EUROPEAN CHEMICALS AGENCY

Helsinki, 30 June 2020

Addressees
Registrants of JS_9002-92-0_[redacted] listed in the last Appendix of this decision

Date of submission for the jointly submitted dossier subject of this decision
28/06/2019

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: Dodecan-1-ol, ethoxylated
EC number: 500-002-6
CAS number: 9002-92-0

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

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (REACH), ECHA requests that you submit the information listed below by the deadline of ***5 October 2021***.

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

1. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method EU B.13/14. / OECD TG 471) with the Substance using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102;

2. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method EU C.2./OECD TG 202) with the Substance;

3. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method EU C.3./OECD TG 201) with the Substance.

B. Requirements applicable to all the Registrants subject to Annex VIII of REACH

1. and 2. Combined repeated dose toxicity study with the reproduction/developmental toxicity screening study (Annex VIII, Sections 8.6.1. and 8.7.1.; test method: OECD 422) in rats, oral route with the registered substance.

3. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method OECD TG 203) with the Substance.

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 Annex VII of REACH, if you have registered a substance at 1-10 tonnes per annum (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;

- you have to comply with the requirements of Annexes VII and VIII of REACH, if you have registered a substance at 10-100 tpa;

Registrants are only required to share the costs of information that they must submit to fulfil the information requirements for their registration.

The Appendix on general considerations addresses issues relevant for several requests while the other Appendices state the reasons for the requests 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. The timeline has been set to allow for sequential testing where relevant.

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.

Authorised[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 general considerations

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

The Substance covered by your registration is "dodecan-1-ol, ethoxylated" (CAS 9002-92-0), with an ethoxylation degree [redacted] Specifically, the test materials used for several of the toxicology studies are different from the Substance which you provided for the endpoints, stated below. Even though they bear the same name and CAS number, the ethoxylation degree of the test material used for these studies is higher than [redacted] This is relevant as higher ethoxylated test material for the Substance is considered as polymers for which differences in absorption and metabolism have been demonstrated (HERA 2009[2]). Therefore, ECHA has evaluated this as a read-across adaptation according to Annex XI, Section 1.5.

You have submitted information with test materials of the Substance indicating a higher ethoxylation degree or with structurally similar substances, collectively referred to as analogue / source substances for the following endpoints,:

- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

ECHA has considered the scientific and regulatory validity of this read-across approach 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[3] and related documents[4, 5].

A. Predictions for toxicological properties

You have not provided a read-across justification document in the dossier but one has been provided in your comments which is addressed below.

The following studies with respective testing material used corresponding to the alkyl chain length (C) and ethoxylate units (EO) are included in the technical dossier:

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[2] Human & Environmental Risk Assessment on ingredients of European household cleaning products (HERA): Alcohol Ethoxylates, 2009; available at http://www.heraproject.com

[3] 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

[4] 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)

[5] 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

Table I

#	Study type	Reference	Reliability indicated by you	Substance name according to reference	Substance name / EC#/ CAS# according to CSR	Substance composition according to Talmage 1994[6]
1	22 day subacute toxicity study	IUCLID: Berberian 1965	2	Laureth-9	Dodecan-1-ol, ethoxylated / 9002-92-0 / 500-002-6	C9-11EO9
2	28 day subacute toxicity study	IUCLID: Grubb 1960	2	polyoxyethylene dodecanol	Dodecan-1-ol, ethoxylated / 9002-92-0 / 500-002-6	C12EO7
3	two-generation reproductive toxicity study, oral route	IUCLID: Talmage 1994; Author: [redacted] 1977	4		Dodecan-1-ol, ethoxylated / 9002-92-0 / 500-002-6	C12EO6
4	two-generation reproductive toxicity study, oral route	IUCLID: HERA 2009; Author: [redacted] 1977	4		Alcohols, C14-15, ethoxylated/68951-67-7/614-831-7,	C14-15EO7
5	two-generation reproductive toxicity study, dermal route	IUCLID: Gingell 1991, Author: [redacted] 1985	2		Alcohols, C9-11, branched and linear, ethoxylated /68439-46-3/500-446-0	C9-11EO6

Since you defined the Substance "Dodecan-1-ol, ethoxylated" with a degree of ethoxylation of [redacted] for registration purposes under REACH, ECHA considers the provided information with the substances "Dodecan-1-ol, 6-9x ethoxylated" provided in Table I above as analogue / source substances, i.e. different substances than the Substance, due to their higher ethoxylation degrees.

You have not provided a reasoning for the prediction of toxicological properties.
ECHA understands that you intend 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 to be quantitatively equal to those of the source substance.

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

Absence of read-across documentation

Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide a justification for the read-across including a hypothesis, explanation of the rationale for the prediction of properties and robust study summary(ies) of the source study(ies).[7]

You have provided studies conducted with substances of higher ethoxylation degree or with

[6] Environmental and Human Safety of Major Surfactants: Alcohol Ethoxylates and Alkylphenol Ethoxylates 1st Edition, Sylvia S. Talmage (Editor), CRC Press 1994, ISBN 9781566700177
[7] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.6.1

other structurally similar substances than your Substance collectively referred to as analogue / source substances in order to comply with the REACH information requirements. You have not provided documentation as to why this information is relevant for your Substance in your dossier submission (submission number [redacted]).

In the absence of such documentation, ECHA cannot verify that the properties of your Substance can be predicted from the data on the analogue / source substances.

Read-across hypothesis

According to Annex XI, Section 1.5., two conditions shall be necessarily fulfilled. 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 source substances and your Substance[8]. It should explain why the differences in the chemical structures should not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern.

In your comments on the draft decision you include a justification document for the read-across adaptation, as well as information on further studies with source substances. You reason that "*based on structural similarity, physical-chemical properties, organic functional groups and several general and endpoint specific mechanistic approach using OECD QSAR toolbox v3.4 [the source substances] were identified as read-across chemical with sufficient data for toxicological evaluations used for the target chemical*". You have not explained how the differences between the sources substance(s) and your Substance impact the prediction.

Your read-across hypothesis is that the similarity in chemical structure and in some of the physicochemical/ ecotoxicological/ toxicological properties between the source substances and your Substance is a sufficient basis for predicting the properties of your Substance for other endpoints.

Similarity in chemical structure and similarity of some of the physicochemical properties does not necessarily lead to predictable or similar human health/ ecotoxicological properties. As described above, a well-founded hypothesis is needed to establish a reliable prediction for a toxicological or ecotoxicological property, based on recognition of the structural similarities and differences between the source substances and your Substance. In particular the differences in metabolism and toxicokinetics between mono- and di-ethoxylated alcohols versus analogues with higher ethoxylation degrees and the resulting toxicodynamics need to be taken into account here

Characterisation of the analogue / source substances and the Substance

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.*"

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

According to the ECHA Guidance, "*the purity and impurity profiles of the substance and the structural analogue need to be assessed*", and "*the extent to which differences in the purity and impurities are likely to influence the overall toxicity needs to be addressed, and where technically possible, excluded*". The purity profile and composition can influence the overall toxicity/properties of the Substance and of the analogue / source substances.[9] Therefore, qualitative and quantitative information on the compositions of the Substance and of the analogue / source substances should be provided to allow assessment whether the attempted predictions are compromised by the composition and/or impurities.

Furthermore, whenever the Substance and/or the analogue / source substances are UVCB substances (Unknown or Variable composition, Complex reaction products or of Biological materials), qualitative compositional information of the individual constituents of the category members needs to be provided; 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.[10]

The references cited in your technical dossier demonstrate that the analogue / source substances are composed of ethoxylated alcohols of various carbon chain lengths. No information on the length of the carbon chain and on the ethoxylation degree of the individual constituents of the source substances is provided.

Without consideration of the distribution of the ethoxylation amongst constituents with different carbon chain length, no qualitative or quantitative comparative assessment of the compositions of the Substance or of the analogue / source substances can be completed. Therefore, ECHA considers that it is not possible to assess whether the attempted predictions are compromised by the composition of the source substance.

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*"[11]. 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 substances.

Supporting information must include bridging studies to compare properties of the Substance and source 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 of the source substances is necessary to confirm that both substance cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substances.

In the read-across justification document that was submitted with your comments on the

[9] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.3.1
[10] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.5.5
[11] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.2.1.f

draft decision you address the structural differences between the Substance and of the source substances *"Deceth 4 (CAS No. 26183-52-8; EC No. 500-046-6)"*, *"Myreth 7 (CAS No. 40036-79-1)" and "Laureth 6 (CAS No. 3055-96-7)"* indicating that they *"are structurally similar having percentage similarity of 80-90%", "60-70%" and "70-80%",* respectively, to the Substance, *"also indicated by the Tanimoto score"* (not given). The Substance and source substances also *"have consistency in Repeated Dose (*[profiler] *HESS)"* (Deceth 4, Laureth 6) and the profiler *"Dart scheme v.1.0 respectively"* (Laureth 6, Myreth 7).

You have assessed the impact of the structural differences using (QSAR) models, i.e. profilers. You report that profilers related to the endpoints covered by read-across did not show any differences between these substances. On that basis you conclude that the source substances *"were identified as read-across chemical with sufficient data for toxicological evaluations used for the target chemical Dodecan-1-ol, ethoxylated"*.

You have provided no bridging studies and no information on the QSAR models to assess their validity and reliability.

Whilst this information may constitute relevant information in support of the read-across approach, considering the complexity of the endpoints under consideration these QSAR and profiler predictions cannot be seen, on their own, as evidence of similarity in the properties of these constituents. This is because the validity and reliability of the source data in the toolbox profiler cannot be evaluated independently. Therefore, any resulting prediction cannot be validated and further (experimental) data is needed to support the adaptation. The data set reported in the technical dossier does not include relevant, reliable and adequate information on the properties under consideration for your Substance and the source substances, e.g. bridging studies of comparable design and duration. In the absence of such information, you have not established that the Substance and the source substances are likely to have similar properties. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

Missing adequate and reliable information

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases adequate and reliable documentation of the applied method shall be provided. According to Article 10(a)(vii) a robust study summary is required for information required under Annexes VII to XI. According to Article 3(28) a detailed summary of the objectives, methods, results and conclusions of a full study report is required, in order to provide sufficient information to make an independent assessment of the study minimising the need to consult the full study report.

For the studies 1-4 listed in the Table I under section A above, deviations from the current relevant guidelines are not recorded. There is no comprehensive listing e.g. of organs subjected to histopathological investigations.

In your comments on the draft decision you provide some information on further studies conducted with source substances: *"Deceth 4, CAS: 26183-52-8 (EC 500-046-6), Myreth-7, CAS No. 40036-79-1, and Laureth 6, CAS: 3055-96-7 (EC 221-282-3)".* However, you did not provide information on the substance identity and composition of the test materials in these source studies, as detailed in the section Characterisation of the analogue / source substances and the Substance.

ECHA considers that these endpoint study records do not allow an independent assessment to the current guideline(s) due to missing information on investigations performed in these studies, missing information on results, and undocumented deviations from the current

relevant guidelines; as well as an absence of details on the effect level (study 1). For the same reasons, in addition to missing literature reference and test material composition, the studies submitted with your comments on the draft decision do not allow an independent assessment.

Therefore, the information provided in these endpoint study records does not meet the requirements of a robust study summary. ECHA considers there is not sufficient information available to make an independent assessment of the study minimising the need to consult the full study report, and accordingly considers that for these studies. There are further issues of adequacy and reliability identified under Sections B.1 and B.2 below.

Therefore, you have failed to meet the requirement of Annex XI, Section 1.5.

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 the analogue / source 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.

Appendix A: Reasons for the requests to comply with Annex VII of REACH

Under Articles 10(a) and 12(1) of REACH, a technical dossier registered at 1 to 10 tonnes or more per year must contain, as a minimum, the information specified in Annex VII to REACH.

1. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)

An *In vitro* gene mutation study in bacteria is a standard information requirement in Annex VII to REACH.

You have provided a key study with the Substance in your dossier :

i. OECD 471 (1987).

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

To fulfil the information requirement, the study has to meet the requirements of OECD TG 471 (1997). The key parameter(s) of this test guideline include:

The test must be performed with 5 strains: four strains of S. typhimurium (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101)

The study provided includes the following strains, TA 98, TA 100, TA 1535, TA 1537, and TA 1538 but it does not include results in the required fifth strain, S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101).

The information provided does not cover key parameter(s) required by OECD TG 471. Therefore, the information requirement is not fulfiled.

In your comments on the draft decision you agree to perform the requested study.

To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471) should be performed using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102.

2. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)

Short-term toxicity testing on aquatic invertebrates is a standard information requirement in Annex VII to REACH.

You have provided results of two experimental (one key and one supporting) studies:

1) Pantani *et al*, 1990 (key study; Exposure duration = 24 hrs; 24 hr LC_{50} = 9.45 mg/L; Species: *Gammarus Italicus*; GLP compliance not specified; LC_{50} stated but ECHA assumes the registrant referres to an EC_{50} value)
2) Database extract (US Library of Medicine, 2017)(Supporting study; Exposure duration = 48 hrs; 48 hr LC_{50} = 6.46 mg/L; Species: *Daphnia magna*;GLP compliance not specified; LC_{50} stated but ECHA assumes the registrant referres to an EC_{50} value)

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

i. Experimental studies

Tests on substances must be conducted in accordance with the OECD test guidelines or other internationally recognised test method (Article 13(3) of REACH).

OECD TG 202 which is the standard test guideline for short-term testing on aquatic invertebrates in combination with the revised OECD Guidance 23, ENV/JM/MONO(2000)6/REV1 requires that the following conditions are met:

1) analytical monitoring of exposure concentrations is performed;
2) effect concentrations based on the measured values rather than nominal values unless the test concentrations are maintained within 20% of the measured initial concentrations throughout testing.

The Substance is surface active (36.3 mN/m at 23 deg C and at 0.1% concentration) and readily biodegradable (based on one key study (OECD Guideline 301 C (Modified MITI Test (I)) under aerobic conditions, % of degradation was determined to be 74, 44 and 62% by BOD, TOC removal and UV-Vis respectively parameter in 28 days) one supporting study (OECD 301D % of degradation was determined to be 74-84% of its theoretical BOD in 30 day) and one supporting QSAR with a statement indicating the test chemical is expected to be readily biodegradable). Therefore it is expected that considerable losses of the Substance, as compared to the nominal concentrations, will occur in aquatic toxicity tests during the exposure period.

For both experimental studies you did not report any analytical monitoring of exposure concentrations and did not demonstrate that the Substance concentrations during the tests were maintained within the required 20% of the measured initial concentrations. Consequently, the aforementioned conditions of the standard OECD test guideline are not met.

In addition, to fulfil an information requirement or to be appropriate for an adaptation, the test material must be representative for the Substance (ECHA Guidance R.4).

The studies you provided, as indicated above, indicate the following test material, Dodecan-1-ol, ethoxylated / 9002-92-0 / 500-002-6;

The Substance covered by your registration is "dodecan-1-ol, ethoxylated" (CAS 9002-92-0), with an ethoxylation degree [redacted] The test material used for the above studies bears the same name and CAS number, but the ethoxylation degree of the test material used is not indicated. Currently, the identity of the testing material regarding the ethoxylation degree cannot be assessed using the information provided in the registration dossier.

ii. Weight of the evidence

In your comments on the draft decision you provided information on four experimental studies.
You propose to adapt this standard information requirement by applying weight of evidence (WoE) adaptation in accordance with Annex XI, section 1.2.

You provided the following information in support:

1. Experimental study (C. Pantani *et. al.*, 1990); Exposure duration = 24 hrs; Species: *Gammarus italicus;* GLP compliance not specified; Test material: a substance identified as Dodecan-1-ol, CAS 9002-92-0 (EC 500-002-6); 24 hr LC_{50} = 9.45 mg/L.
2. Experimental "*study from authoritative database (2018) secondary source (2019)*"; Exposure duration = 48 hrs; Species: *Daphnia magna;* GLP compliance not specified; Test material: a substance identified as Dodecan-1-ol, CAS 9002-92-0 (EC 500-002-6) 48 hr LC_{50} = 6.46 mg/L.
3. Experimental study (Study report, 2019) according to OECD TG 202; Exposure duration = 48 hrs; Species: *Daphnia magna;* GLP compliance not specified; Test material: a substance identified as Dodecan-1-ol, CAS 9002-92-0 (EC 500-002-6) ("*target chemical*

used contains 12 carbon chain length along with 1-2.5 ethoxylated units (i.e, [redacted] *) and [...] its purity is considered to be 100%"*); 48 hrs median EC_{50} = 5.2 mg/l (nominal concentration).

4. Experimental study (C. Pantani et. al., 1997 and secondary source, 2019); Exposure duration = 96 hrs; Species: *Gammarus italicus* and *Echinogammarus tibaldii;* GLP compliance not specified; Test material: a substance identified as Dodecan-1-ol, CAS 9002-92-0 (EC 500-002-6); 96 hrs LC_{50} = 7.6 mg/L (nominal concentration) for *Gammarus italicus* and 96 hrs LC_{50} = 3.6 mg/L (nominal concentration) for *Echinogammarus tibaldii*.

ECHA understands that you claim that all these studies were conducted with the Substance.

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

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.

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.

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

To fulfil the information requirement, normally a study performed according to OECD TG 202 must be provided. OECD TG 202 requires the study to investigate the following key parameter of daphnids:

- immobilization.

Two of the provided sources of information (3. and 2.) may provide relevant information on the immobilization of daphnids. Furthermore, other two provided sources of information (4. and 1.) may provide relevant information on the immobilization of other aquatic invertebrates but not on daphnids and, therefore, are not relevant for the above key investigation.

However, the reliability of all four sources of information is significantly affected by a number of deficiencies.

ECHA understands that two of the reported studies have already been reported in the registration dossier and quality deficiencies of these studies (respectively, 1. and 2.) affecting their reliability have already been noted above. There is no new information addressing deficiencies of these studies provided in your comments.

- Identity of the test material

The test material in studies according to OECD TG 202 must be representative for the Substance (ECHA Guidance R.4.1).

The unambiguous characterisation of the composition of the Substance and test material used to generate the data is required to evaluate the representativeness of the test material. The composition of the selected test material must be reported in the respective endpoint study record, under the test material section.

For the sources of information (3. and 4.) comprehensive reporting of all constituents present in the test material (including their identity and concentrations) is missing. Without consideration of the presence (or absence) of constituent with various carbon chain lengths, branched/unsaturated constituents, of the distribution (or absence) of ethoxylation amongst constituents with different carbon chain length/branching, no qualitative or quantitative comparative assessment of the compositions of the test material and registered substance can be completed.

- Quality of the sources of information (3. and 4.)

The conditions of the OECD TG 202 or the EU Method C.2 (Article 13(3) of REACH) and the conditions of OECD GD 23 (ENV/JM/MONO(2000)6/REV1), if the substance is difficult to test, specify the following:

- The results can only be based on nominal or measured initial concentration if the concentration of the test material has been satisfactorily maintained within 20 % of the nominal or measured initial concentration throughout the test (see also ECHA Guidance R.7b, Section R.7.8.4.1);
- The median of the concentrations that are measured after the decline would be more appropriate as a surrogate for the mean exposure concentration only for the studies where loss processes of the test material are very fast (ECHA Guidance R.7b);
- At least 20 animals are used at each test concentration and for the controls;
- The test is conducted on *Daphnia magna* or other suitable *Daphnia* species.

Regarding the first condition: Information on the details of verification of exposure concentrations throughout the test is not available for two sources of information (3. and 4.):
- for the source information 3., raw data on the test material exposure concentrations throughout the test duration and details on the analytical method used to verify exposure concentrations are missing;
- for the source information 4., there is no information whether or not test material exposure concentrations throughout the test duration were verified and maintained within the required 20% of the measured initial concentrations.

Regarding the second condition: For the source of information 3., you stated in your comments: "*test chemical concentrations were verified analytically at day 0 and day 2 which has been satisfactorily maintained within ± 20 % of the nominal initial concentration throughout the test*". Thus, loss processes of the test material was not very fast, so effect concentrations should be expressed in terms of the mean exposure concentrations.

Regarding the third condition: For the source information 3., "*Total 10 Daphnids were exposed to test chemical in 25 ml beakers in a volume of 20 ml of liquid solution containing both the chemical and media*".

Regarding the fourth condition: For the source of information 4., non-OECD 202 standard test organisms were used, without any justification on how such data should be used for the purpose of risk assessment under REACH and classification/labelling.

On that basis, the conditions of OECD TG 202 and OECD GD 23 are not met.

As a conclusion, sources of information, as indicated above, provide information on the immobilization of daphnids or other aquatic invertebrates, but the provided information is not reliable and/or not adequate.

Thus, it is not possible to conclude, based on any source of information alone or considered together, whether the Substance has or has not the particular dangerous property foreseen to be investigated in an OECD TG 202 study.

Therefore, the information provided does not fulfil the information requirement.

Due to the UVCB nature, surface activity and ready biodegradability of the Substance you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6/REV1 (6 July 2018) and ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested aquatic toxicity tests and for calculation and expression of the result of the tests.

The substance is difficult to test due to the surface activity and ready biodegradability. OECD TG 202 specifies that for difficult to test substances, the OECD Guidance 23 is to be followed. To get reliable results, the substance properties need to be considered when performing the test, in particular with regard to the test design; including exposure system, test solution preparation, and sampling. OECD GD 23 (Table 1) describes testing difficulties related to a specific property of the Substance. You may use the approaches described in OECD GD 23 or other approaches if more appropriate for your Substance. The approach selected must be justified and documented. Due to the Substance properties it may be difficult to achieve and maintain the exposure concentrations. Therefore, you have to demonstrate that the concentration of the substance is stable throughout the test (i.e. measured concentrations remains within 80-120% of the nominal concentration). If it is not possible to demonstrate the stability, you must express the effect concentration based on measured values as described in the applicable test guideline. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the test solution preparation method applied was sufficient to maximise the concentration of the Substance in the test solution.

In case you decide to use the Water Accommodated Fraction (WAF) approach in your ecotoxicity tests, please note that this approach may not be adequate to determine the toxicity of multi-component substances where its poorly soluble components are of concern, as in the case of your Substance. In general, it is critical that a robust chemical analysis is carried out prior the test, to identify those constituents present in the water to which the test organisms are exposed. Additionally, chemical analysis to demonstrate attainment of equilibrium in WAF preparation and stability during the conduct of the test is required. Methods capable of identifying gross changes in the composition of WAFs with time, such as e.g. ultra-violet spectroscopy or total peak area, are required for this purpose. The method used to prepare the WAF should be fully described in the test report and evidence of the compositional stability of the test substance over time should be provided.

Appendix D includes further technical advice on testing UVCB substances.

3. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)

Growth inhibition study aquatic plants is a standard information requirement in Annex VII to REACH.

You have provided results of three experimental (one key and two supporting) studies:

1) Wind *et al*, 2006 (key study; Exposure duration = 72 hrs; 72 hr ErC50 = 0.2369 mg/L; Species: *Desmodesmus subspicatus* (previous name: *Scenedesmus subspicatus*); GLP compliance not specified)
2) Nyberg *et al*, 1987(Supporting study; Exposure duration = 48 hrs; 48 hr IC50 = > 5 - < 10 mg/L; Species: *Pseudokirchneriella subcapitata* (previous names: *Raphidocelis subcapitata*, *Selenastrum capricornutum*); GLP compliance not specified)
3) Database extract (US Library of Medicine, 2017) (Supporting study; Exposure duration = 8 days; 8 days EC50 = 3.3 mg/L; Species: *Scenedesmus quadricauda*; GLP compliance not specified)

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

Tests on substances must be conducted in accordance with the OECD test guidelines or other internationally recognised test method (Article 13(3) of REACH).

- Quality of reported studies

OECD TG 201 which is the standard test guideline for short-term testing on aquatic invertebrates in combination with the revised OECD Guidance 23, ENV/JM/MONO(2000)6/REV1 requires that the following conditions are met (among others):

i. adequate exposure duration of the test (i.e. 72 hours);
ii. analytical monitoring of exposure concentrations is performed;
iii. effect concentrations based on the measured values rather than nominal values unless the test concentrations are maintained within 20% of the measured initial concentrations throughout testing;
iv. the median of the concentrations that are measured after the decline would be more appropriate as a surrogate for the mean exposure concentration only for the studies where loss processes of the test material are very fast (ECHA Guidance R.7b);
following validity criteria are fulfilled:

- exponential growth in the control cultures is observed over the entire duration of the test;
- at least 16-fold increase in biomass is observed in the control cultures by the end of the test;
- the mean coefficient of variation for section-by-section specific growth rates (days 0-1, 1-2 and 2-3, for 72-hour tests) in the control cultures is ≤ 35%;
- the coefficient of variation of average specific growth rates during the whole test period in replicate control cultures is ≤ 7% in tests with *Pseudokirchneriella subcapitata.*

As explained in Appendix A, section 2 above, it is expected that considerable losses of the test substance, as compared to the nominal concentrations, will occur in aquatic toxicity tests during the exposure period.

Regarding condition i: Exposure duration of one of the supporting studies (2) was 48 hours.

Regarding conditions ii and iii: For all three experimental studies provided in the registration dossier you did not report any analytical monitoring of exposure concentrations and did not demonstrate that the test substance concentration during the test was maintained within the required 20% of the measured initial concentrations.

In your comments on the draft decision you reported information on four experimental studies. ECHA understands that two of the reported studies have already been reported in the registration dossier and quality deficiencies of these studies (respectively, 1 and 3)

affecting their reliability have already been noted above.

You provided the following information on new studies in your comments:

4) Experimental study (Study report, 2019) according to OECD TG 201; Exposure duration = 72 hrs; Species: *Pseudokirchneriella subcapitata;* GLP compliance not specified; "*The highest and lowest concentration of exposed test chemical was verified analytically at day 0 and day 3, which has been satisfactorily maintained within ± 20 % of the nominal initial concentration throughout the test.*").
5) Experimental study according to EC Directive 92/69/EWG. Exposure duration = 72 hrs; Species: *Scenedesmus subspicatus*; GLP compliance not specified; Test material: a substance identified as Dodecan-1-ol, CAS 9002-92-0 (EC 500-002-6); 72 hrs ErC_{50} = 0.43 mg/l (nominal concentration). No information on the analytical verification of exposure concentrations was provided.

For the experimental studies 4 and 5 there is no raw data on biological observations provided.

ECHA understands that you claim that all studies reported in your comments on the draft decision were conducted with the Substance.

In your comments on the draft decision you provided additional information for the experimental study 1: "*Analytical monitoring of test chemical conc. was carried out by GC analysis. [...] As test concentrations are maintained within 20% of the measured initial concentrations throughout the test, the median effect concentrations (EC50) reported was considered as nominal concentrations.*".

ECHA notes, however:
- Condition i is not met for experimental study 2.
- Conditions ii and iii are not met for experimental studies 2, 3 and 5.
- Condition iii is not met for experimental studies 4 and 1 (considering additional information provided in the comment on the draft decision), as raw data on the test material exposure concentrations throughout the test duration and details on the analytical method used to verify exposure concentrations are missing.
- Condition iv: Regarding your additional comment on experimental study 1: "*As test concentrations are maintained within 20% of the measured initial concentrations throughout the test*", loss processes of the test material are not very fast, so effect concentrations should be expressed in terms of the mean exposure concentrations.
- Condition v: for the experimental studies 4 and 5 there is no raw data on biological observations provided, which would allow independently assess and confirm fulfilment of validity criteria of the test method.

Therefore, none of the studies provided meet the above requirements and they are therefore rejected.

- Identity of the test material

To fulfil an information requirement or to be appropriate for an adaptation, the test material must be representative for the Substance (ECHA Guidance R.4).

The three studies you provided in the registration dossier, as indicated above, are performed on the following test material, Dodecan-1-ol, ethoxylated / 9002-92-0 / 500-002-6.

The Substance covered by your registration is "dodecan-1-ol, ethoxylated" (CAS 9002-92-0), with an ethoxylation degree [redacted] The test material used for the above studies

bears the same name and CAS number, but the ethoxylation degree of the test material used is not indicated.

In your comments on the draft decision you provided additional information for the experimental study 1: Test material: a substance identified as Dodecan-1-ol, CAS 9002-92-0 (EC 500-002-6) ("*test chemical used contains 12 carbon chain length along with 2 ethoxylated units (i.e,* [redacted] *) and has a purity of 100%*")."

Based on the information in the registration dossier, the identity of the testing material regarding the ethoxylation degree cannot be assessed using the information provided in the registration dossier.

For the experimental study 1, ECHA understands that the testing material is of UVCB nature. In that case, even with improved reporting of the test material in your comments, comprehensive reporting of all relevant constituents present in the test material (including their identity and concentrations) is missing. Without consideration of the presence (or absence) of constituent with various carbon chain lengths, branched/unsuturated constituents, of the distribution (or absence) of ethoxylation amongst constituents with different carbon chain length/branching, no qualitative or quantitative comparative assessment of the compositions of the test material and registered substance can be completed.

The same deficiency applies to experimental studies 4 and 5 reported in the comments to the draft decision.

As a conclusion, as indicated above, information provided in your dossier and in your comment must be rejected.

Due to the UVCB nature, surface activity and ready biodegradability of the Substance you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6/REV1 (6 July 2018) and ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested aquatic toxicity tests and for calculation and expression of the result of the tests.

The substance is difficult to test due to the surface activity and ready biodegradability. OECD TG 201 specifies that for difficult to test substances, the OECD Guidance 23 is to be followed. To get reliable results, the substance properties need to be considered when performing the test, in particular with regard to the test design; including exposure system, test solution preparation, and sampling. OECD GD 23 (Table 1) describes testing difficulties related to a specific property of the Substance. You may use the approaches described in OECD GD 23 or other approaches if more appropriate for your Substance. The approach selected must be justified and documented. Due to the Substance properties it may be difficult to achieve and maintain the exposure concentrations. Therefore, you have to demonstrate that the concentration of the substance is stable throughout the test (i.e. measured concentrations remains within 80-120% of the nominal concentration). If it is not possible to demonstrate the stability, you must express the effect concentration based on measured values as described in the applicable test guideline. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the test solution preparation method applied was sufficient to maximise the concentration of the Substance in the test solution.

In case you decide to use the Water Accommodated Fraction (WAF) approach in your ecotoxicity tests, please note that this approach may not be adequate to determine the toxicity of multi-component substances where its poorly soluble components are of concern, as in the case of your Substance. In general, it is critical that a robust chemical analysis is carried out prior the test, to identify those constituents present in the water to which the test organisms are exposed. Additionally, chemical analysis to demonstrate attainment of equilibrium in WAF preparation and stability during the conduct of the test is required. Methods capable of identifying gross changes in the composition of WAFs with time, such as e.g. ultra-violet spectroscopy or total peak area, are required for this purpose. The method used to prepare the WAF should be fully described in the test report and evidence of the compositional stability of the test substance over time should be provided.

Therefore, the information provided does not fulfil the information requirement.

Appendix B: Reasons for the requests to comply with Annex VIII of REACH

Under Articles 10(a) and 12(1) of REACH, a technical dossier registered at 10 to 100 tonnes or more per year must contain, as a minimum, the information specified in Annexes VII and VIII to REACH.

1. Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)

A Short-term repeated dose toxicity study (28 days) is a standard information requirement in Annex VIII to REACH. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have provided a key study and a supporting study for the endpoint repeated dose toxicity (Annex VIII Section 8.6.1) in your dossier:

1) Sub-acute oral toxicity study, Berberian (1965, 22 days exposure, C9-11EO9)
2) Sub-acute oral toxicity study, Grubb (1960, C12EO7)

We have assessed this information and identified the following issues:

The test materials are not the same as the Substance. Therefore, ECHA has assessed the provided information according to the rules of *grouping of substances and read-across approach* under Annex XI, Section 1.5. As explained in the Appendix on general considerations your adaptation is rejected.

In addition, the following endpoint-specific deficiencies have been identified:

To be considered compliant with the endpoints, you need to submit a study performed according to the OECD TG 407, or a valid adaptation according to either the specific rules of Column 2, Annex VIII, Section 8.6.1. or the general rules of Annex XI .

Under the OECD TG 407, a study must fulfil *inter alia* the following key parameters:

i. The exposure duration is 28 days.
ii. The dose selection aims to induce toxicity.

You did not justify why some deviations listed below from the guidelines can be considered acceptable:

i. The duration of the source study **1** is 22 days.
ii. The highest dose level in all studies (**1-2**) did not induce any toxicity and were not performed up to the limit dose of 1000 mg/kg bw/day. The NOAEL for these source substances in sub-chronic repeated dose toxicity studies is 300-500 mg/kg bw/d.

Therefore, the studies were not performed according to the key parameters of the OECD TG 407. In particular, ECHA concludes that the dose selection did not aim to induce toxicity and thus the dose level selection was too low. Therefore, the studies do not fulfil all relevant key parameters set in OECD TG 407.

Based on the above, the information you provided do not fulfil the information requirement.

When there is no information available neither for the 28-day repeated dose toxicity endpoint (EU B.7, OECD TG 407), nor for the screening study for reproductive/ developmental toxicity (OECD TG 421 or TG 422) (see section 2 below), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided. Such an approach offers the possibility to avoid carrying out a 28-day study according to OECD TG 407, because the OECD

TG 422 can at the same time fulfil the information requirement of REACH Annex VIII, 8.6.1 and that of REACH Annex VIII, 8.7.1.[12]

ECHA has evaluated the most appropriate route of administration for the study. Referring to the criteria in Annex VIII, Section 8.6.1, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity. The substance is a liquid of very low vapour pressure and no uses with spray application are reported that could potentially lead to aerosols of inhalable size. The oral route is the preferred route of administration 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. . Hence, the test shall be performed by the oral route using the test method OECD TG 422.

According to the test method OECD TG 422, the test is designed for use with rats. On the basis of this default assumption, ECHA considers testing should be performed with rats.

2. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

A Screening for reproductive/developmental toxicity study (test method: OECD TG 421 or OECD TG 422) is a standard information requirement under Annex VIII Section 8.7.1. , if there is no evidence from analogue substances, QSAR or *in vitro* methods that the Substance may be a developmental toxicant. In this case, there is no information available in your dossier indicating that your Substance may be a developmental toxicant.

You have adapted the standard information requirement according to Annex XI, Section 1.2. Weight of evidence.

You have provided the following information:

1) Two-generation reproductive toxicity study with an analogous substance, [redacted] (1977, C12EO6)
2) Two-generation reproductive toxicity study with an analogous substance, [redacted] (1977, C14-15EO7)
3) Two-generation reproductive toxicity study by the dermal route with an analogous substance, [redacted] (1985/1991, C9-11EO6 "Neodol 91-6")

Annex XI, Section 1.2 states that there may be sufficient weight of evidence (WoE) 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. According to ECHA Guidance R.4.4, a WoE adaptation involves an assessment of the relative values/weights of different pieces of the available information which is defined by e.g. the reliability of the data, consistency of results/data, nature and severity of effects, and relevance of the information for the given regulatory endpoint. Subsequently, the lines of evidence should be integrated considering their relative values or weights in order to draw a conclusion. Adequate and reliable documentation shall be provided to describe your WoE approach, the assessment of relative weights of individual piece of information and the subsequent conclusions drawn.

ECHA has evaluated the individual pieces of information separately below.

You have not submitted any explanation why the sources of information provide sufficient weight of evidence leading to the conclusion/assumption that the Substance has or has not a

[12] ECHA Guidance, Section R.7.6.2.3.2., pages 484 to 485 of version 6.0 – July 2017. (https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf)

particular dangerous property.

Read-across adaptation can be used to adapt the standard information requirement, provided that the criteria in Annex XI, Section 1.5. are fulfilled. As explained in the Appendix on general considerations your read-across adaptation is rejected. Therefore, it cannot be used as part of a weight of evidence adaptation according to Annex XI, Section 1.2.

Based on the assessment above, 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 property foreseen to be investigated in an OECD TG 421/422 study. Your adaptation is rejected and the information requirement is not fulfilled.

In addition, the following deficiencies have been identified:

To be considered compliant with the endpoints, you need to submit a study performed according to the OECD TG 421 or OECD TG 422, or a valid adaptation according to either the specific rules of Column 2, Annex VIII, Section 8.7.1. or the general rules of Annex XI.

Under the OECD TG 421-422, a study must fulfil the following key parameters:

i. the dose selection aims to induce toxicity.
ii. Oral route

The studies were not performed according to the criteria of the OECD TG 421 or OECD TG 422, and you did not justify why some deviations listed below from the guidelines can be considered acceptable:

iii. The highest dose level in all studies (**1-3**) did not induce any toxicity and were not performed up to the limit dose of 1000 mg/kg bw/day. The NOAEL for these source substances in sub-chronic repeated dose toxicity studies is 300-500 mg/kg bw/d.
iv. Study **3** has been conducted by the dermal route administering the test substance on three instead of five days per week.

ECHA concludes that the dose selection did not aim to induce toxicity.

Therefore, the dose level selection was too low, and the studies do not fulfil the key paramaters set out in OECD TGs 421 or 422.

Based on the above, the information you provided do not fulfil the information requirement.

When there is no information available neither for the 28-day repeated dose toxicity endpoint (EU B.7, OECD TG 407) (as explained above under section 1.), nor for the screening study for reproductive/developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided. Such an approach offers the possibility to avoid carrying out a 28-day study according to OECD TG 407, because the OECD TG 422 can at the same time fulfil the information requirement of REACH Annex VIII, 8.6.1 and that of REACH Annex VIII, 8.7.1.[13]

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. The Substance is a liquid of very

[13] ECHA Guidance, Section R.7.6.2.3.2., pages 484 to 485 of version 6.0 – July 2017. (https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf)

low vapour pressure and no uses with spray application are reported that could potentially lead to aerosols of inhalable size. ECHA concludes that testing should be performed by the oral route.

According to the test methods OECD TG 422, the test is designed for use with rats. On the basis of this default assumption ECHA considers testing should be performed with rats.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit information derived with the registered substance subject to the present decision: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (test method: OECD TG 422) in rats by the oral route.

3. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)

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

You have provided results of three experimental (one key and two supporting) studies

1) Wildish, 1973 (key study; Exposure duration = 96 hrs; 96 hr LC_{50} = 1.5 mg/L; Species: *Salmo salar*; GLP compliance not specified)
2) Database extract (US Library of Medicine, 2017) (Supporting study; Exposure duration = 48 hrs; 48 hr LC50 = 8.61 mg/L; Species: *Poecilia reticulata*; GLP compliance not specified)
3) Database extract (US Library of Medicine, 2017) (Supporting study; Exposure duration = 48 hrs; 48 hr LC50 = 3.72 mg/L; Species: *Cyprinus carpio*; GLP compliance not specified)

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

i. Experimental studies

Tests on substances must be conducted in accordance with the OECD test guidelines or other internationally recognised test method (Article 13(3) of REACH).

OECD TG 203 which is the standard test guideline for short-term testing on aquatic invertebrates in combination with the revised OECD Guidance 23, ENV/JM/MONO(2000)6/REV1 requires that the following conditions are met (among others):

1) adequate exposure duration of the test (i.e. 96 hours);
2) analytical monitoring of exposure concentrations is performed;
3) effect concentrations based on the measured values rather than nominal values unless the test concentrations are maintained within 20% of the measured initial concentrations throughout testing.

As explained in Appendix A, section 2 above, it is expected that considerable losses of the test substance, as compared to the nominal concentrations, will occur in aquatic toxicity tests during the exposure period.

For all three experimental studies you did not report any analytical monitoring of exposure concentrations and did not demonstrate that the test substance concentration during the test was maintained within the required 20% of the measured initial concentrations. Consequently, the aforementioned conditions (2 and 3) of the standard OECD test guideline are not met.

Moreover, exposure duration of both supporting studies was 48 hours. Consequently, the aforementioned condition 1 of the standard OECD test guideline is not met.

In addition, to fulfil an information requirement or to be appropriate for an adaptation, the test material must be representative for the Substance (ECHA Guidance R.4).

The studies you provided, as indicated above, are performed on the following test material, Dodecan-1-ol, ethoxylated / 9002-92-0 / 500-002-6;

The Substance covered by your registration is "dodecan-1-ol, ethoxylated" (CAS 9002-92-0), with an ethoxylation degree [redacted] The test material used for the above studies bears the same name and CAS number, but the ethoxylation degree of the test material used is not indicated. Currently, the identity of the testing material regarding the ethoxylation degree cannot be assessed using the information provided in the registration dossier.

i. Weight of the evidence

In your comments on the draft decision you provided information on four experimental studies. You propose to adapt this standard information requirement by applying weight of evidence (WoE) adaptation in accordance with Annex XI, section 1.2.

You provided the following information in support:

i. Experimental study ([redacted] 1984) according to Japanese Industrial Standard (JIS) K0102 (1981) Testing methods for Industrial Wastewater; Exposure duration = 48 hrs; Species: *Oryzias latipes;* GLP compliance not specified; Test material: a substance identified as Dodecan-1-ol, CAS 9002-92-0 (EC 500-002-6) ("*test chemical used contains twelve carbon chain length along with three ethoxylated units and has a purity of 100%*"); 48 hrs LC_{50} = 2.4 mg/l (nominal concentration).
ii. Database extract (Authoritative database, 2018 and secondary source, 2019); Exposure duration = 48 hrs; Species: *Cyprinus carpio*; GLP compliance not specified; "*Test chemical concentration was not verified analytically*"; Test material: a substance identified as Dodecan-1-ol, CAS 9002-92-0 (EC 500-002-6); 48 hrs LC_{50} = 3.72 mg/L (nominal concentration).
iii. Database extract (authoritative database (2018) and secondary source (2019)); Exposure duration = 48 hrs; Species: *Poecilia reticulata*; GLP compliance not specified; "*Test chemical concentration was not verified analytically*"; Test material: a substance identified as Dodecan-1-ol, CAS 9002-92-0 (EC 500-002-6); 48 hrs LC_{50} = 8.61 mg/L (nominal concentration).
iv. Experimental study with analogue substance; Exposure duration = 96 hrs; Species: *Salmon salar;* GLP compliance not specified; Test material: a substance identified as Polyoxyethylene (4) lauryl ether (Laureth 4), CAS 5274-68-0 (EC 226-097-1); 96 hrs LC_{50} = 1.5 mg/l.

ECHA understands that you claim that studies under sources of information (i, ii and iii) were conducted with the Substance.

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

Annex XI, Section 1.2 states that there may be sufficient 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.

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.

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

To fulfil the information requirement, normally a study performed according to OECD TG 203 must be provided. OECD TG 203 requires the study to investigate the following key parameter of juvenile fishes:

- mortality.

All four of the provided sources of information may provide relevant information on the mortality of fish. However, the reliability of these sources of information is significantly affected by the number of deficiencies.

ECHA understands that two of the provided sources of information (ii and iii) are reported in the registration dossier and quality deficiencies of these studies affecting their reliability have already been noted above. There is no new information addressing deficiencies of these studies provided in the comments on the draft decision .

- Identity of the test material

The test material in studies according to OECD TG 202 must be representative for the Substance (ECHA Guidance R.4.1).

The unambiguous characterisation of the composition of the Substance and test material used to generate the data is required to evaluate the representativeness of the test material. The composition of the selected test material must be reported in the respective endpoint study record, under the test material section.

ECHA understands that the study (source information i) was performed with mono-constituent substance. Bearing in mind that the Substance is UVCB, relevance of source of information i for the purpose of risk assessment under REACH and classification/labelling should be considered and justified in the registration dossier.

Therefore, source of information (i) is not considered reliable.

- Quality of the sources of information (i and iv)

A study must comply with the conditions of OECD TG 203 and OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test. Therefore, the following requirements must be met:

- Information on the study design (number of replicates and number of test fishes per exposure concentration) needs to be reported;
- The results can only be based on nominal or measured initial concentration if the concentration of the test material has been satisfactorily maintained within 20 % of the nominal or measured initial concentration throughout the test (see also ECHA Guidance R.7b, Section R.7.8.4.1);

- The test duration is 96 hours or longer.

Information on number of replicates and number of test fishes per exposure concentration is not available for sources of information (i and iv).
Furthermore, for these sources of information there is no information whether or not test material exposure concentrations throughout the test duration were verified and maintained within the required 20% of the measured initial concentrations.
For the source of information i, exposure duration of the study was 48 hours.
Consequently, the condition of the standard OECD test are not met for sources of information i and iv.

- Read-across as part of weight of evidence

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.

ECHA understands that you predict the properties of the Substance using a read-across hypothesis with source of information iv 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.

Read-across hypothesis
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[14]. It should explain why the differences in the chemical structures should not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern.

In the comments of the draft decision you summarise that prediction of short-term fish toxicity from the source substance (Polyoxyethylene (4) lauryl ether, CAS 5274-68-0, EC No 226-097-1) is applicable for the Substance "*Based on structurSupporting al similarity, physical-chemical properties, organic functional groups and several general and endpoint specific mechanistic approach using OECD QSAR toolbox v3.4, Polyoxyethylene (4) lauryl ether (CAS no. 5274-68-0; EC no. 226-097-1) was identified as read-across chemical with sufficient data for ecotoxicological evaluations used for the target chemical Dodecan-1-ol, ethoxylated (CAS no. 9002-92-0; EC no. 500-002-6).*" Furthermore, you noted that the "*use profile for the target substance and read-across analogue Polyoxyethylene (4) lauryl ether (CAS no. 5274-68-0) are similar. Both chemicals used as a surfactant.*"

While structural similarity is a prerequisite for applying the grouping and read-across approach, such similarity, as well as physico-chemical similarity, does not necessarily lead to predictable or similar ecotoxicological properties. You have not provided a well-founded hypothesis to establish a reliable prediction for the short-term fish toxicity, based on recognition of the structural and physico-chemical similarities and differences between the source substance and your Substance.

Supporting information

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

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*"[15]. 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 [toxicokinetic information on the formation of the common compound/supporting information/bridging studies to compare properties of the Substance and source substances/ information to confirm your claimed worst-case prediction/information on the impact of exposure parent compounds on the prediction/...]

In your comment on the draft decision, there is supporting information to compare short-term toxicity to fish of the Substance with this of the source substance from DNA and protein binding alerts predicting tools, acute aquatic toxicity classification by Verhaar, by OASIS and by ECOSAR tools, and overview of functional groups similarity. However, there is no reliable bridging studies to compare properties of the Substance and source substances and/or information to confirm your claimed worst-case prediction.

Thus, the data set reported in the technical dossier does not include sufficient relevant, reliable and adequate information for the Substance and of the source substance to support your read-across hypothesis.

In the absence of such information, you have not established that the Substance and of 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.

Characterisation of the source substance
According to the ECHA Guidance, "*the purity and impurity profiles of the substance and the structural analogue need to be assessed*", and "*the extent to which differences in the purity and impurities are likely to influence the overall toxicity needs to be addressed, and where technically possible, excluded*". The purity profile and composition can influence the overall toxicity/properties of the Substance and of the source substance(s).[16] Therefore, qualitative and quantitative information on the compositions of the Substance and of the source substance(s) should be provided to allow assessment whether the attempted predictions are compromised by the composition and/or impurities.

Furthermore, whenever the Substance and/or the source substance) are UVCB (Unknown or Variable composition, Complex reaction products or of Biological materials) substances qualitative compositional information of the individual constituents of the substances needs to be provided; 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.[17]

Your documents provided with the comments on the draft decision do not contain compositional information for the source substance. Moreover, bearing in mind that the Substance is UVCB, relevance of source of information (iv) for the purpose of risk assessment

[15] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.2.1.f
[16] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.3.1
[17] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.5.5

under REACH and classification/labelling should be considered and justified in the registration dossier.

Therefore, ECHA considers that it is not possible to assess whether the attempted prediction is compromised by the composition of the source substance.

Furthermore, quality of the source of information (iv) is addressed above.

As a conclusion on the proposed WoE approach, sources of information, as indicated above, provide information on the mortality of fish, but provided information is not reliable and/or relevant.

Thus, it is not possible to conclude, based on any source of information alone or considered together, whether the Substance has or has not the particular dangerous property foreseen to be investigated in an OECD TG 203 study.

Due to the UVCB nature, surface activity and ready biodegradability of the Substance you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6/REV1 (6 July 2018) and ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested aquatic toxicity tests and for calculation and expression of the result of the tests.

The substance is difficult to test due to the surface activity and ready biodegradability. OECD TG203 specifies that for difficult to test substances, the OECD Guidance 23 is to be followed. To get reliable results, the substance properties need to be considered when performing the test, in particular with regard to the test design; including exposure system, test solution preparation, and sampling. OECD GD 23 (Table 1) describes testing difficulties related to a specific property of the Substance. You may use the approaches described in OECD GD 23 or other approaches if more appropriate for your Substance. The approach selected must be justified and documented. Due to the Substance properties it may be difficult to achieve and maintain the exposure concentrations. Therefore, you have to demonstrate that the concentration of the substance is stable throughout the test (i.e. measured concentrations remains within 80-120% of the nominal concentration). If it is not possible to demonstrate the stability, you must express the effect concentration based on measured values as described in the applicable test guideline. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the test solution preparation method applied was sufficient to maximise the concentration of the Substance in the test solution.

In case you decide to use the Water Accommodated Fraction (WAF) approach in your ecotoxicity tests, please note that this approach may not be adequate to determine the toxicity of multi-component substances where its poorly soluble components are of concern, as in the case of your Substance. In general, it is critical that a robust chemical analysis is carried out prior the test, to identify those constituents present in the water to which the test organisms are exposed. Additionally, chemical analysis to demonstrate attainment of equilibrium in WAF preparation and stability during the conduct of the test is required. Methods capable of identifying gross changes in the composition of WAFs with time, such as e.g. ultra-violet spectroscopy or total peak area, are required for this purpose. The method used to prepare the WAF should be fully described in the test report and evidence of the compositional stability of the test substance over time should be provided.

Therefore, the information provided does not fulfil the information requirement.

Appendix C: Procedural history

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 compliance check was initiated on 12 July 2018.

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

ECHA took into account your comments and did not amend the requests.

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

As no amendments were proposed, ECHA took the decision according to Article 51(3) of the REACH Regulation.

Appendix D: Observations and technical guidance

1. This compliance check decision does not prevent ECHA from initiating further 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 the Member States.

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 shall 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'[18].

4. Test material
Selection of the test material(s) for UVCB susbstacnces
The registrants of the Substance are responsible for agreeing on the composition of the test material to be selected for carrying out the tests required by the present decision. The test material selected must be relevant for all the registrants of the Substance, i.e. it takes into account the variation in compositions reported by all members of the joint submission. The composition of the test material(s) must fall within the boundary composition(s) of the Substance.
While selecting the test material you must take into account 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. Any constituents that have harmonised classification and labelling according to the CLP Regulation (Regulation (EC) No 1272/2008) must be identified and quantified using the appropriate analytical methods.
The OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring, Number 11 [ENV/MC/CHEM(98)16] requires a careful identification of the test material and description of its characteristics. In addition, the Test Methods Regulation (EU) 440/2008, as amended by Regulation (EU) 2016/266, requires that "if the test method is used for the testing of a [...] UVCB [...] sufficient information on its composition should be made available, as far as possible, e.g. by the chemical identity of its constituents, their quantitative occurrence, and relevant properties of the constituents".
In order to meet this requirement, all the constituents of the test material used for each test must be identified as far as possible. For each constituent the concentration value in the test material must be reported in the Test material section of the endpoint study record.
Technical Reporting of the test material for UVCB substances

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

The composition of the selected test material must be reported in the respective endpoint study record, under the Test material section. The composition must include all constituents of the test material and their concentration values and an indication of the ethoxylation degree ≤2,5. Without such detailed reporting, ECHA may not be able to confirm that the test material is relevant for the Substance and to all the registrants of the Substance.
Technical instructions are available in the manual "How to prepare registration and PPORD dossiers" on the ECHA website[19].

5. Environmental testing for UVCB substances

Your Substance is a UVCB 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.

6. List of references of the ECHA Guidance and other guidance/ reference documents[20]

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 in this decision.

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 in this decision.

ECHA Read-across assessment framework (RAAF, March 2017)[21]

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

[19] https://echa.europa.eu/manuals
[20] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[21] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

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.

OECD Guidance documents[22]

Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD23.

Guidance Document on Mammalian Reproductive Toxicity Testing and Assessment – No 43, referred to as OECD GD43.

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

Appendix E: 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 fufilled
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[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.