EUROPEAN CHEMICALS AGENCY

~~Confidential~~

Helsinki, 26 January 2021

Addressees
Registrants of ethoxylated [redacted] listed in the last Appendix of this decision

Date of submission for the jointly submitted dossier subject of a decision
23/09/2019

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: 2,4,7,9-Tetramethyldec-5-yne-4,7-diol, ethoxylated
EC number: 500-022-5
CAS number: 9014-85-1

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

DECISION ON A TESTING PROPOSAL

Based on Article 40 of Regulation (EC) No 1907/2006 (REACH), ECHA requests that you submit the information listed below by the deadline of ***2 February 2022***.

A. Requirements applicable to all the Registrants subject to Annex IX of REACH

1. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method OECD TG 414) in a first species (rat or rabbit), oral route with the Substance.

Conditions to comply with the requests

You are bound by the request for information corresponding to the REACH Annexes applicable to their own registered tonnage of the Substance at the time of evaluation of the jointly submitted dossier.

To identify your legal obligations, please refer to the following:

- you have to comply with the requirements of Annexes VII to IX of REACH, if you have registered a substance at 100-1000 tpa.

The Appendix entitled "Reasons for the requirements applicable to all the Registrants subject to Annex IX of REACH" states the reasons for the request for information to fulfil the requirements set out in the respective Annexes of REACH.

The Appendix entitled Observations and technical guidance addresses the generic approach for the selection and reporting of the test material used to perform the required studies and provides generic recommendations and references to ECHA guidance and other reference documents.

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

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, has to 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.

Approved[1] under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

[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 A: Reasons for the requirements applicable to all the Registrants subject to Annex IX of REACH

This decision is based on the examination of the testing proposals you submitted.

1. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species

A pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is a standard information requirement under Annex IX, Section 8.7.2. to REACH.

You have submitted a testing proposal for a PNDT study according to OECD TG 414 with the analogue substance 2,4,7,9-tetramethyldec-5-yne-4,7-diol (EC No 204-809-11), in the rat, by the oral route.

You provided your considerations concluding 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 have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5 using the following:

1) a read-across adaptation based on a category "Acetylenic geminalic diols"
2) a read-across based on an analogue approach

ECHA has evaluated your proposal to perform the test with the analogue substance 2,4,7,9-tetramethyldec-5-yne-4,7-diol (EC No 204-809-11).

We have assessed this information and identified the following issue(s):

Grouping of substances and read-across approach

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.

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance[2] and related documents[3,4].

ECHA has evaluated the category approach under section I below and the analogue approach under section II. The arguments presented for the prediction of properties are similar between the two approaches and, therefore, only addressed under section II.

[2] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals. 2008 (May) ECHA, Helsinki. 134. pp. Available online: https://echa.europa.eu/documents/10162/13632/information_requirements_r6_en.pdf/77f49f81-b76d-40ab-8513-4f3a533b6ac9

[3] Read-Across Assessment Framework (RAAF). 2017 (March) ECHA, Helsinki. 60 pp. Available online: Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across)

[4] Read-across assessment framework (RAAF) - considerations on multi-constituent substances and UVCBs. 2017 (March) ECHA, Helsinki. 40 pp. Available online: https://doi.org/10.2823/794394

I. Assessment of the Grouping of substances and read-across approach under Annex XI, Section 1.5. (category)

A. Scope of the grouping

i. Description of the grouping

In your registration dossier you have formed a group (category) of 'Acetylenic geminalic diols'. You have provided a read-across justification document in IUCLID Section 0.

For the purpose of this decision, the following abbreviations are used for the group members:
[1] Surfynol 104 2,4,7,9-tetramethyldec-5-yne-4,7-diol (EC No. 204-809-1);
[2] Surfynol 124 2,5,8,11-tetramethyldodec-6-yne-5,8-diol (EC No. 269-348-0);
[3] Surfynol 440 ethoxylated 2,4,7,9-tetramethyldec-5-yne-4,7-diol (EC No. 500-022-5);
[4] Surfynol 2502 ethoxylated propoxylated 2,4,7,9-tetramethyldec-5-yne-4,7-diol (EC No. 638-783-1);
[5] Envirogem AD01 2,4,7, 9-tetramethyl-4,7-dodecanediol (EC No. 451-160-7).

The Substance is not listed in this justification document.

You provide the following reasoning for the grouping the substances: *"Acetylenic geminalic diols are considered a chemical category based on structural similarity and similar properties in environmental and biological systems."*

You define the structural basis for the grouping as *"members of the category begin with an acetylene group as their core structure; in one member, this acetylene group has been fully hydrogenated. [...] Alpha to the acetylene are the geminal hydroxyl groups, which can be derivatized with ethoxylates and propoxylates in order to achieve desired functionalities of surfactants. Distal to the geminal hydroxyl groups is either an isobutyl group (methyl isopropyl) or an isopentyl group (ethyl isopropyl). These are short chain alkyls displaying an incremental increase in carbon chain length. All substances have two stereogenic centers (chiral carbons) in alpha-position to the carbon triple bond."* ECHA understands that this is the applicability domain of the grouping and will assess your predictions on this basis.

ii. Assessment of the grouping

ECHA notes the following shortcomings with regards to your grouping approach.

Characterisation of the group members

Annex XI, Section 1.5 of the REACH Regulation provides that *"substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of chemical similarity may be considered as group."*

According to the ECHA Guidance, *"in identifying a category, it is important that all potential category members are described as comprehensively as possible"*, because the purity profile and composition can influence the overall toxicity/properties of the potential category members.[5] Therefore, qualitative and quantitative information on the compositions of the category members should be provided to confirm the category membership.

[5] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.4.1

Furthermore, the provided information for categories consisting of UVCB (Unknown or Variable composition, Complex reaction products or of Biological materials) substances needs to include qualitative compositional information of the individual constituents of the category members; as well as quantitative characterisation in the form of information on the concentration of the individual constituents of these substances; to the extent that this is measurable.[6]

You have defined the applicability domain of the category as explained above. Your read-across justification document contains compositional information for the members of your category. Several category members (Surfynol 440, Surfynol 2502) are UVCBs including ethoxylated and propoxylated diols of various carbon chain lengths. The degree of ethoxylation or propoxylation is not provided for these category members. The same applies to the Substance, which is not included as category member.

Without consideration of the distribution of the ethoxylation and propoxylation amongst constituents with different carbon chain lengths, and information on the composition of test materials, no qualitative or quantitative comparative assessment of the different category members can be completed. Therefore, the category membership cannot be confirmed.

B. Predictions for toxicological properties

You have presented a hypothesis and arguments similar to those for a separate analogue approach. They are rejected for the same reasons described below (see section **II** below)).

C. Conclusion on the read-across category approach

As explained above, you have not demonstrated that the established category can be used as a basis to predict properties of the Substance from data on the analogue substances. Therefore, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

II. Assessment of the Grouping of substances and read-across approach under Annex XI, Section 1.5. (analogue approach)

A. Predictions for toxicological properties

You have provided a justification document in IUCLID Section 13.

You read-across between the structurally similar substances, Surfynol 104 (2,4,7,9-tetramethyldec-5-yne-4,7-diol), EC No. 204-809-1 (CAS No. 126-86-3), and Surfynol 440 (2,4,7,9-Tetramethyl-5-decyne-4,7-diol, ethoxylated (3.8)), EC No. 500-022-5 (CAS No. 9014-85-1) as source substances and the Substance Surfynol 420 (2,4,7,9-Tetramethyldec-5-yne-4,7-diol, ethoxylated (1.3)), EC No. 500-022-5 (CAS No. 9014-85-1) as target substance.

You have provided the following reasoning for the prediction of (eco-)toxicological properties: *"This read-across is based on the hypothesis that source and target substances have similar toxicological and ecotoxicological properties. [...] For most endpoints, data are available for the source substances 2,4,7,9-Tetramethyl-5-decyne-4,7-diol, ethoxylated (3.8) and 2,4,7,9-Tetramethyl-5-decyne-4,7-diol. The results are interpolated to the target substance, where appropriate, or the worst-case result is used for chemical safety assessment."*.

[6] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.5.5

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance, or, for selected endpoints, based on a worst-case approach.

You intend to predict the properties of the Substance from information obtained from the following source substances:

Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Surfynol 104 (OECD TG 414, Testing proposal)

ECHA notes the following shortcomings with regards to predictions of toxicological properties.

1. *Supporting information*

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*"[7]. 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).

Supporting information must include bridging studies to compare properties of the Substance and the source substances.

a. *Missing supporting information to compare properties between analogue substances*

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 the source substance is necessary to confirm that both substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the category members.

In your read-across hypothesis, there are no experimental studies conducted with the Substance, which could serve as bridging studies to compare toxicological profiles between source substances and the Substance). The data set reported in the technical dossier does not include relevant, reliable and adequate information for the target substance in order to compare to the source substances to support your read-across hypothesis.

In the absence of such information, you have not established that the Substance and the source substance(s) are likely to have similar properties. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

b. *Missing supporting information to substantiate worst-case*

As indicated above, your read-across hypothesis is in some cases based on the assumption that the source substance constitutes a worst-case for the prediction of the property under

[7] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.2.1.f

consideration of the Substance. 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 a conservative prediction of the properties of the Substance from the data on the source substance(s). Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance(s).

In your read-across hypothesis, you indicate that "*The only difference between the target substance and the source substances is the degree of Ethoxylation. [...] Ethoxylation seems to lead to lower toxicity as demonstrated by higher effect levels in the subchronic toxicity studies as well as in the QSAR calculations performed for short-term toxicity to fish, Daphnia, and algae. Thus, using the toxicity and ecotoxicity results obtained with the non-ethoxylated source substance* [Surfynol 104] *is a sufficiently conservative approach to fill the data gaps of the target substance.*"

However, in your read-across hypothesis, you have not considered the impact of the ethoxylation status and the degree of ethoxylation on the bioavailability of the Substance and source substances:

- the Substance is more polar than the source substance Surfynol 104 due to ethoxylation, and
- the Substance has a lower molecular weight than the source substance Surfynol 440 due to a higher proportion of constituents with short ethoxylated chains (i.e. with 1-2 ethoxylate units).

You did not provide any toxicokinetic data for the Substance and source substances to compare their bioavailability. You also did not provide comparable toxicological studies, which could establish a worst-case on the basis of toxicological properties.

There are multiple factors potentially determining toxicological properties, such as bioavailability. In this case, (1) you have not addressed how the ethoxylation status, degree of ethoxylation, polarity and molecular weight (i.e. proportion of constituents with short ethoxylated chains) may impact bioavailability. Furthermore (2) you have not demonstrated lower toxicity of the source substance Surfynol 104 (see section a. above).

In the absence of such supporting information, you have not established that the source substances Surfynol 104 and Surfynol 124 constitute worst-case for the prediction of the property under consideration of the Substance. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

B. Conclusions on the read-across analogue approach

As explained above, you have not established that relevant properties of the Substance can be predicted from data on the analogue substances. Therefore, your grouping and read-across approach does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

Conclusion on the testing proposal

Based on the above, your proposal to test the analogue substance 2,4,7,9-tetramethyldec-5-yne-4,7-diol (EC No 204-809-11) is rejected according to Annex XI, Section 1.5.

ECHA considers that the proposed study requires modification to fulfil the information requirement of Annex IX, Section 8.7.2. of the REACH Regulation.

Species

You proposed testing with the rat as a first species. You may select between the rat or the rabbit because both are preferred species under the OECD TG 414[1].

Route

You proposed testing by the oral route. ECHA agrees with your proposal on the route.

The oral route is the most appropriate route of administration to investigate reproductive toxicity[8].

Outcome

Under Article 40(3)(d) and (c) of REACH, your proposed test is rejected and you are requested to carry out a pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method OECD TG 414) in a first species (rat or rabbit), oral route with the Substance.

[8] ECHA Guidance R.7a, Section R.7.6.2.3.2.

Appendix B: Procedural history

ECHA started the testing proposal evaluation in accordance with Article 40(1) on 24 September 2019.

ECHA held a third party consultation for the testing proposals from 25 November 2019 until 9 January 2020. ECHA did not receive information from third parties.

For the purpose of the decision-making, this decision does not take into account any updates of registration dossiers after the date on which you were notified the draft decision according to Article 50(1) of REACH.

The decision making followed the procedure of Article 51 of the REACH Regulation, as described below:

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

ECHA did not receive any comments within the notification period.

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 C: Observations and technical guidance

1. This testing proposal examination decision does not prevent ECHA from initiating compliance checks at a later stage on the registrations present.

2. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State(s).

3. Test guidelines, GLP requirements and reporting

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

   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.

   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: 'How to report robust study summaries'[9].

4. 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:

a) the variation in compositions reported by all members of the joint submission,
b) the boundary composition(s) of the Substance,
c) 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

a) 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.
b) The reported composition must include the careful identification and description of the characteristics of the Tests Materials in accordance with OECD GLP (ENV/MC/CHEM(98)16) and EU Test Methods Regulation (EU) 440/2008 (Note, Annex), namely all the constituents must be identified as far as possible as well as their concentration. Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods,

[9] https://echa.europa.eu/practical-guides

With that detailed information, ECHA can confirm whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Appendix D: List of references - ECHA Guidance and other supporting documents

Evaluation of available information
Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 where relevant.

QSARs, read-across and grouping
Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 where relevant.

Read-across assessment framework (RAAF, March 2017)[10]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017) [11]

Physical-chemical properties
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

Data sharing
Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

[10] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[11] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316

OECD Guidance documents[12]
Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

Guidance document on transformation/dissolution of metals and metal compounds in aqueous media – No 29, referred to as OECD GD 29.

Guidance Document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption – No 150, referred to as OECD GD 150.

Guidance Document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD 151.

[12] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Appendix E: Appendix G: Addressees of this decision and the corresponding information requirements applicable to them

You must provide the information requested in this decision for all REACH Annexes applicable to you.

Registrant Name	Registration number	(Highest) Data requirements to be fulfilled
[redacted]	[redacted]	[redacted]

Note: where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas the decision is sent to the actual registrant.