~~Confidential~~

Helsinki, 5 May 2022

Addressees
Registrants of RECONSILE EC# 240-816-6 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
11/03/2016

Registered substance subject to this decision ("the Substance")
Substance name: Dimethoxymethylvinylsilane
EC number: 240-816-6

Decision number: Please refer to the REACH-IT message which delivered this communication (in format CCH-D-XXXXXXXXXX-XX-XX/F)

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***10 August 2023***.

Requested information must be generated using the Substance unless otherwise specified.

Information required from all the Registrants subject to Annex VII of REACH

1. Skin sensitisation (Annex VII, Section 8.3.; test method: in vivo skin sensitisation (Annex VII, Section 8.3.2.; test method: EU B.42./OECD TG 429)

The reasons for the decision(s) are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The addressees of the decision and their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

You are only required to share the costs of information that you must submit to fulfil your information requirements.

How to comply with your information requirements

To comply with your information requirements, you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also **update the chemical safety report, where** relevant, including any changes to classification and labelling, based on the newly generated information.

You must follow the general requirements for testing and reporting new tests under REACH, see Appendix 4.

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to

http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

Authorised[1] under the authority of Mike Rasenberg, Director of Hazard Assessment

Appendix 1: Reasons for the decision
Appendix 2: Procedure
Appendix 3: Addressees of the decision and their individual information requirements
Appendix 4: Conducting and reporting new tests under REACH

[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 for the decision

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Reasons related to the information under Annex VII of REACH

1. Skin sensitisation

1 Skin sensitisation is an information requirement under Annex VII to REACH (Section 8.3.). Under Section 8.3., Column 1, the registrants must submit information allowing (1) A) a conclusion whether the substance is a skin sensitiser and B) whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A), and (2) risk assessment, where required.

1.1. Information provided

2 You have adapted this standard information requirement according to Annex XI, Section 1.2. of REACH (weight of evidence). In support of your adaptation, you have provided the following sources of information:

(i) guinea pig maximisation test according to [redacted] 1970 (1988) with triethoxy(vinyl) silane, EC No. 201-081-7

(ii) guinea pig maximisation test (2000) with trimethoxy(vinyl)silane, EC No. 220-449-8.

3 Based on the presented sources of information, you argue that the available data gives sufficient information to conclude on the non skin sensitising property of the Substance because these are reliable data from related aloxysilanes, which have similar toxicological properties, being structurally similar and hydrolysing to similar silane-containing hydrolysis products. They are therefore "*read across as weight of evidence.*"

1.2. Assessment of the information provided

4 We have assessed this information and identified the following issues:

1.2.1. Assessment whether the Substance causes skin sensitisation

5 Annex XI, Section 1.2 states that there may be sufficient weight of evidence weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

6 According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude that the Substance has or has not the (dangerous) property investigated by the required study.

7 Annex XI, section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence adaptation.

8 You provide summaries of studies (i. and ii) in IUCLID endpoint study records. In those summaries you briefly present each of the sources of information, describe the results and conclude in the endpoint summary that this information can be used as weight of evidence to predict the toxicological properties of the Substance for skin sensitisation.

9 However, whilst these reports can be regarded as integrated summaries of the data sets, your justification does not include any explanation why the sources of information provide

sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

10 Irrespective of the above mentioned deficiencies on the documentation, which in itself could lead to the rejection of the adaptation, ECHA has assessed the provided sources of information.

11 Relevant information that can be used to support weight of evidence adaptation for the information requirements of Section 8.3 at Annex VII includes similar information to that investigated by the internationally recognised in vitro, in chemico and/or in vivo test methods on skin sensitisation. The key investigations of such test methods address each of the 3 key events of skin sensitisation, either individually or in an integrated approach as follows:

1. investigation of cell proliferation in the draining lymph nodes (local lymph node assay), or
2. investigation of local responses in animals or humans (guinea pig assays or human studies), or
3. investigation of molecular interaction with proteins, inflammatory response in keratinocytes and activation of dendritic cells (in vitro and in chemico assays).

12 The sources of information (i. and ii.) provide relevant information on skin sensitisation, as they investigate local responses in animals (guinea pig assays).

13 However, the studies (i.-ii.) have the following deficiencies affecting their reliable contribution to the weight of evidence approach.

1.2.1.1. Reliability of the information with analogue substances

14 ECHA understands that you intend to predict the toxicological properties of the Substance for skin sensitisation from data obtained with source substances in a read-across analogue approach, as part of the weight of evidence approach.

1.2.1.1.1. Grouping of substances and read-across approach

15 Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group.

16 Additional information on what is necessary when justifying a read-across approach can be found in the Guidance on IRs and CSA, Chapter R.6. and related documents (RAAF, 2017; RAAF UVCB, 2017).

17 You provide a read-across justification in IUCLID Section 7.4 under the endpoint summary.

18 You predict the properties of the Substance from information obtained from the source substances triethoxy(vinyl) silane, EC No. 201-081-7 (source substance 1) and trimethoxy(vinyl)silane, EC No. 220-449-8 (source substance 2).

19 You provide the following reasoning for the prediction of toxicological properties: *"source and target substances have similar toxicological properties because they are structurally similar and hydrolyse to similar silicon-containing hydrolysis products. The non-silanol hydrolysis products, methanol and ethanol, do not contribute to any adverse effects for sensitisation at the relevant concentrations based on publicly available information"*.

20 ECHA understands that your read-across hypothesis assumes that different compounds have the same type of effects. You predict the properties of your Substance to be quantitatively equal to those of the source substance.

21 We have identified the following issues with the predictions of toxicological properties:

Missing supporting information

22 Annex XI, Section 1.5 of the REACH Regulation states that "physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)". For this purpose "it is important to provide supporting information to strengthen the rationale for the read-across" (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.). The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

23 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar substances cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary to confirm that both substances cause the same type of effects.

24 For the source substances, you provide the experimental skin sensitisation studies, with negative results, used in the prediction in the registration dossier. Furthermore, you provide information on the hydrolysis of the Substance (to methylvinylsilanediol and methanol) and estimated half-lives for the hydrolysis of the source substances to vinylsilanetriol and ethanol (source substance 1), vinylsilanetriol and methanol (source substance 2), to show that the hydrolysis "*at physiological pH [is] generally comparable*", in order to support your similarity argument. You state that "*during dermal exposure similar levels of parent and hydrolysis products will be present and so read-across from triethoxy(vinyl)silane and trimethoxy(vinyl)silane to dimethoxy(methyl)vinylsilane for sensitisation is valid*".

25 The Substance and source substances all contain a vinylsilane core structure. However, the Substance and sources substances differ structurally in the number of methoxy/ethoxy groups bound to the silicon as well as in the additional methyl group for the Substance. Despite potentially having similar hydrolysis properties, they form non-common hydrolysis products. The non-common silicon-containing hydrolysis products are methylvinylsilanediol for the Substance and vinylsilanetriol for the source substances, which differ structurally, in analogy to the substances.

26 You consider that the substances have similar properties for skin sensitisation despite these structural differences. However, your read-across justification or the registration dossier does not include data that address the impact of these differences on the properties and would explain why the structural differences between the substances do not influence the toxicological properties.

27 Furthermore, ECHA notes that the source substance 2 has a harmonised classification as Skin sensitiser Cat 1B, while source substance 1 is not classified as skin sensitiser. You do not provide any explanation why this information has been disregarded and not taken into account in the prediction of the toxicological properties of the Substance from the toxicological properties of source substance 2. This difference in the toxicity profiles of the substances seems to contradict your read-across hypothesis whereby the substances have similar non-sensitising properties.

28 You have not established that the Substance and the source substances are likely to have similar properties. You have not provided sufficient supporting information to strengthen the rationale for the read-across.

29 In the absence of reliable read-across from analogue substances, the properties of your Substance cannot be predicted from the data on the analogue substances. Therefore, the information from the analogue substances submitted under your weight-of-evidence adaptation is not considered reliable and does not contribute to the weight of evidence adaptation.

1.2.1.1.2. Reliability of the study on the source substance (study ii.)

30 The evaluation of the reliability of the contribution of each relevant line of information to the weight of evidence approach includes an assessment of each source of information against the specifications of the test guideline followed.

31 The OECD TG 406 test guideline specifies that the induction concentration should be the highest causing mild-to-moderate irritation to the skin and the challenge dose should be the highest non-irritation concentration.

32 In the provided source study (ii), which was conducted following the OECD TG 406, the doses used for induction and challenge were the same (5% in mineral oil), but no mild-to-moderate irritation was noted in the topical induction.

33 In the study, there were solubility issues with the source substance in mineral oil, as also stated in the opinion of the Committee for Risk Assessment (RAC)[2]: "A primary irritation study was performed […]. The 5% intradermal concentration caused mild/moderate irritation and was therefore used as induction dose. For dermal application, 5% in mineral oil was chosen for both topical induction and challenge doses. The selection of topical doses is not according to OECD TG 406 recommendations, but higher concentrations than 5% of [the Substance] in mineral oil resulted in what was described as "polymerisation" of the test substance." ECHA notes however that studies done on the same source substance with other oil based vehicles did not have solubility issues, as indicated in the RAC report.

34 Because of the solubility issues of the source substance in the vehicle, the selection of topical doses is lower than specified in the OECD TG 406. Therefore the study does not provide reliable information for hazard identification because too low doses have been used which might lead to underestimation of the hazard.

35 Based on the above, the reliability of the contribution of the results obtained from this study to the weight of evidence is limited.

1.2.1.2. Conclusion on the weight of evidence

36 All the source of information (i.-ii.) provide relevant information, as they investigate local effects in animals (guinea pig assays).

37 However, as a result of the deficiencies described in section 1.2.1.1 above, the information provided with the source substances in the read-across approach cannot reliably contribute to the weight of evidence approach.

38 Therefore, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in skin sensitisation studies.

39 Therefore, your adaptation is rejected and the information requirement is not fulfilled.

1.2.2. No assessment of potency

[2] Committee for Risk Assessment, RAC. Opinion proposing harmonised classification and labelling at EU level of trimethoxyvinylsilane; trimethoxy(vinyl)silane. EC Number: 220-449-8; CAS Number: 2768-02-7. CLH-O-0000001412-86-214/F. Adopted 8 June 2018

40 To be considered compliant and enable a conclusion in cases where the substance is considered to cause skin sensitisation, the information provided must also allow a conclusion whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

41 As the currently available data does not allow to conclude whether the Substance causes skin sensitisation (see section 1.2.1 above), this condition cannot be assessed.

42 On this basis, the information requirement is not fulfilled.

1.3. Specification of the study design

43 An *in vivo* skin sensitisation test is required, as the intrinsic properties of the Substance cannot be investigated using the currently available *in vitro/in chemico* methods. The Substance is expected to hydrolyse under the conditions of the *in vitro* tests. The results from these *in vitro* test would then be anticipated to inform on the properties of the hydrolysis products of the Substance rather than on the properties of the Substance.

44 Therefore, to fulfil the information requirement for the Substance an *in vivo* skin sensitisation study must be performed and the murine local lymph node assay (EU Method B.42/OECD TG 429) is considered as the appropriate study for the potency estimation.

45 In the comments to the draft decision, you agree to perform the requested study.

References

The following documents may have been cited in the decision.

Guidance on information requirements and chemical safety assessment (Guidance on IRs & CSA)

Chapter R.4 Evaluation of available information; ECHA (2011).
Chapter R.6 QSARs, read-across and grouping; ECHA (2008).
Appendix to Chapter R.6 for nanoforms; ECHA (2019).
Chapter R.7a Endpoint specific guidance, Sections R.7.1 – R.7.7; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Chapter R.7b Endpoint specific guidance, Sections R.7.8 – R.7.9; ECHA (2017).
Appendix to Chapter R.7b for nanomaterials; ECHA (2017).
Chapter R.7c Endpoint specific guidance, Sections R.7.10 – R.7.13; (ECHA 2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Appendix R.7.13-2 Environmental risk assessment for metals and metal compounds; ECHA (2008).
Chapter R.11 PBT/vPvB assessment; ECHA (2017).
Chapter R.16 Environmental exposure assessment; ECHA (2016).

Guidance on data-sharing; ECHA (2017).

All Guidance on REACH is available online: https://echa.europa.eu/guidance-documents/guidance-on-reach

Read-across assessment framework (RAAF)

RAAF, 2017 Read-across assessment framework (RAAF), ECHA (2017)
RAAF UVCB, 2017 Read-across assessment framework (RAAF) – considerations on multi- constituent substances and UVCBs), ECHA (2017).

The RAAF and related documents are available online:
https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

***OECD Guidance documents* (OECD GDs)**

OECD GD 23 Guidance document on aquatic toxicity testing of difficult substances and mixtures; No. 23 in the OECD series on testing and assessment, OECD (2019).
OECD GD 29 Guidance document on transformation/dissolution of metals and metal compounds in aqueous media; No. 29 in the OECD series on testing and assessment, OECD (2002).
OECD GD 150 Revised guidance document 150 on standardised test guidelines for evaluating chemicals for endocrine disruption; No. 150 in the OECD series on testing and assessment, OECD (2018).
OECD GD 151 Guidance document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test; No. 151 in the OECD series on testing and assessment, OECD (2013).

Appendix 2: Procedure

This decision does not prevent ECHA from initiating further compliance checks at a later stage on the registrations present.

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

The compliance check was initiated on 04 June 2021.

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

In your comments you agreed to the draft decision. ECHA took your comments into account and did not amend the request.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

Appendix 3: Addressees of this decision and their corresponding information requirements

In accordance with Articles 10(a) and 12(1) of REACH, the information requirements for individual registrations are defined as follows:

- the information specified in Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa;
- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa;
- the information specified in Annexes VII to X to REACH, for registration at more than 1000 tpa.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.

Appendix 4: Conducting and reporting new tests for REACH purposes

1. Requirements when conducting and reporting new tests for REACH purposes

1.1. Test methods, GLP requirements and reporting

(1) Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.

(2) Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

(3) Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[3].

1.2. Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

(1) Selection of the Test material(s)
The Test Material used to generate the new data must be selected taking into account the following:
- the variation in compositions reported by all members of the joint submission,
- the boundary composition(s) of the Substance,
- the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.

(2) Information on the Test Material needed in the updated dossier
- You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
- The reported composition must include all constituents of each Test Material and their concentration values and other parameters relevant for the property to be tested.

This information is needed to assess whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[4].

[3] https://echa.europa.eu/practical-guides
[4] https://echa.europa.eu/manuals