EUROPEAN CHEMICALS AGENCY

Helsinki, 19 July 2018

Addressee: [redacted]

Decision number: TPE-D-2114432420-65-01/F
Substance name: 3-(triethoxysilyl)propanethiol
EC number: 238-883-1
CAS number: 14814-09-6
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.

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

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 (rat or rabbit), oral route using the registered substance.**

While your originally proposed test for In vivo mammalian erythrocyte micronucleus test (EU B.12./OECD TG 474) using the registered substance is rejected, you are requested to perform:

3. **In vivo mammalian alkaline comet assay (Annex IX, Section 8.4., column 2; test method: OECD TG 489) in rats, oral route, on the following tissues: liver, glandular stomach and duodenum using the registered substance.**

While your originally proposed test for Long-term toxicity testing on aquatic invertebrates (Daphnia magna reproduction test, EU C.20./OECD TG 211) using the analogue substance 3-trimethoxysilylpropane-1-thiol (EC No. 224-588-5, CAS No. 4420-74-0) is rejected, you are requested to perform:

4. **Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: Daphnia magna reproduction test, EU C.20./OECD TG 211) using the registered substance**

You are additionally requested to perform:

5. **Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.; test method: Fish, early-life stage (FELS) toxicity test, OECD TG 210) using the registered substance**
6. **Growth inhibition study on aquatic algae and cyanobacteria (Annex VII,Section 9.1.2.; test method: Freshwater alga and cyanobacteria, growthinhibition test, OECD 201) using the registered substance**

7. **Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method: Daphnia sp. Acute immobilisation test, EU C.2./OECD TG 202) using the registered substance**
8. **Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: Fish, Acute Toxicity Test, OECD 203) using the registered substance**

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI of the REACH Regulation. In order to ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective Annex, and an adequate and reliable documentation.

You are required to submit the requested information in an updated registration dossier by **26 January 2021**. 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 3-(triethoxysilyl)propanethiol, CAS No 14814-09-6 (EC No 238-883-1) (hereafter referred to as "target substance") taking into account the updated dossier.

In relation to the human health related testing proposals, you propose testing on the registered substance and ECHA's assessment is provided in Sections 1 to 3 below.

In relation to the environment relating testing proposals , you propose a testing strategy intending to fulfil the standard information requirement for: Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.).

In your testing strategy you propose to test the following analogue substance hereafter referred to as "source substance": 3-trimethoxysilylpropane-1-thiol (CAS No. 4420-74-0, EC No 224-588-5). The results from the structural analogue(s) 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.

To the extent that the proposed aquatic testing and the justification provided for the current read-across for aquatic endpoints relies upon the 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 (Section 4 below) and additional information requests related to the aquatic toxicity endpoint (Sections 5-8 below).

In the updated dossier (submission number: [redacted]) you have acknowledged the shortcomings communicated to you in a draft decision, provided further read-across justification and proposed a stepwise strategy how to address the ecotoxicological requirements relevant to the current decision. ECHA has assessed the new information provided.

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 testing programmes 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 approaches in general terms:

"*The substance is part of an analogue group of thiols.*" (Section 1.4 Analogue group approach, CSR)

The registered substance is part of a group of three thiols for which a separate Analogue report: Ecotoxicity of thiols document has been provided. In the report the following is given (section 2.1): "*For the purposes of this report, the thiol analogue group includes substances which contain a terminal thiol (SH) group present on a Silicon side chain. A methoxy, ethoxy or hydroxyl group will be attached directly to the silicone. A thiol group is also known as a sulphydryl or mercaptan group.*"

The group is further categorised as III-20 which is characterised as follows: "*This is a chemical group with some known effects from non-Si chemistry and (eco)toxicology.*" (Section 8.7, Reconsile Category/Analogue/QSAR strategy)
The basis of the read across is the hydrolytic stability and relevance of the silanetriol hydrolysis products. The hydrolysis half-life of the substance has been predicted using a validated QSAR.
The analogue methodology takes into account the properties of all hydrolysis products and the choice of read-across substance is described on a case-by-case basis for individual endpoints." (Section 1.4 Analogue group approach, CSR)

With regards to the ecotoxicological properties addressed in this decision, you provide the following justifications in the new read-across justification report [redacted] which was submitted in the dossier update: "*There are no measured data for 3-(triethoxysilyl)propanethiol for short-term or long-term aquatic ecotoxicity endpoints. This document describes the analogue approach for fulfilling these endpoints by read-across from the source substance 3-trimethoxysilylpropane-1-thiol according to the Read-across Assessment Framework (RAAF).*" ... "*Read-across is proposed in accordance with RAAF Scenario 1*"

"*The registered substance, 3-(triethoxysilyl)propanethiol, and the substance used for read-across, 3-trimethoxysilylpropane-1-thiol, are trialkoxysilanes with an ethoxy and a methoxy group respectively, in addition to a thiol group present in the side chain. The substances are considered to be structural analogues, the toxicity of which is dominated by the presence of the thiol group. The two substances are susceptible to abiotic degradation by hydrolysis, and produce an identical silanol hydrolysis product, 3-(trihydroxysilyl)propanethiol. The non-silanol hydrolysis products are ethanol and methanol, respectively.*"

"*3-(Triethoxysilyl)propanethiol has a predicted hydrolysis half-life of approximately 19 h at 20-25°C and pH 7 , a measured log Kow value of 2.7, a calculated water solubility of 82 mg/l and a molecular weight of 238.2. If 3-(triethoxysilyl)propanethiol were tested in standard aquatic ecotoxicity test media, it would hydrolyse under the conditions of the studies to produce 3-(trihydroxysilyl)propanethiol, and ethanol.*"

"*3-Trimethoxysilylpropane-1-thiol has a predicted hydrolysis half-life of 2.6 h at pH 7 and 20°C, a calculated log Kow value of 1.7, calculated water solubility of 2800 mg/l and a molecular weight of 196.3. In the aquatic ecotoxicity studies that have been conducted, it would have hydrolysed under the conditions of the studies to produce 3-(trihydroxysilyl)propanethiol, and methanol.*"

"The silanol hydrolysis product, 3-(trihydroxysilyl)propanethiol, has a log Kow value of -1.4, is soluble in water (predicted) and has a MW of 154.2. It is not readily biodegradable."

"The toxicity is expected to be driven by the thiol group and as suggested by ECOSAR v.1.11 (2012) and in literature available in the public domain, invertebrates are the most susceptible trophic level. The sources also suggest that there is only a weak correlation between log Kow and thiol toxicity to fish. Hence, although there is a difference in log Kow between the registered substance and the silanol hydrolysis product, this is not considered to affect the validity of the read-across."

"Methanol and ethanol are well characterised in the public domain literature and are not hazardous at the concentrations relevant to the studies; the short-term EC50 and LC50 values for these substances are in excess of 1000 mg/l (OECD 2004a - SIDS for methanol, CAS 67-56-1, OECD 2004b - SIDS for ethanol, CAS 64-17-5). Therefore, at the loading rates experienced in these tests it is unlikely that the presence of either would significantly affect the results of the tests."

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

You have provided several documents as separate attachments in IUCLID, Section 13, relevant to the ecotoxicological properties addressed in this decision:

[redacted]

In the updated dossier you submitted also the two following documents:

[redacted]

The provided Dissociation Constant of Hydrolysis Products of Organosilicon Substances document ([redacted]) in ECHA's understanding is an overview of the grouping of organosilicon substances with a half-life of < 12 hours and which are known to generate silanol hydrolysis product, and how the dissociation constant is determined/predicted. In addition, in ECHA's understanding the document does not include substance specific data to support the read-across hypothesis subject to this decision. ECHA notes that the substance subject to the current decision is not included in the document.

The provided Reconsile Category/Analogue/QSAR strategy [redacted] is an overview of the grouping and read-across methods of Reconsile REACH submissions. In ECHA's understanding the document describes the general principles applied but does not provide any substance-specific information. According to the report, *"each technical dossier needs to describe clearly whether Category, Analogue or QSAR methods have been applied, and which endpoints they are applied to"*.

The provided Biodegradation group approach ([redacted]) presents "*a foundation*" for "*a group of analogues for the property ready biodegradation*". In the analogue group hypothesis it is given that "*substances within this main analogue group indicates that in general these substances are not readily biodegradable.*" Data matrix of ready biodegradation studies is provided. ECHA notes that no substance-specific information regarding the proposed read-across approach has been provided.

The provided grouping report for Toxicity to sewage treatment plant microorganisms ([redacted]) presents "*the foundation*" for "*a group of analogues for the property toxicity to sewage treatment plant microorganisms*". A definition of analogue group and its members is provided together with a data matrix. ECHA notes that the substance subject to the current decision is not included in the document.

The provided Ecotoxicity of thiols document ([redacted]) "*outlines the approach to grouping thiol-containing substances, (R(4-x)-SiOR'x, for ecotoxicity properties*" and in ECHA's understanding a hypothesis for analogue group approach regarding ecotoxicity is described. A list of endpoints covered is provided together with a data matrix. ECHA notes that no substance-specific information regarding the read-across approach has been provided.

In the new read-across justification report ([redacted]) submitted in the dossier update you further explain why you believe that the properties of the registered substance can be predicted from studies performed with the source substance, according to Scenario 1 of the RAAF (Analogue approach, (Bio)transformation to common compound(s)).

You have also provided the substance specific read-across justification for environmental hazard assessment, in the technical dossier, under the endpoint summary Ecotoxicological information, in Section 6 and in the Chemical Safety Report (CSR) in section 7.0.

The information justifying the read-across prediction for the registered substance includes description of the properties of substances in the class of trialkoxysilanes and possible mode of action of thiols in general terms, followed by specific information regarding the read-across approaches from the source substance to the target substance, taking into account structure, hydrolysis rate, physico-chemical properties and ecotoxicological properties.

In addition you have provided in the technical dossier of the target substance the following ecotoxicological studies for the source substance:

- Short-term aquatic toxicity study on fish (EU Method C.1, GLP, [redacted] 1995)
- Short-term aquatic toxicity study on *Daphnia* (EU Method C.2; GLP; [redacted] 1995)
- Toxicity to aquatic algae study (EU Method C.3, [redacted] 1995)
- Toxicity to aquatic microorganisms study (other guideline: EG-Nr. L 133/118 from 30.5.1988, [redacted] 1995)

No ecotoxicological data on the target substance has been submitted in its technical dossier.

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 thiols 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 provided by you for the registered substance, ECHA understands that no category hypothesis

/justification has been included and the proposed prediction is based on the analogue approach using 3-trimethoxysilylpropane-1-thiol (CAS No. 4420-74-0) as a source substance.

According to ECHA's understanding you suggest that based on their structural similarities the target and source substance have similar properties; they undergo similar hydrolysis process and as a result the same silanetriol hydrolysis products are formed. In your analogue methodology you consider the formation and the properties of the hydrolysis products to be most relevant.

ECHA understands also that the basis of your hypothesis is the postulation that the hydrolysis of the parent substances is moderately rapid, leading to the formation of the same silanol hydrolysis products 3-(trihydroxysilyl)propanethiol, and ethanol and methanol. Furthermore, ECHA understands you to suggest that it is more relevant to test the source substance than the target due to source's shorter half-life. You also consider that the as the toxicity is driven by the thiol group which is still present after the hydrolysis, the hydrolysis rate is a secondary consideration.

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

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 and relevance of the proposed silananol hydrolysis product as the most relevant substance to be studied to determine the ecotoxic effects of the registered substance.

(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.

In the Ecotoxicity of thiols document you state that "*Detailed information on the purity/impurity profiles of the substances in the analogue group is not given in this report for reasons of commercial confidentiality. Substance-specific Substance Identity Profiles (SIPs) are available for all registered substances and these are included in the appropriate technical dossiers. In general, the substances in this group are typically mono-constituent substances of high purity (>90%). Typical impurities are other alkoxysilanes, thiols, alcohols or closely related substances. It is not expected that the specific identity of any impurities, or the small number of cases where the substances are multi-constituent, would impact upon the approaches used or the conclusions made in this report. In cases where a classified impurity is identified the implications of this will be described in the individual CSR(s).*" In the CSR of the target substance you state that its impurities are alkoxysilanes, siloxanes and alcohols present at 0-7 %, 0-7 % and 0-1 %, respectively.

In the new read-across justification report ([redacted] you provide more specific information on the purity of the source substance (>98% SIP purity, 95.5% purity of tested material in existing studies). However, you still maintain that the composition is considered confidential and provide further descriptions on the types of impurities you expect to be present in the target and in the source substances, i.e. organosilanes, siloxanes and alcohols, and why you consider them not to influence the prediction. However, only a general description and no clear information on the identity of the organosilanes and siloxanes impurities are given.

ECHA notes that the above general statements and the updated information on the purity of the source substance are not sufficient, for the following reasons. Firstly, the statement from the read-across justification is not supported by substance specific analysis of the possible differences in the composition and impurity profiles of the source and target substance and the impact they may have on the proposed prediction. Similarly the information provided in the CSR of the target substance is of generic nature. Secondly, ECHA notes that the source substance has not been registered under REACH, which prevents ECHA from assessing the relevant data contained therein. Finally, as already indicated by you, commercial confidentiality is at stake – which may also prevent ECHA from discussing with you the implications of potential substances' differences if it would be based solely on the data present in another registrant's dossier.

ECHA considers that currently the composition and the impurity profile of the source and target substances cannot be adequately compared using the information provided in the registration dossier. Therefore, ECHA cannot analyse the impact of the possible differences in the composition and impurity profiles that the source and target substances may have on the proposed prediction. Hence ECHA cannot reach a conclusion that 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 in this specific case that structural similarity *per se* is sufficient to enable the prediction of ecotoxicological properties of a substance, since structural similarity does not always lead to predictable or similar ecotoxicological 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 indicating that they are considered to be structural analogues and that both substances belong to *"the thiol analogue group"* which *"includes substances which contain a terminal thiol (SH) group present on a Silicon side chain. A methoxy, ethoxy or hydroxyl group will be attached directly to the silicone"*. You further state that their toxicity is driven by the thiol group.

ECHA notes that you state that the substances are *"structural analogues"* but at the same time acknowledge that they have differences in that they contain an exthoxy and methoxy group, respectively. Therefore, ECHA notes that in addition to the structural similarities, structural differences can be observed as the target substance has three ethoxy groups attached to the silicone whereas the source substance has three methoxy groups.

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 main silanol hydrolysis product 3-(trihydroxysilyl)propanethiol.

ECHA acknowledges that based on the structures of the two substances, the main hydrolysis product appears to be the same. However, ECHA observes that due to the described structural differences of target and source substances the silanol hydrolysis products formed from the parent substances are formed in different rates. You also acknowledge that *"the rate of hydrolysis is, however, highly dependent on the identity and the number of the groups and the pH of the test medium"* indicating that due to the structural differences, the hydrolysis rates may differ.

In addition, ethanol is formed in the hydrolysis of the target substance and methanol in the hydrolysis of the source substance. ECHA understands that you consider that methanol and ethanol *"are not hazardous at the concentrations relevant to the studies".*

ECHA has addressed the potential differences in hydrolysis rates and influence of the non-silanol hydrolysis products below in section (iii). The QSAR based hydrolysis information submitted by you to support your claims has been assessed by ECHA in section (iv) below.

In conclusion ECHA notes that you have not provided adequate information on how the structural differences in the parent substances affect the possibility to predict properties of the target substance from the data obtained with the source substance. Specifically, noting that the hydrolysis half-lifes may differ and the differences in the hydrolysis rates may impact the toxicity of the substances (see section iii below).

(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 structural 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 describe the physico-chemical parameters/properties of the target and the source substances and the main hydrolysis product. You state that the target substance has *"a log Kow value of 2.7, water solubility of 82 mg/l and a MW of 238.2",* whereas the source substance *"has a log Kow value of 1.7, water solubility of 2800 mg/l (predicted) and a MW of 196.3.".* With regards to the proposed hydrolysis product you state that *"The silanol hydrolysis product has a log Kow value of -1.4, is soluble in water (predicted) and has a MW of 154.2."* ECHA observes that the water solubility of the source substance is about 30 fold higher as that of the target substance, and logKow of the target substance is 1.3 log units higher than that of the source substance.

ECHA notes that you acknowledge the difference in the properties such as log Kow between the target and the hydrolysis product/source substance, but in your new read-across justification report submitted in the dossier update you consider that *"there is only a weak correlation between log Kow and thiol toxicity to fish. Hence, although there is a difference in log Kow between the registered substance and the silanol hydrolysis product, this is not considered to affect the validity of the read-across*". You state that this information is based on *"ECOSAR v.1.11 (2012)"* and *"in literature available in the public domain"* but give no further references or information. In your Analogue report: ecotoxicity of thiols you write that *"Log Kow is thought to affect toxicity to fish only in this analogue group, as indicated by the thiol and mercaptan Quantity Structure Activity Relationships (QSARs) for fish, invertebrates and algae (ECOSAR, 2011). The QSAR indicates that there is a good*

correlation between toxicity to fish and log Kow, but not for aquatic invertebrates and algae."

ECHA notes that your justification and mechanistic explanation for the relationship between logKow and toxic effects of thiols is unclear. ECHA understands that you imply any toxicity of thiols to be caused by the thiol group and that the ethoxy and methoxy groups present in the target and source substances, respectively, do not affect the prediction. ECHA notes that you have not provided reliable evidence/data to support this claim.

However, ECHA notes that in general, existence of differences in physicochemical and degradation properties between source and target substances, or hydrolysis product and the target substance, indicate the likelihood of differences in bioavailability and bioaccumulation potential, and consequently in the degree of toxic effects. In particular, based on the information provided in the new read-across justification report you expect the target substance to hydrolyse slower than the source substance. Considering that the test organisms would be exposed to the parent substances (and potentially longer to the target substance due to expected slower hydrolysis), the potential effects of the parent substances should be considered in your read-across justification (as per RAAF[2], Scenario 1, AE 1.3 and 1.4). However, you do not account for that. ECHA further notes that the information on hydrolysis half-lives for the target and source substances reported in the new read-across justification report includes some uncertainties which further hampers the comparison of the duration of exposure to the parent substances (see section (iv) below).

Furthermore, in the Ecotoxicity of thiols document you on one hand consider that *"Hydrolysis rate is a secondary consideration when choosing surrogate substances because the toxicity is driven by the thiol group which is still present even after hydrolysis has taken place"*, but at the same time state that with regards to any difference in ecotoxic effects between ethoxy and methoxysilanes the differences in hydrolysis rates should be considered. However, without valid hydrolysis data (see section (iv) below) it is not possible to compare the rates and the impact their difference may have on the property to be predicted.

With regards to aquatic toxicity you acknowledge that *"No data are available for the submission substance, 3-(triethoxysilyl)propanethiol"* and that *"reliable test data are available for a structurally analogous substance 3-trimethoxysilylpropane-1-thiol (CAS 4420-74-0)."* ECHA observes that there are no short- or long-term toxicity data provided in the technical dossier for the target substance. The data provided for Short-term aquatic toxicity on fish and Daphnia and Toxicity to aquatic algae study and Toxicity to aquatic microorganisms study has all been carried out on the source substance. In absence of any ecotoxicological data on the target substance it is not possible to exclude the possibility that the effects would not be influenced by the exposure to the parent substances and thus to validate your claim of similar ecotoxicological properties.

In summary, 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 regarding aquatic toxicity. 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.

[2] Read-Across Assessment Framework (RAAF)
https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

(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 moderately rapid hydrolysis and they form the same main silanol hydrolysis product, 3-(trihydroxysilyl)propanethiol. You propose in your CSR 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".* In your read-across justification you consider further that *"Long-term exposure will be mostly relevant to the hydrolysis products of the substances rather than the parent substances because of their moderately fast hydrolysis rates and retention time in the WWTP"*.

You have provided the hydrolysis half life values in the new read-across justification document (19h for the target, 2.6h for the source substance in pH 7). ECHA observes that hydrolysis half-lifes are based on assumptions which are not substantiated by valid data. ECHA notes that in IUCLID section 5.1.2. you have submitted one endpoint study record (ESR) for the hydrolysis of the target substance based on QSAR predictions (19h half life in pH of 7). In the updated dossier you have submitted documentation (QMRF and QPRF) for this hydrolysis prediction. ECHA however notes that the QMRF and QPRF documentation does not include the training set of the QSAR model and therefore it cannot be confirmed that the target substance falls within the applicability domain of the model used. In addition to QSAR estimation, in the updated dossier you have also indicated to perform a new experimental hydrolysis study according to OECD TG 111. ECHA acknowledges that a conduct of the hydrolysis study according to OECD TG 111 would provide reliable information on the hydrolysis half life for the target substance, which is currently not available.

ECHA notes that information on the hydrolysis of the source is merely described in the endpoint summary text. As no further information on the QSAR prediction of the hydrolysis of the source substance is provided ECHA is not able to assess its acceptability.

Consequently, ECHA considers that the QSAR predictions provided to support your claim of moderately fast hydrolysis cannot be accepted. In the light the criteria established in Section 1.3. of Annex XI to the REACH Regulation, adequate and reliable documentation of the applied method should be provided in order to support the predictions. ECHA notes that no adequate and reliable documentation of the applied method is provided and consequently it is not clear whether the substances fall within the applicability domain of the (Q)SAR models. Therefore ECHA considers that your postulation that the hydrolysis of the parent substances is moderately rapid, leading to the formation of the same silanol hydrolysis products 3-(trihydroxysilyl)propanethiol, and ethanol and methanol is not evidenced by data and cannot be accepted.

Finally in the initial draft decision, ECHA noted that you have not addressed adequately how the formation of the non-silanol hydrolysis products influences the prediction. In the new read-across justification document submitted in the dossier update, you state that methanol and ethanol would not significantly affect the results of the tests (*"the short-term EC50 and LC50 values for these substances are in excess of 1000 mg/l (OECD 2004a - SIDS for methanol, CAS 67-56-1, OECD 2004b - SIDS for ethanol, CAS 64-17-5)."* ECHA acknowledges that these hydrolysis product likely do not influence the prediction.

In summary, ECHA considers that given the lacking evidence on the rate of formation of the hydrolysis products, your hypothesis cannot be confirmed. Therefore, 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 environmental 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 and the current read-across data provided for aquatic endpoints is not appropriate to fulfil the information requirements of the substance subject to the present decision.

The decision of ECHA is based on the examination of the testing proposals submitted by you and scientific information submitted by third parties.

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

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

A sub-chronic toxicity study (90 day) is a standard information requirement as laid down in Annex IX, Section 8.6.2. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

You have submitted a testing proposal for a sub-chronic toxicity study (90 day) in rats by the oral route according to EU B.26/OECD TG 408.

ECHA notes that in the updated dossier you provided your considerations for alternative methods to fulfil the information requirement for Sub-chronic toxicity (90-day): oral. You concluded that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

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 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 7 mg/m^3). Hence, the test shall be performed by the oral route using the test method EU B.26./OECD TG 408.

You proposed testing in rats. 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 your comments to the draft decision you did not provide considerations to this specific endpoint.

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

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)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

A pre-natal developmental toxicity study for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

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

ECHA notes that in the updated dossier you provided your considerations for alternative methods to fulfil the information requirement for Reproductive toxicity (pre-natal developmental toxicity). You concluded that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

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

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

In your comments to the draft decision you did not provide considerations to this specific endpoint.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study with the registered substance subject to the present decision: Pre-

natal developmental toxicity study in a first species (rats or rabbits), oral route (test method: EU B.31/OECD TG 414).

Notes for your consideration

For the selection of the appropriate species you are advised to consult ECHA *Guidance on information requirements and chemical safety assessment* (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).

3. In vivo mammalian alkaline comet assay (Annex IX, Section 8.4., column 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.

"Mutagenicity" is an information requirement as laid down in Annex VIII, Section 8.4. of the REACH Regulation. Column 2 of Annex IX, Section 8.4. provides that "If there is a positive result in any of the *in vitro* genotoxicity studies in Annex VII or VIII and there are no results available from an *in vivo* study already, an appropriate *in vivo* somatic cell genotoxicity study shall be proposed by the Registrant."

The technical dossier contains an *in vitro* study *In vitro* Mammalian Cell Gene Mutation Assay (Thymidine Kinase Locus/TK+/-) in Mouse Lymphoma L5178Y Cells with 3-(triethoxysilyl)propanethiol performed according to *OECD Guideline 476 (In vitro Mammalian Cell Gene Mutation Test)* with the registered substance that show positive results without metabolic activation. In addition, an increase in the number of small colonies was observed without metabolic activation, suggesting a clastogenic effect. The positive results indicate that the substance is inducing gene mutations and chromosomal aberrations under the conditions of the test.

An appropriate *in vivo* genotoxicity study to follow up the concern on gene mutations and chromosomal aberrations is not available for the registered substance but shall be proposed by the Registrant.

Hence, you have submitted a testing proposal for a OECD TG 474 (mammalian erythrocyte micronucleus test) in rat by oral administration.

You did not specify the species to be used for testing. You did not specify the route for testing.

ECHA notes that in the updated dossier you provided your considerations for alternative methods to fulfil the information requirement for Genetic toxicity in vivo. You concluded that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

Following proposals for amendment (PfAs) from one of the Member State Competent Authorities (MSCAs) it was noted that the proposed study is not an appropriate test to further investigate effects seen with the registered substance. Specifically, due to the high reactivity of the substance there is a concern for chromosomal aberrations in the initial site of contact tissues, which cannot be evaluated by performing a Mammalian Erythrocyte Micronucleus Test (OECD TG 474), since the latter only measures effects in the bone marrow (distant tissue). If you perform a Mammalian Erythrocyte Micronucleus Test (OECD TG 474), the concern for gene mutation as well as the concern for chromosomal aberrations in initial sites of contact will not be clarified. Also, as described in the ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017), a Mammalian Erythrocyte Micronucleus Test (OECD TG 474) investigates effects on chromosome aberrations and does not address gene mutations *in vivo*. For all the above reasons, the Mammalian Erythrocyte Micronucleus Test (OECD TG 474) is not an appropriate test, and so your testing proposal is rejected.

In view of the above concerns, ECHA considers that according to the ECHA Guidance on information requirements and chemical safety assessment R.7a, chapter R.7.7.6.3 (version 6.0, July 2017), the *in vivo* mammalian alkaline comet assay (OECD TG 489) is the suitable study to follow up the positive result *in vitro* showing gene mutation and chromosomal aberrations for substances of high reactivity. The *in vivo* mammalian alkaline comet assay is appropriate to address the concerns noted in the positive *in vitro* study (OECD TG 476). Moreover, it enables the generation of information regarding potential genotoxic effects at the site of contact.

According to the test method OECD TG 489, the comet assay shall be performed in rats. Having considered the anticipated routes of human exposure and adequate exposure of the target tissue(s), performance of the comet assay by the oral route is appropriate.

In line with the test method OECD TG 489, the test shall be performed by analysing tissues from liver as primary site of xenobiotic metabolism; glandular stomach and duodenum as sites of contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the substance, and probable different local absorption rates of the substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to analyse both tissues to ensure a sufficient evaluation of the potential for genotoxicity at the site of contact in the gastro-intestinal tract.

In your comments to the draft decision you did not provide considerations to this specific endpoint.

b) Consideration of the information received during third party consultation

ECHA received third party information concerning the testing proposal during the third party consultation.

Third party information 1: "As evidence both for gene mutations and clastogenic effects is reported the in vivo mammalian alkaline Comet assay according to the recently adopted OECD Test Guideline 489 could be an appropriate alternative to the mammalian erythrocyte micronucleus test. For animal welfare and economic reasons genotoxicity testing should preferably be incorporated into the proposed oral 90-day repeated dose toxicity study."

In the third party comments it was proposed that the comet assay should be performed instead of a micronucleus assay. As explained above, following a PfA from one of the

MSCAs, ECHA has agreed to request only the *in vivo* mammalian alkaline comet assay (OECD 489). As regards combining this assay to a repeated dose toxicity study you may consider this option (see "*Notes for your consideration*").

c) Outcome

You are requested to carry out, pursuant to Article 40(3)(c) of the REACH Regulation the additional study with the registered substance subject to the present decision:

In vivo mammalian alkaline comet assay (test method: OECD TG 489) in rats, oral route, on the following tissues: liver, glandular stomach and duodenum.

While your originally proposed test for a Mammalian Erythrocyte Micronucleus Test (OECD TG 474) is rejected according to Article 40(3)(d) of the REACH Regulation.

d) *Notes for your consideration*

Germ cell testing

You are reminded that according to Annex IX, Section 8.4., column 2 of the REACH Regulation, if positive results from an *in vivo* somatic cell study are available, "the potential for germ cell mutagenicity should be considered on the basis of all available data, including toxicokinetic evidence. If no clear conclusions about germ cell mutagenicity can be made, additional investigations shall be considered".

You may consider examining gonadal cells, as it would optimise the use of animals. ECHA notes that a positive result in whole gonads is not necessarily reflective of germ cell damage since gonads contain a mixture of somatic and germ cells. However, such positive result would indicate that the substance and/or its metabolite(s) have reached the gonads and caused genotoxic effects. This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

Combining a comet assay with a repeated dose toxicity test

You may consider to combine a comet assay with a repeated dose toxicity study as long as this will not impair the validity of and the results from each individual study.

Hence, if you decide to combine both assays you should consider a number of practical aspects, which may prove challenging, such as (i.) the selection of dosing, which should use the maximum tolerated dose (as defined in OECD TG 489, para.36) or maximum (limit) dose, and which should avoid administration via feed or drinking water (OECD TG 489, para. 12 and Annex 3(2)); (ii.) historical control values should take into account the different age of test animals; (iii.) careful consideration should be given to the tissue sampling for comet analysis alongside the requirements of tissue sampling for other types of toxicological assessments; harvesting 24 hours after the last dose, which is typical of a general toxicity study, is not appropriate for the comet assay where samples are usually collected 2-6 h after the last treatment (see OECD TG 489, para. 33); and (iv) address OECD TG 489 para. 34.

4. and 5. Long-term aquatic toxicity testing on invertebrates and fish (Annex IX, Sections 9.1.5 and 9.1.6.)

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.

"Long-term toxicity testing on aquatic invertebrates" and "Long-term toxicity testing on fish" are standard information requirements as laid down in Annex IX, Section 9.1.5. and Section 9.1.6. of the REACH Regulation.

In the submission based on which the initial draft decision was prepared on (submission number [redacted] you submitted a testing proposal for testing the analogue substance 3-(trimethoxysilyl)propane-1-thiol (EC no 224-588-5) for long-term toxicity testing on aquatic invertebrates (*Daphnia magna* reproduction test, EU C.20/OECD TG 211). ECHA rejected the read-across testing proposed for the reasons described in Section 0 to this document and required testing on the registered substance.

With regards to long-term toxicity testing on fish, you initially sought to adapt the information requirement according to Annex IX, Section 9.1.6., column 2. ECHA considered your adaptation based on Chemical Safety Assessment not acceptable and additionally requested testing of fish conditional to the outcome of the other aquatic toxicity studies requested.

In the updated dossier (submission number [redacted]) although you have unticked the box for the testing proposal on aquatic invertebrates you have stated that: "*This information will be submitted later based on ECHA draft decision, communication number TPE-D-2114331354-58-01/D*". ECHA understands that you aknowlegde that further data has to be generated for this endpoint and you have an intention to do so. ECHA continues the decision making to authorise you to do such testing (as further explained in footnote 1).

You have also indicated the following for both long-term aquatic information requirements: "*A stepwise testing strategy is proposed to address the requirements. Please refer to the attachment in Section 13. The PNEC may be revised once further data are available.*"

In this document, you propose to conduct an experimental hydrolysis study according to OECD TG 111 on the registered substance, and based on that you propose various ways how to fulfil ecotoxicological information requirements addressed in this decision.

First, ECHA understands that you intend to focus the chemical safety assessment solely on hydrolysis products in case the hydrolysis half-life is lower than 12 hours. ECHA notes that ECHA Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017) refers to recommendations of the OECD Guidance Document 23 (Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures) by which the parent compound should be considered when the Disappearance Time 50 (DT50) is higher than 3 days, and the breakdown products for DT50 lower than 1h and case-by-case basis for anything in between.

Based on the current information on hydrolysis half life of the registered substance and the advice given in OECD GD 23, the registered substance requires case-by-case consideration when deciding whether to test the parent substance and/or hydrolysis products. ECHA considers that the 12 hour threshold you proposed to follow for choosing the parent or the hydrolysis products for testing is not appropriate but case specificity must be considered (e.g. the hazard profile of the registered parent substance).

Second, ECHA notes that the hydrolysis study you proposed to conduct is not yet available and therefore analysis of the testing strategy cannot be currently made.

With regards to long-term toxicity testing on fish, in the testing strategy document you indicate that you will consider the results from short-term tests according to OECD TGs 202 and 203/236, and if the invertebrate EC50 is substantially lower (factor of at least 10, expected outcome) then propose to waive long term toxicity testing on fish. ECHA notes that currently there is no reliable information relevant for the registered substance (see requests 6-8) that would allow to reach such a conclusion. ECHA notes that the prediction of relative species sensitivity based on studies with the analogue substance (CAS 4420-74-0) cannot be made due to several deficiencies of the read-across approach, as described in Section 0 of this decision.

In summary, currently the information on these endpoints are not available for the registered substance but need to be present in the technical dossier to meet the information requirements. Consequently, there are information gaps and it is necessary to provide information for these endpoints.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 3.0, February 2016) *Daphnia magna* reproduction test (test method EU C.20. / OECD TG 211) is the preferred test to cover the standard information requirement of Annex IX, Section 9.1.5.

ECHA considers that for the endpoint of long-term toxicity testing on fish pursuant to Annex IX, section 9.1.6., the FELS toxicity test according to OECD 210 is the most sensitive of the standard fish tests available as it covers several life stages of the fish from the newly fertilised egg, through hatch to early stages of growth and should therefore be used (see ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, February 2016), Chapter R7b, Figure R.7.8-4). For these reasons, ECHA considers the FELS toxicity test using the test method OECD 210 as appropriate and suitable.

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, you are required to carry out the following additional studies using the registered substance subject to the present decision:

- Long-term toxicity testing on aquatic invertebrates (Annex IX, 9.1.5.; test method: *Daphnia magna* reproduction test, EU C.20/OECD 211) and
- Fish, early-life stage (FELS) toxicity test (Annex IX, 9.1.6.1.; test method: Fish, early-life stage toxicity test, OECD 210).

  while your originally proposed *Daphnia magna* reproduction test (EU C.20/OECD TG 211), using analogue substance 3-(trimethoxysilyl)propane-1-thiol (EC no 224-588-5) is rejected according to Article 40(3)(d) of the REACH Regulation.

6. Growth inhibition study on aquatic algae and cyanobacteria (Annex VII, Section 9.1.2.)

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

"Growth inhibition study aquatic plants" is a standard information requirement regarding aquatic toxicity as laid down in Annex VII, Section 9.1.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a Algal inhibition test (EU Method C.3) with the analogue substance 3-(trimethoxysilyl)propane-1-thiol (EC no 224-588-5). However, as explained above in Appendix 1, Section 0 of this decision, your adaptation of the information requirement for aquatic endpoints cannot be accepted. Furthermore, there are doubts about the validity of the study itself due to a high initial cell count.

In addition to the read-across data submitted for this endpoint, in the updated dossier you provided a testing strategy document wherein you indicate your plan to perform experimental hydrolysis study and depending on the result consolidate the read-across justification and consider the need to perform a growth inhibition study according to OECD TG 201. ECHA notes however that currently the results of the experimental hydrolysis study on the registered substance are not yet available and therefore assessment of the testing strategy cannot be currently made (see requests 4-5). Also, there are deficiencies identified in your read-across approach as explained in Section 0 of this decision which currently prevent prediction of the relevant property from the source data to the target substance.

According to ECHA *Guidance on information requirements and chemical safety assessment* (May 2008), Chapter R10 (Section R.10.3.1 including Table R.10-4), in order to derive PNECaquatic, it is necessary to provide at least one short-term L(E)C50 from each of the three trophic levels: Primary producers (plants), represented by algae; plant eating animals, represented by invertebrates (e.g. *Daphnia*) and predators, represented by fish.

Therefore, 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.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 2.0, November 2014) Algae growth inhibition test (test method EU C.3. / OECD TG 201) is the preferred test to cover the standard information requirement of Annex VII, Section 9.1.2.

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, you are required to carry out the additional study using the registered substance subject to the present decision: Algae growth inhibition test, EU C.3./OECD TG 201.

7. and 8. Short-term aquatic toxicity testing on invertebrates and fish (Annex VII, Section 9.1.1. and Annex XI Section 9.1.3.)

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

"Short-term toxicity testing on aquatic invertebrates" and "Short-term toxicity testing on fish" are standard information requirements as laid down in Annex VII, Section 9.1.1. and Annex VIII, Section 9.1.3. of the REACH Regulation, respectively. Adequate information on these endpoints need to be present in the technical dossier for the registered substance to meet these information requirements.

You have sought to adapt these information requirements according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for Acute Toxicity for Daphnia (EU Method C.2) and Acute Toxicity for Fish (EU Method C.1) with the analogue substance 3-(trimethoxysilyl)propane-1-thiol (EC no 224-588-5). However, as explained above in

Appendix 1, section 0 of this decision, your adaptation of the information requirement for aquatic endpoints cannot be accepted. Furthermore, due to instability of the source substance and lack of analytical monitoring it is unclear what organisms were exposed to.

In addition to the read-across data submitted for this endpoint, in the updated dossier you provided a testing strategy document wherein you indicate your plan to perform experimental hydrolysis study and depending on the result consolidate the read-across justification and consider the need to perform short-term toxicity studies according to OECD TG 202 and 203. ECHA notes however that currently the results of the experimental hydrolysis study on the registered substance are not yet available and therefore assessment of the testing strategy cannot be currently made (see requests 4-5). Also, there are deficiencies identified in your read-across approach as explained in Section 0 of this decision which currently prevent prediction of the relevant property from the source data to the target substance.

With regards to your intention to perform a test according to OECD TG 236 instead of 203, ECHA notes that currently results obtained from a study performed according to the guideline OECD 236 alone are not considered to fulfil standard information requirement on short-term toxicity testing on fish. As reported in the ECHA commissioned study on "Analysis of the relevance and adequateness of using Fish Embryo Acute Toxicity test (FET) Test Guideline (OECD 236) to fulfil the information requirements and addressing concerns under REACH", published on ECHA website May 2016, there is a lack of evidence to indicate that the embryo toxicity would not underestimate the toxicity to juvenile/adult fish. Results from an OECD TG 236 test may be used in a Weight of Evidence approach, and would require other lines of evidence to conclude on acute fish toxicity. A study performed according to the OECD TG 203 is considered relevant to address information requirement on short-term toxicity to fish.

According to ECHA *Guidance on information requirements and chemical safety assessment* (May 2008), Chapter R10 (Section R.10.3.1 including Table R.10-4), in order to derive PNECaquatic, it is neccesary to provide at least one short-term L(E)C50 from each of the three trophic levels: Primary producers (plants), represented by algae; plant eating animals, represented by invertebrates (e.g. *Daphnia*) and predators, represented by fish.

Therefore, the information on these endpoints are not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently, there are information gaps and it is necessary to provide information for these endpoints.

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, you are required to carry out the following additional studies using the registered substance subject to the present decision:

- *Daphnia* sp. Acute immobilisation test, EU C.2./OECD TG 202).
- Fish, acute toxicity test (test method: EU C.1./OECD TG 203).

Notes for consideration in relation to aquatic toxicity testing (sections 4-8 above)

Pursuant to column 2 of Annex VII, Section 9.1.1. and Annex VIII, Section 9.1.3. the short-term toxicity testing on invertebrates and fish need not be conducted if a long-term study on invertebrates and fish, respectively, is available. Thus the Registrant may choose to perform the long-term toxicity on fish (Annex IX, 9.1.6.1.; test method: Fish, early-life stage toxicity test, OECD 210) and long-term toxicity testing on aquatic invertebrates (Annex IX, 9.1.5.; test method: *Daphnia magna* reproduction test, EU C.20/OECD 211) and waive the short-term toxicity on invertebrates and fish.

You have indicated in your testing strategy document that you intend to adapt the information requirement on long-term toxicity testing on fish, based on the results from short-term tests and the following comparison on species sensitivity. ECHA acknowledges that according to the Integrated Testing Strategy (ITS) described in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R7b (Section R.7.8.5., including Figure R.7.8-4) if there is compelling evidence to suggest that the fish value is at least a factor of about 10 less sensitive than invertebrates or algae there are no further requirements for fish testing.

Furthermore if based on reliable acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially more sensitive, long-term studies may be required on both. In such case, according to the ITS, the *Daphnia* study is to be conducted first. If based on the results of the long-term *Daphnia* study and the application of a relevant assessment factor, no risks are observed (PEC/PNEC<1), no long-term fish testing may need to be conducted. However, if a risk is indicated, the long-term fish study needs to be conducted.

Appendix 2: Procedural history

ECHA received your registration containing the testing proposal(s) for examination pursuant to Article 40(1) on 29 April 2013.

ECHA held a third party consultation for the testing proposal(s) from 16 October 2014 until 1 December 2014. ECHA received information from third parties (see Appendix 1).

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.

You were notified that the draft decision does not take into account any updates after 6 July 2016, 30 calendar days after the end of the commenting period.

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 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.

ECHA received proposals for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendments.

ECHA referred the draft decision to the Member State Committee.

You did not provide any comments on the proposed amendment(s).

The Member State Committee reached a unanimous agreement on the draft decision during its MSC-60 meeting and ECHA took the decision according to Article 51(6) 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.