EUROPEAN CHEMICALS AGENCY

Helsinki, 26 January 2021

Addressees
Registrants of JS_451-160-7 listed in the last Appendix of this decision

Date of submission for the jointly submitted dossier subject of a decision
29/05/2019

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: 2,4,7,9-Tetramethyl-4,7-decanediol
EC number: 451-160-7
CAS number: 17913-76-7

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 August 2022***.

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

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 ;

2. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method EU C.20./OECD TG 211);

3. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.; test method OECD TG 210) ;

Your originally proposed following test(s) using the an analogue substance, 2,4,7,9-Tetramethyl-5-decyne-4,7-diol (TMDD), EC 204-809-1, CAS 126-86 are rejected, according to Article 40(3)(d):

Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method EU C.20./OECD TG 211)

Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.; test method OECD TG 210)

Conditions to comply with the requests

Each addressee of this decision is bound by the requests 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 Appendices state the reasons for the requests for information to fulfil the requirements set out in the respective Annexes of REACH.

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 testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". In addition, you should follow the general recommendations provided under the Appendix entitled "General recommendations when conducting and reporting new tests for REACH purposes". For references used in this decision, please consult the Appendix entitled "List of references".

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.

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 on Reasons common to several requests

(i) Assessment of the Grouping of substances and read-across approach, in light of the requirements of Annex XI, Section 1.5.

You seek to adapt the following standard information requirements by applying (a) read-across approach(es) in accordance with Annex XI, Section 1.5:

- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method EU C.20./OECD TG 211)
- Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.; test method OECD TG 210)

ECHA has considered the scientific and regulatory validity of your read-across approach(es) in general before assessing the specific standard information requirements in the following appendices.

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 (addressed under 'Assessment of prediction(s)').

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].

A. Predictions for, physico-chemical and (eco)toxicological properties for the following aquatic endpoints; Long-term toxicity testing on aquatic invertebrates and Long-term toxicity testing on fish

To support a read-across adaptation for your two environmental testing proposals you have provided the following reasoning for the prediction of long-term toxicity to invertebrates and fish in IUCLID Sections 6.1.2 and 6.1.4 (REACH Annex IX, Section 9.1.5. and Section 9.1.6.1.): "*Based on acute toxicity data it is evident that* [" 2,4,7,9-Tetramethyl-5-decyne-4,7-diol (*TMDD*), EC 204-809-1, CAS 126-86-3] *is a more toxic substance than the target substance. Evaluation of long-term tox data can be considered as worst case in this proposed read across (RA)-approach*". In addition you have provided a read-across justification in IUCLUD Section 13 for endpoints other than those for which you have submitted testing proposals.

You propose to read-across between the structurally similar substances, 2,4,7,9-Tetramethyl-5-decyne-4,7-diol (TMDD) (EC 204-809-1, CAS 126-861) as source substance and the

[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

Substance as target substance for long-term toxicity to aquatic invertebrates and fish.

ECHA has evaluated the information provided in IUCLID Sections 6.1.2 and 6.1.4. Furthermore, ECHA has evaluated the read-across justification, provided in IUCLID Section 13, only as relevant to the endpoints of the testing proposals, Long-term toxicity testing on aquatic invertebrates and Long-term toxicity testing on fish, according to Annex XI Section 1.5.

As this communication is an assessment of your testing proposals, ECHA understands that you propose to 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 based on a worst-case approach.

ECHA notes the following deficiencies with regard to the proposed read-across for the ecotoxicological properties:

a) Read-across hypothesis

According to Annex XI, Section 1.5., two conditions shall be necessarily fulfilled to apply grouping and read-across. 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 (read-across approach).

A read-across hypothesis needs to be provided, establishing why a prediction for a toxicological or ecotoxicological property is reliable. This hypothesis should be based on recognition of the structural similarities and differences between the substances[5]. It should explain why the differences in the chemical structures should not influence the toxicological/ ecotoxicological/physico-chemical properties or should do so in a regular pattern.

While structural similarity is a prerequisite for applying the grouping and read-across approach, it does not necessarily lead to predictable or similar ecotoxicological and physico-chemical properties. Your read-across hypothesis is that different compounds have the same type of effects. The properties of your Substance are predicted based on a worst-case approach. You state that *"Since the central acetylene group in the source substance is sterically shielded by the neighbouring functional groups, this structural difference does not lead to major differences in reactivity and/or toxicity, which is demonstrated based on the available toxicological data"*. However, your proposal to predict that the structural difference does not lead to major differences in reactivity and/or toxicity, contradicts your read-across hypothesis which is based on a worst-case approach.

Thus, you have not provided a well-founded hypothesis to establish a reliable prediction for the Long-term toxicity testing on aquatic invertebrates and fish and physico-chemical properties, based on recognition of the structural similarities and differences between the source substance and your Substance also considering that both substances are flagged by you in the read-across justification document as multi-constituent.

In the absence of such information, you have not established that the source substance constitutes a worst-case for the prediction of the properties under consideration of the

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

Substance. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

b) Missing 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*"[6]. 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 source substance.

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

Furthermore, a read-across justification must be specific to the endpoint or property under consideration due to the different nature of each endpoint and consequent difference in scientific considerations (e.g. key test design parameters, biological targets), as indicated in ECHA's Read-Across Assessment Framework (RAAF, March 2017).

You have not provided any information with regard to acute aquatic toxicity of your source substance, neither in your read-across justification document nor in IUCLID Sections 6.1.4 and 6.1.2. in order to compare properties of the Substance and source substance.

Furthermore, you have not provided justification supported by scientific evidence on why and how the results of the acute studies would support the predictions for long-term toxicity testing on aquatic invertebrates and fish endpoints. Thus, ECHA considers that your read-across justification is lacking the relevant reasoning specific to the endpoints of long-term toxicity testing on aquatic invertebrates and fish.

In the absence of such information, you have not established that the source substance constitutes a worst-case for the prediction of the properties under consideration of the Substance. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

c) Physico-chemical properties of the target and source substance

According to Annex XI, Section 1.5., 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.

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

According to ECHA Guidance R.7a for octanol-water partitioning coefficient (Kow) determination for surfactants: *"A working approach for surfactants might be the comparison of measured solubilities in octanol and water. However, it would then be prudent to take the critical micelle concentration in water (CMC) as a solubility limit, in order to avoid the artefact of unrealistically low Kow values"*. Furthermore, in the same Guidance document it is noted that *"It is therefore important to ensure that the results presented for the physico-chemical tests represent each component rather than the mixture being treated as a single component."*

In your read-across justification document you outline the relevant physico-chemical properties of the target and sources substances. You state that "they have similar physicochemical properties...". In this document you note that *"The source substance .... are acetylenic geminalic diol surfactants"* and that *"The source substance has a lower log Kow than the target substance and is therefore expected to have a slightly higher bioavailability than the target substance."*

Based on the information provided in the registration dossier, the Substance is a surfactant (surface tension 33.4 mN/m at 20° C and technical function as surfactant). With regard to physico-chemical properties, the intrinsic surface activity of the source substance and of the Substance interfere with the determination of physico-chemical properties. You have not considered surface activity of your substances to more accurately indicate the partition properties of these substances. The experimental methods used to measure values for Kow are not well suited for surfactants and need specific considerations before being used for such substances, which was not the case here.

Furthermore, as noted in the read-across justification document provided in the registration dossier the source substance and the Substance are indicated as multi-constituent substances. Therefore, each specific constituent present in these substances, needs to be considered when physico-chemical properties of the substances are estimated.

Thus, due to the issues listed above similarity of the physico-chemical properties of the source substance and your Substance cannot be confirmed.

B. Conclusions on the read-across approach

As explained above, you have not established that relevant properties of the Substance can be predicted from data on your source substance. 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.

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

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.

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 proposed testing with the rat as a first species and by the oral route. ECHA agrees with your proposal. You may select between the rat or the rabbit because both are preferred species under the OECD TG 414[2]. The oral route is the most appropriate route of administration to investigate reproductive toxicity[7].

Under Article 40(3)(a) of REACH, you are requested to carry out the proposed test with the Substance.

2. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)

Long-term toxicity testing on aquatic invertebrates is a standard information requirement in Annex IX to the REACH Regulation.

You have submitted a testing proposal for a *Daphnia magna* Reproduction Test (OECD TG 211) using an analogue substance, 2,4,7,9-Tetramethyl-5-decyne-4,7-diol (TMDD), EC 204-809-1, CAS 126-86.:

You have proposed to adapt this information requirement by using a read-across approach under Annex XI, Section 1.5.

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

Grouping and read-across rejected according to Article 40(3)(d)

As explained in the Appendix on Reasons common to several requests your proposal for adaptation is rejected.

Currently in your registration dossier there is no long-term toxicity to aquatic invertebrates for your Substance.

In your comments on the draft decision you requested a deadline extension, please refer to Appendix D of the draft decision.

Consequently, under Article 40(3)(c) of the REACH Regulation, you are requested to carry out the proposed test on the Substance.

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

Study design
As the Substance is surface active, you need to consult the OECD Guidance Document (GD) 23 and ECHA Guidance, Chapter R7b, Table R.7.8-3 relating to the aquatic toxicity testing of difficult substances, so that you choose the most appropriate design of the requested ecotoxicity test(s) and you best calculate and report the results of the test(s).

3. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

Long-term toxicity testing on fish is a standard information requirement in Annex IX to REACH.

You have submitted a testing proposal for a Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.; test method OECD TG 210) using the an analogue substance, 2,4,7,9-Tetramethyl-5-decyne-4,7-diol (TMDD), EC 204-809-1, CAS 126-86.

You have proposed to adapt this information requirement by using a read-across approach under Annex XI, Section 1.5.

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

Grouping and read-across rejected according to Article 40(3)(d)

As explained in the Appendix on Reasons common to several requests your proposal for adaptation is rejected.

Currently in your registration dossier there is no long-term toxicity to fish for your Substance.

There was no considerations for alternative methods to fulfil the information requirement for Long-term toxicity to fish in your registration dossier.

Based on the available acute aquatic toxicity testing on the Substance in your registration dossier, it appears to indicate that fish may be the most sensitive species due to the 96-hour LC50 of 53.2 mg active ingredient/L based on measured concentrations. According to the "Guidance on information requirements and chemical safety assessment Chapter R.7b: Endpoint specific guidance, R.7.8.5.3" (ECHA, 2008), long-term testing of fish should only be conducted if it represents the most sensitive taxonomic group. The Guidance Document states that if invertebrates are likely to be more sensitive than fish and algae or the relative sensitivity of invertebrates cannot be predicted, long-term testing on Daphnia sp. should be preferred instead of fish."

ECHA considers that the proposed study is appropriate to fulfil the information requirement of Annex IX, Section 9.1.6. to REACH.

In your comments onthe draft decision you requested a deadline extension, please refer to Appendix D of the draft decision.

Consequently, under Article 40(3)(c) of the REACH Regulation, you are required to carry out the proposed test on the Substance.

Study design
As the Substance is surface active, you need to consult the OECD Guidance Document (GD) 23 and ECHA Guidance, Chapter R7b, Table R.7.8-3 relating to the aquatic toxicity testing of difficult substances, so that you choose the most appropriate design of the requested ecotoxicity test(s) and you best calculate and report the results of the test(s).

Appendix B: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. 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[8].

B. Test material

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.

With that detailed information, ECHA can confirm whether the Test Material is relevant for the Substance.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[9].

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

Appendix C: General recommendations when conducting and reporting new tests for REACH purposes

A. Testing strategy for aquatic toxicity testing

You are advised to consult ECHA Guidance R.7b, (Section R.7.8.5) which describes the Integrated Testing Strategy, to determine the sequence of aquatic toxicity tests and testing needed.

B. Environmental testing for substances containing multiple constituents

Your Substance contains multiple constituents and, as indicated in ECHA Guidance R.11 (Section R.11.4.2.2), you are advised to consider the following approaches for persistency, bioaccumulation and aquatic toxicity testing:

- the "known constituents approach" (by assessing specific constituents), or
- the "fraction/block approach, (performed on the basis of fractions/blocks of constituents), or
- the "whole substance approach", or
- various combinations of the approaches described above

Selection of the appropriate approach must take into account the possibility to characterise the Substance (i.e. knowledge of its constituents and/or fractions and any differences in their properties) and the possibility to isolate or synthetize its relevant constituents and/or fractions.

Appendix D: Procedure

ECHA started the testing proposal evaluation in accordance with Article 40(1) on 5 June 2019.

ECHA held a third party consultation for the testing proposal from 17 September 2019 until 1 November 2019. ECHA did not receive information from third parties. ECHA did not receive information from third parties.

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

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 took into account your comments and did not amend the request(s) but amended the deadline.

Deadline to submit the requested information in this decision

The timeline indicated in the draft decision to provide the information requested is 12 months from the date of adoption of the decision.

In your comments on the draft decision, you requested an extension of the timeline to 18 months. You justified your request on two grounds, firstly foreseen technical analytical problems due to the properties of the substance, which will need to be addressed first and secondly on the grounds of laboratory capacity. As stated above under study design, due to the properties of the substance, testing is foreseen to be difficult. Your comments included information from the laboratory outlining their capacity. Therefore, on these grounds, ECHA has granted the request and set the deadline to 18 months.

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 E: List of references - ECHA Guidance[10] 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)[11]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)**Error! Bookmark not defined.**

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.

OECD Guidance documents[12]

[10] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[11] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[12] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

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.

Appendix F: List of the registrants to which the decision is addressed and the corresponding information requirements applicable to them

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.