal to perform the test with the analogue substance trimethylsilanol CAS No 1066-40-60 (EC No 213-914-1). As explained in the section 0 '*Read-across approach*' of this decision, your adaptation of the information requirement cannot be accepted and information submitted in the updated dossier do not change this conclusion. Hence there is a need to test the registered substance.

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

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 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) 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 proposed to use existing information to fulfil the information requirement: *"We refer to an overview of existing information on the registered substance and the proposed read-across compound. The similarities in structural, physicochemical and toxicological characteristics may support the read-across justification to be provided by the registrant. A combined repeated dose toxicity study with the reproduction/ developmental toxicity screening assay conducted via the inhalation route at concentrations of 25, 100 and 400 ppm of the read-across substance did not show evidence of a reproductive or developmental toxicity potential."*

A third party has provided information on an OECD 422 screening study performed with the analogue substance hexamethyldisilazane (HMDZ, CAS No 999-97-3, EC No 213-668-5). However, ECHA notes that an OECD 422 screening study is not a test method that corresponds to the standard information requirement of Annex IX, Section 8.7.2 for a pre-natal developmental toxicity study because it does not provide equivalent information. The screening study does not cover the key parameters of a pre-natal developmental toxicity study which are, for example, examinations of the foetuses for skeletal and visceral malformations.

In addition, the information provided by the third party is insufficient for demonstrating that the conditions of Annex XI, Section 1.5. of the REACH Regulation are met, for the reasons explained in Section 0. above. Therefore, the information provided by the third party is not sufficient to adapt the standard information requirement.

c. 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 a pre-natal developmental toxicity test (OECD 414) with the analogue substance trimethylsilanol CAS No 1066-40-60 (EC No 213-914-1) 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).

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 12 December 2014 until 26 January 2015. ECHA received information from third parties (see Appendix 1).

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 11 July 2016.

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 27 June 2017. ECHA took the information in the updated registration 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.