~~Confidential~~

Helsinki, 15 June 2021

Addressees
Registrant(s) of JS_2-butyloctanoic acid as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
27/05/2020

Registered substance subject to this decision ("the Substance")
Substance name: 2-butyloctanoic acid
EC number: 248-570-1
CAS number: 27610-92-0

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***20 September 2022***.

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

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

1. Surface tension (Annex VII, Section 7.6.; test method: EU A.5./OECD TG 115)

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

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

B. Information required from all the Registrants subject to Annex VIII of REACH

1. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.; test method: OECD TG 473) or In vitro micronucleus study (Annex VIII, Section 8.4.2.; test method: OECD TG 487)

2. If negative results are obtained in test performed for the information requirement of Annex VIII, Section 8.4.2. then: In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)

3. Short-term repeated dose toxicity (28 days; Annex VIII, Section 8.6.1.) to be combined with the Screening for reproductive/developmental toxicity below

4. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.64/OECD TG 422) by oral route, in rats

5. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: OECD TG 203)

Reasons for the request(s) are explained in the following appendices:

- Appendix entitled "Reasons common to several requests";
- Appendices entitled "Reasons to request information required under Annexes VII to VIII of REACH", respectively.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH:

- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa.

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

How to comply with your information requirements

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

You must follow the general testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil 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.

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 Reasons common to several requests

1. Assessment of your read-across approach under Annex XI, Section 1.5.

You seek to adapt the information requirements for the following standard information requirements by grouping substances and applying a read-across approach in accordance with Annex XI, Section 1.5:

- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)

You have provided the following two read-across adaptations:

1) a read-across adaptation based on a category "Isocarb" (for all properties mentioned above)
2) a read-across based on an analogue approach (for ecotoxicological properties)

ECHA has considered the scientific and regulatory validity of your grouping and 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 (addressed under 'Scope of the grouping'). 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 R.6. and related documents[2,3].

ECHA has evaluated the category approach under section I below and the analogue approach under section II.

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

A. Scope of the grouping

i. Description of the grouping

In your registration dossier you have formed a category of 'the substances ISOCARB 11, 12, [redacted], 24 and Docosanoic acid'. You have provided a read-across justification document in

[2] 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)

[3] 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

IUCLID Section 13.

For the purpose of this decision, the following abbreviations are used for the group members:
[1] ISOCARB 11 (Reaction mass of 2-methyldecanoic acid and 2-ethylnonanoic acid and 2-propyloctanoic acid and 2-butylheptanoic acid, EC No. 941-570-9);
[2] ISOCARB 12 (2-butyloctanoic acid, CAS No. 27610-92-0, EC No. 248-570-1);
[3] ISOCARB 24 (2-decyltetradecanoic acid, CAS No. 93778-52-0, EC No. 298-190-5);
[4] [redacted] and
[5] Docosanoic acid, CAS No. 112-85-6, EC No. 204-010-8.

You provide the following reasoning for the grouping the substances. *"In this particular case the similarity of the ISOCARB category members is justified,* […] *on basis of scope of variability and overlapping of composition, representative molecular structure, physico-chemical properties, toxicological, ecotoxicological profiles and supported by various QSAR methods*. […]".

You define the applicability domain of the category as follows: *"ISOCARB are aliphatic branched carboxylic acids and include substances with carbon chain lengths of C11 to C24. Their only functional group is the carboxyl group, which they share in common. As can be seen from the graphical representation a single branching exists at the C2 position, where the branches differ in chain length from methyl to decyl".*

ii. Assessment of the grouping

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

Applicability domain of the category

According to the ECHA Guidance, a category (grouping) hypothesis should address "*the set of inclusion and/or exclusion rules that identify the ranges of values within which reliable estimations can be made for category members for the given endpoint".*[4] Particularly, "*the applicability domain of a (sub)category would identify the structural requirements and ranges of physico-chemical, environmental fate, toxicological or ecotoxicological properties within which reliable estimations can be made for the (sub)category members*".[5] Therefore, to reliably predict properties within a category the applicability domain should be described including the borders of the category, for which chemicals the category does not hold and a justification for the inclusion and/or exclusion rules.

You describe the applicability domain of the substances covered by the grouping as: "*ISOCARB are aliphatic branched carboxylic acids and include substances with carbon chain lengths of C11 to C24. Their only functional group is the carboxyl group, which they share in common. As can be seen from the graphical representation a single branching exists at the C2 position, where the branches differ in chain length from methyl to decyl".*

First, this applicability domain defines branched substances with one functional group and a chain length of C11 to C24. However, category members [4] and [5] do not fullfill the criteria of branched C2 position which is used to define the applicability domain of the ISOCARB category: [5] is linear and [4] is a multi-constituent substance where one of the constituents

[4] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.4.1
[5] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.1.2

is linear.

Second, the applicability domain of your category does not identify the structural requirements and ranges of physico-chemical, environmental fate, toxicological or ecotoxicological properties within which reliable estimations can be made for the category members

Therefore, the applicability domain does not describe the borders of the category covering all category members nor unambiguously identifies the structural requirements and ranges of physico-chemical, environmental fate, toxicological or ecotoxicological properties within which reliable estimations can be made for the (sub)category members.

B. Predictions for properties

a. Prediction for toxicological properties

You have provided the following reasoning for the prediction of toxicological properties: *"All available experimental data indicate that the target and source substances are not acutely toxic and do not have sensitizing properties. Repeated dose toxicity was shown to be low for all substances. None of the substances showed mutagenic effects or toxicity to reproduction. Only the Category Member 1 has skin and eye irritating properties whereas all other Category Member are not skin or eye irritating".*

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

You intend to predict the properties for the category members from information obtained from the following source substances:

In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- Substance [1], ISOCARB 11 (EC No. 941-570-9), OECD TG 473 (2015)
- Substance [5], docosanoic acid (EC No. 204-010-8), OECD TG 473 (2002)

In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Substance [3], ISOCARB 24 (EC No. 298-190-5), OECD TG 476 (2015)
- Substance [1], ISOCARB 11 (EC No. 941-570-9), OECD TG 476 (2015)

Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Substance [1], ISOCARB 11 (EC No. 941-570-9), OECD TG 407 (2015)
- Substance [5], docosanoic acid (EC No. 204-010-8), OECD TG 422 (2002)

Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Substance [5], docosanoic acid (EC No. 204-010-8) OECD TG 422 (2002)

ECHA notes the following shortcoming(s) with regards to prediction(s) of toxicological properties.

1. *Read-across hypothesis contradicted by existing data*

Annex XI, Section 1.5. provides that "substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances. The ECHA

Guidance[6] indicates that "*it is important to provide supporting information to strengthen the rationale for the read-across*". 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 category members. The observation of differences in the toxicological properties among some members of a category is a warning sign. An explanation for such a difference resulting in a contradiction between the similarities in properties claimed in the read-across hypothesis and the observation of different properties needs to be provided and supported by scientific evidence.

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar category members cause the same type of effect(s).

In the technical dossier and in the "mammalian toxicity" data matrix (table 4) of your justification document, the results on prenatal developmental toxicity obtained with the Substance differ from the results obtained from the studies mentioned above. Specifically, the NOAEL identified for maternal systemic toxicity in that study was 25 mg/kg bw/d, whereas the data from the short-term repeated dose toxicity with substance [1] and the combined repeated dose toxicity study with the reproduction/developmental toxicity screening study with substance [5] both resulted in NOAELs of 1000 mg/kg bw/d for systemic toxicity.

You have not provided any explanation for this difference.

In your comments to the draft decision, you attribute this difference to an assumed higher sensitivity of pregnant animals used in the OECD TG 414 study with the Substance. You also indicate your intention to improve your read-across justification by providing additional argumentation for the existing results.

With your comments, you have not provided new supporting (experimental) data to support a read-across adaptation.

In addition, ECHA notes that no maternal systemic toxicity was observed in the OECD TG 422 study with substance [5], which also used pregnant rats treated orally but for an exposure period longer than the one used in an OECD TG 414 (52 days, from 2 weeks before gestation to 3 days after gestation, vs. 14 days, from gestation day 6 to gestation day 19). If the Substance and substance [5] had similar toxic properties towards pregnant animals, signs of maternal systemic toxicity would have been expected with substance [5] in the OECD TG 422 study. This was not the case.

ECHA cannot conclude on the reliability of the read-across approach proposed in the comments because the acceptability will depend on the relevance of the supporting information.

Please note that this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation).

The available set of data on the category members indicates differences in the toxicological properties of the substances. This contradicts your read-across hypothesis whereby the structurally similar category members cause the same type of effect(s). Therefore, you have not demonstrated and justified that the properties of the category members are likely to be similar despite the observation of these differences.

[6] Guidance on information requirements and chemical safety assessment (version 6.0, July 2017), Chapter R.6, Section R.6.2.2.1.f

2. *Supporting information*

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*"[7]. The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on other category members.

Supporting information must include bridging studies to compare properties of the category members.

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar category members cause the same type of effects. In this context, relevant, reliable and adequate information allowing to compare the properties of the category members 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 category members.

In the read across justification document you claim that: *"All available experimental data indicate that the target and source substances are not acutely toxic and do not have sensitizing properties. Repeated dose toxicity was shown to be low for all substances. None of the substances showed mutagenic effects or toxicity to reproduction. Only the Category Member 1 has skin and eye irritating properties whereas all other Category Member are not skin or eye irritating. All of the studies presented in the dossier were reliable, means assessed as Klimisch 1 or 2."*

In your comments to the draft decision, you indicate your intention to "*[…] revise the Category Approach of the Guerbet acids (Isocarb Category). Instead of a category approach for all Isocarb products* [you] *will create an analogue justification for 2-butyloctanoic acid. […] Only for the endpoint reproductive/developmental toxicity* [you] *still consider the whole category including docosanoic acid (C22)."* To support your new read-across hypothesis, you also intend to perform additional testing to demonstrate that the presence of carbon-chain branching in the Substance has no effect on toxicity compared to that of some of the analogue substances.

Your dossier contains information generated with source substances [1], [3] and [5], for the endpoints which you intend to adapt. It does not contain information with the Substance for these endpoints except for gene mutation in bacteria.

The data set reported in the technical dossier does not include relevant, reliable and adequate information for the target substance, the Substance, to support your read-across hypothesis. As discussed in the section *Assessment of the grouping* above, substance [5] does not fullfill the criteria you defined for the category and you have not demonstrated that data on that substance can be used for prediction. Therefore, with information from source substance [1] or [3], it is not possible to compare properties with the Substance.

The information in your comments is not sufficient for ECHA to make an assessment, because you have not provided new supporting (experimental) data to support a read-across adaptation. Furthermore, ECHA cannot conclude on the reliability of the read-across approach proposed in the comments because acceptability will depend on the outcome of the proposed studies and the relevance of the supporting information.

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

Furthermore, ECHA observes that your intention to strengthen the approach does not include the generation of information on repeated dose toxicity and reproductive and developmental toxicity with the target substance, and that the deficiency identified in this subsection is likely to remain.

Please note that this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation).

In the absence of such information, you have not established that all category members are likely to have similar properties. Therefore you have not provided reliable and adequate bridging studies to strengthen the rationale for the read-across.

b. Predictions for ecotoxicological properties

You have provided the following reasoning for the prediction of ecotoxicological properties: *"The structural similarities result in the same mode of ecotoxicological action.[…] The available study results indicate that the toxicity of the ISOCARB decrease with increasing carbon chain lengths, due to the declining water solubility."*.

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted based on an identified trend within the group.

Based on the Table 5 in the read-across justification document, you intend to predict the properties for the category members from information obtained from the following source substances:

Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Substance [1], information on the calculated value of effect concentration is not reported in the registration dossier under the specific endpoint.
- Substance [2], study according to OECD TG 202 (1999) and effect concentration predicted by ECOSAR version 1.00.
- Substance [3], study is not reported in the registration dossier under the specific endpoint.
- Substance [4], study according to OECD TG 202 (2014).

Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Substance [1], information on the calculated value of effect concentration is not reported in the registration dossier under the specific endpoint.
- Substance [2], effect concentration predicted by ECOSAR version 1.00.
- Substance [3], study is not reported in the registration dossier under the specific endpoint.
- Substance [4], study according to OECD TG 201 (2014).

Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)
- Substance [1], information on the calculated value of effect concentration is not reported in the registration dossier under the specific endpoint.
- Substance [2], effect concentration predicted by ECOSAR version 1.00.
- Substance [3], study is not reported in the registration dossier under the specific endpoint.

ECHA notes the following shortcoming(s) with regards to prediction(s) of aquatic toxicity.

a. Adequacy of information on aquatic toxicity

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across should:

- be adequate for the purpose of classification and labelling and/or risk assessment;
- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).
- have adequate and reliable documentation of the applied method.

- *Experimental aquatic toxicity studies*

Specific issues of adequacy and reliability of studies submitted to predict the properties for the category members are identified and addressed in the relevant endpoint-specific reasons in appendices A-B.

Due to these shortcomings, ECHA concludes that the studies are unreliable and are not adequate for the purpose of classification and labelling and/or risk assessment.

- *Effect concentrations predicted by ECOSAR version 1.00*

For the same reasons as reasons explained below in the section 2 on Assessment of the (Q)SAR adaptation under Annex XI, Section 1.3., you have not demonstrated that the prediction for the Substance is adequate for the purpose of classification and labelling and/or risk assessment.

- *Studies and information not reported in the registration dossier*

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).[8]

You have not provided in the registration dossier:

- documentation for the calculated values of effect concentrations for Substance [1]; and
- robust study summary(ies) for Substance [3], study is not reported in the registration dossier under the specific endpoint.

In the absence of such documentation, ECHA cannot verify that the properties of your Substance can be predicted from the data on the source substances, so such data are not adequate for the purpose of classification and labelling and/or risk assessment.

- *Relevance of short-term aquatic toxicity studies for source substance [3]*

Poorly water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests does not give a true measure of toxicity for this type of substances and the long-term test is required. A substance is regarded as poorly water soluble if, for instance, it has a water solubility below 1 mg/L or below the detection limit of the analytical method of the test material (ECHA Guidance R.7.8.5).

In the read-across justification document for the source substance [3], you noted that aqueous solubility is "*practically insoluble*" and in the published registration dossier of the source substance [3] (2-decyltetradecanoic acid - Registration Dossier - ECHA (europa.eu)) it is noted that "*The water solubility was determined to be < 0.5 mg/l (detection limit).*

[8] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.6.2

Additionally was the water solubility calculated used the program WATERNT v1.01 (part of US EPA EPI Suite v4.11) for 2 -decyltetradecanoic acid to be 0.0000122 mg/l.", i.e. this substance is poorly water soluble with a water solubility below 1 mg/l.

Therefore, ECHA concludes that short-term aquatic toxicity studies with invertebrates and fish do not give a true measure of toxicity for the Substance [3] and are not adequate to predict short-term aquatic toxicity for the members of the category and thus is not adequate for the purpose of classification and labelling and/or risk assessment.

- *test material identity (source substance [4])*

The unambiguous characterisation of the composition of the source substance and test material used to generate the source data is required to evaluate the reliability and uncertainty associated with predicting properties of substances with potential substantial compositional differences. The composition of the selected test material must be reported in the respective endpoint study record, under the test material section.

Your technical dossier contains limited compositional information for the source substance [4]. The identification/naming information on test material provided in your dossier is limited to the name of this multi-constituent substance and numerical identifier. The concentrations of the constituents are not provided for the test material.

Without comprehensive reporting of all constituents present in the test material (including their identity and concentrations), no qualitative or quantitative comparative assessment between the compositions of the different substances as source substance/test material on the one hand, and of the Substance on the other hand, can be completed.

ECHA is unable to confirm that the test material which is a multi-constituent is relevant for the Substance and to all the registrants of the Substance. Therefore, ECHA concludes that it is not possible to assess whether the attempted predictions are compromised by the composition of these test materials and that you have not provided adequate and reliable documentation nor demonstrates that the results are adequate for the purpose of classification and labelling and risk assessment for the Substance.

Thus, ECHA concludes that information used to predict the properties for the category members from the source substances and the Substance is not adequate for the purpose of classification and labelling and/or risk assessment.

b. 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*"[9]. 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 other category members.

Supporting information must include bridging studies to compare properties of the category members.

As indicated above, your read-across hypothesis is based on the assumption that the

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

structurally similar category members cause the same type of effects. In this context, relevant, reliable and adequate information allowing to compare the properties of the category members 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 category members.

You claim in the Read across justification document that: *"Based on the data, it appears that the species of all trophic levels are similar sensitive. The available study results indicate that the toxicity of the ISOCARB decrease with increasing carbon chain lengths, due to the declining water solubility".*

In support of this claim you have noted in the Table 5 of the read-across justification document information obtained from the source substances from which you intend to predict aquatic toxicity properties for the category members.

As explained in the section *'a. Adequacy of information on aquatic toxicity'* above, information used to predict the properties for the category members from the source substances and the Substance is not adequate for the purpose of classification and labelling and/or risk assessment. Thus, you have not provided reliable and adequate bridging studies to support your read-across hypothesis.

In the absence of such information, you have not established that all category members are likely to have similar properties. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

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

A. Predictions for ecotoxicological properties

a. 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).[10]

You have provided aquatic toxicity studies conducted with other substance (lauric acid, EC 205-582-1, CAS 143-07-7) than your Substance in order to comply with the REACH information requirements for:

- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)

You have not provided documentation as to why this information is relevant for your Substance.

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

b. Adequacy and reliability of aquatic toxicity studies

[10] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.6.2

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across should:

- be adequate for the purpose of classification and labelling and/or risk assessment;
- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).
- have adequate and reliable documentation of the applied method.

Additional issues of adequacy and reliability of studies submitted are identified and addressed in the relevant endpoint-specific reasons in appendices A-B.

Due to these shortcomings, ECHA concludes that the studies are unreliable.

III. Conclusions on the grouping of substances and read-across approach

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

2. Assessment of the (Q)SAR adaptation under Annex XI, Section 1.3.

You seek to adapt the following standard information requirements by applying (a) (Q)SAR approach(es) in accordance with Annex XI, Section 1.3:

- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)

Furthermore, you used effect concentrations predicted by (Q)SAR (ECOSAR version 1.00) to support grouping of substances and application of a read-across approach in accordance with Annex XI, Section 1.5.

ECHA has considered the scientific and regulatory validity of your (Q)SAR adaptation(s) in general before assessing the specific standard information requirements in the following appendices.

Under Annex XI, Section 1.3., the following conditions must be fulfilled whenever a (Q)SAR approach is used:

1. the prediction needs to be derived from a scientifically valid model,
2. the substance must fall within the applicability domain of the model,
3. results need to be adequate for the purpose of risk assessment or classification and labelling, and
4. adequate and reliable documentation of the method must be provided.

With regard to these conditions, we have identified the following issue(s):

a. The prediction is not adequate due to low reliability

Under ECHA Guidance R.6.1.3.4 a prediction is adequate for the purpose of classification and labelling and/or risk assessment when the model is applicable to the chemical of interest with the necessary level of reliability. ECHA Guidance R.6.1.5.3. specifies that, among others, the following cumulative conditions must be met:

- reliable input parameters are used

In regard of Kow for surfactants the following is noted in various parts of ECHA Guidance documents which is relevant for assessing the reliability of input parameters:

- R.7a (p. 78-79): None of the experimental methods is very well suited for determining the Kow of surface active substances. 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.
- R.7b (p. 83) for aquatic toxicity: QSAR modelling is potentially very difficult since the Kow cannot usually be measured.

In the registration dossier you have provided estimation of aquatic toxicity effect concentrations (by ECOSAR v1.00 model) for the Substance. For the aquatic toxicity estimations you note that there are "ECOSAR l*imitations: If the log Kow value is greater than 5.0, or if the compound is solid and the LC50 exceeds the water solubility by 10X, no effects at saturation are predicted. However, the log KOW of 2 -butyl octanoic acid is estimated 4.33 and falls therefore in the applicability domain*.".

There is no evidence provided in the dossier that CMC was used for the estimation of Kow for the Substance.

Based on the structure, the Substance is ionisable and a potential surfactant, which may be confirmed based on the surface active information requested below (the Substance contains lipophilic (long alkyl chain) and hydrophilic (carboxylic group) moieties).

In the absence of any consideration of CMC and its potential impact on the reliability of the input parameters, you have not demonstrated that QSAR estimations of aquatic toxicity effect concentrations based on Kow are not reliable for the Substance.

Consequently, you have not demonstrated that the prediction for the Substance is adequate for the purpose of classification and labelling and/or risk assessment.

b. Inadequate documentation of the model (QMRF)

Under Appendix C of the OECD Guidance document on the validation of (Q)SAR models (ENV/JM/MONO(2007)2) and ECHA Guidance R.6.1.6.3., adequate and reliable documentation must include a (Q)SAR Model Reporting Format document (QMRF) which reports, among others, the following information:

- the predicted endpoint, including information on experimental protocol and data quality for the data used to develop the model;
- an unambiguous definition of the algorithm, the descriptor(s) of the model and its applicability domain,
- an estimate of the goodness-of-fit and of the predictivity of the model, including information on training set and validation statistics.

You have not provided information about the model listed above.

In absence of such information, ECHA cannot establish that the model can be used to meet this information requirement.

c. Lack of or inadequate documentation of the prediction (QPRF)

ECHA Guidance R.6.1.6.3 states that the information specified in or equivalent to the (Q)SAR Prediction Reporting Format document (QPRF) must be provided to have adequate and reliable documentation of the applied method. For a QPRF this includes, among others:

- the model prediction(s), including the endpoint,
- a precise identification of the substance modelled,
- the relationship between the modelled substance and the defined applicability domain,
- the identities of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

You have not provided QPRF addressing information listed above. Therefore, you have not provided sufficient information about the prediction.

In absence of such information, ECHA cannot establish that the prediction can be used to meet these information requirements.

Consequently, ECHA cannot verify that the cumulative conditions of Annex XI, Section 1.3 listed above are met. Therefore, the provided information based on application of QSARs and your adaptations are rejected.

Appendix A: Reasons to request information required under Annex VII of REACH

1. Surface tension

Surface tension is a standard information requirement in Annex VII to REACH.

You have adapted the information under Annex VII, Section 7.6., Column 2, providing the following information:

i. In accordance with column 2 of REACH Annex VII, the surface tension of the substance does not need to be tested because due to its chemical structure, no surface activity is predicted.

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

According to Annex VII, Section 7.6, Column 2, the study need only be conducted if:

- based on structure, surface activity is expected or can be predicted, or
- surface activity is a desired property of the material.

You have provided no explanation to your adaptation.
The Substance, however, contains lipophilic (long alkyl chain) and hydrophilic (carboxylic group) moieties.

Therefore, surface activity can be expected, and an experimental study is required.

In your comments to the draft decision, you indicate that an OECD 115-study on the Substance is available and that you will provide this information in an update of your registration dossier. You state that the surface tension of the aqueous solution is 71.8 mN/m at a temperature of 20 °C indicating that the Substance has no surface activity.

The information in your comments is not sufficient for ECHA to make an assessment, because you have not provided a full report of the study.

Please note that, as indicated in the *Appendix on Reasons common to several requests*, this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation").

Therefore, the adaptation is rejected.

2. Short-term toxicity testing on aquatic invertebrates

Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII to REACH (Section 9.1.1.).

You have provided the following information:

i. OECD TG 202 key study with the Substance (1999)
ii. Adaptation by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. supported by:
    a. OECD TG 202 supporting study with the analogue substance: source substance [4].
    b. OECD TG 202 supporting study with the analogue substance: lauric acid.
    c. data listed under i. and iii.
iii. Adaptation according to Annex XI, section 1.3. supported by effect concentration predicted by ECOSAR version 1.00.

We have assessed this information and identified the following issues:

Reliability of key study (i.)

To fulfil the information requirement, a study must comply with OECD TG 202 and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

- a reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available;
- the concentrations of the test material are measured at least at the highest and lowest test concentration, at the beginning and end of the test;
- the effect values 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);
- adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations are provided;

Your registration dossier provides an OECD TG 202 showing the following:

- Exposure concentrations were measured with TOC only at the beginning of the test.
- TOC concentration of the dilution water (before the Substance is added to it) is not reported.
- You have not provided performance parameters of the analytical method (e.g. LOD, LOQ, recovery).

The Substance is difficult to test due to the structure, the Substance is ionisable and a potential surfactant, which may be confirmed based on the surface active information requested above. The Substance contains lipophilic (long alkyl chain) and hydrophilic (carboxylic group) moieties.

Based on the above, there are critical methodological deficiencies resulting in the rejection of the key study i. results. More, specifically, due to the absence of analytical determination of exposure concentrations at the end of the test it cannot be confirmed if the concentration of the test material has been satisfactorily maintained within 20% of the nominal or measured initial concentration throughout the test. Furthermore, it cannot be estimated what is the contribution of the Substance to the TOC concentration measured at the beginning of the test. Thus, the study is not reliable.

Therefore, the requirements of OECD TG 202 are not met for the key study i.

Rejection of adaptations according to Annex XI, section 1.5.

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

Rejection of adaptation according to Annex XI, section 1.3.

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

On this basis, the information requirement is not fulfilled.

Study design

As explained, the Substance is difficult to test due to the structure, the Substance is ionisable and a potential surfactant (which may be confirmed based on the surface active information requested above) (the Substance contains lipophilic (long alkyl chain) and hydrophilic (carboxylic group) moieties). OECD TG 202 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 202. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

In your comments to the draft decision, you agree to perform the study with the Substance, according to OECD TG 202.

3. Growth inhibition study aquatic plants

Growth inhibition study aquatic plants is an information requirement under Annex VII to REACH (Section 9.1.2.).

You have provided the following information:

i. Adaptation by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. supported by:
   a. OECD TG 201 key study with the analogue substance: source substance [4].
   b. OECD TG 201 supporting study with the analogue substance: lauric acid.
   c. data listed under ii.

ii. Adaptation according to Annex XI, section 1.3. supported by effect concentration predicted by ECOSAR version 1.00.

We have assessed this information and identified the following issues:

Rejection of adaptation according to Annex XI, section 1.5.

As explained in the *Appendix on Reasons common to several requests* your adaptation is rejected. The following endpoint-specific deficiencies have also been identified in your read-across adaptation:

Reliability of studies

As explained in the Appendix on reasons common to several requests, if grouping concept is applied then in all cases the results must have adequate and reliable coverage of the key parameters of the corresponding test methods, in this case OECD TG 201 with OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test. For that, the following specification apply:

- the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form;
- the concentration of solvent should not exceed 100 µl/L;

- the results can be based on nominal or measured initial concentration only if the concentration of the test material has been maintained within 20 % of the nominal or measured initial concentration throughout the test.

Your registration dossier provides OECD TG 201 studies i.a. and i.b. showing the following:

- tabulated data on the algal biomass determined daily for each treatment group and control are not reported;
- the concentration of the solvent (HCO-50) in the final test solution: 100 mg/l (study i.b.);
- measured concentrations at the end of the test were app. 60-70% of the initial measured concentrations and the results of the study are based on initial measured concentrations (study i.b.).

Based on the above, there are critical methodological deficiencies resulting in the rejection of the study results. Specifically,

- Data on the algal biomass determined daily for each treatment group and control are not reported. Therefore, the reporting of the studies is not sufficient to conduct an independent assessment of its reliability.
- The concentration of the solvent used in study i.b. is 1000 times higher than allowed by the OECD TG 201. Therefore, the study is not reliable.
- The results of the study i.b. are based on initial measured concentrations while measured concentrations at the end of the test were below 80% of the initial measured concentrations. Thus, the results of this study are not adequate for the purpose of classification and labelling and/or risk assessment.

Therefore, the requirements of OECD TG 201 are not met

Rejection of adaptation according to Annex XI, section 1.3.

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

On this basis, the information requirement is not fulfilled.

Study design

OECD TG 201 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix A.2.

In your comments to the draft decision, you agree to perform the study with the Substance, according to OECD TG 201.

Appendix B: Reasons to request information required under Annex VIII of REACH

1. In vitro cytogenicity study in mammalian cells or In vitro micronucleus study

In vitro cytogenicity study in mammalian cells is a standard information requirement in Annex VIII to REACH (Section 8.4.2.).

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

In support of your adaptation, you have provided the following sources of information:

i. OECD TG 473 study (2015) with the source substance [1] ISOCARB 11 (EC No. 941-570-9),
ii. OECD TG 473 study (2002) with the source substance [5] docosanoic acid (EC No. 204-010-8).

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

Therefore, the information requirement is not fulfilled.

In your comments to the draft decision, you agree to perform the study with the Substance, according to the OECD TG 473.

Study design

To fulfil the information requirement for the Substance, either *in vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) or *in vitro* micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) are considered suitable.

2. In vitro gene mutation study in mammalian cells

In vitro gene mutation study in mammalian cells is a standard information requirement in Annex VIII to REACH (Section 8.4.3.) in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

In support of your adaptation, you have provided the following sources of information:

i. OECD TG 476 study (2015) with the source substance [3] ISOCARB 24 (EC No. 298-190-5),
ii. OECD TG 476 study (2015) with the source substance [1] ISOCARB 11 (EC No. 941-570-9).

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

Therefore, the information requirement is not fulfilled.

Consequently, you are required to provide information for this endpoint, if the *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study provides a negative result.

In your comments to the draft decision, you agree to perform the study with the Substance, according to the OECD TG 476 or OECD TG 490.

Study design

To fulfil the information requirement for the Substance, either the *in vitro* mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

3. Short-term repeated dose toxicity (28 days)

Short-term repeated dose toxicity (28 day) is a standard information requirement in Annex VIII to REACH (Section 8.6.1.).

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

In support of your adaptation, you have provided the following sources of information:

i. OECD TG 407 study (2015) with the source substance [1] ISOCARB 11 (EC No. 941-570-9),
ii. OECD TG 422 study (2002) with the source substance [5] docosanoic acid (EC No. 204-010-8).

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

In your comments to the draft decision, you indicate your intention to submit a read-across justification for the repeated dose toxicity endpoints. Please refer to ECHA's reply in the Appendix on *reasons common to several requests.*

Please note that, as indicated in the *Appendix on Reasons common to several requests*, this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation").

You further refer to animal welfare and the use of the Substance mainly as cosmetics to support your disagreement to perform an OECD TG 407 or OECD TG 422 study.

Registrants of substances that use the substance also for non-cosmetic uses (i.e. mixed-use substances) may perform animal testing to fulfil the REACH information requirements, as a last resort, for all human health endpoints.[11]

In your dossier you indicate that your substance is manufactured in the EU and report widespread uses by professionals other than cosmetic uses; formulation and re-packing uses at industrial sites; consumer uses in cosmetic products.

As your registration dossier reports other uses, beyond cosmetic uses, you are not prevented

[11] See Commission Communication on the animal testing and marketing ban in the Cosmetics Regulation: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52013DC0135&from=EN. See also ECHA's factsheet on the interface between REACH and Cosmetics Regulations, developed jointly with the European Commission at https://echa.europa.eu/documents/10162/13628/reach_cosmetics_factsheet_en.pdf. The ECHA factsheet clarifies the practical meaning and implication of the Commission Communication. See also the ECHA questions and answers on animal testing available at https://echa.europa.eu/documents/10162/0/cosmetics_reach_interface_animal_testing_en.pdf/a1c91da8-bad8-64c3-400a-82db0085406a.

from performing the requested vertebrate test for the purposes of assessing the hazards of the Substance under the present information requirement.

Therefore, the information requirement is not fulfilled.

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), 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]

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, because the Substance is a liquid of very low vapour pressure. Although the information provided in your dossier indicates that human exposure to the Substance by the inhalation route is likely, the available oral developmental toxicity study in rat (1998) indicates a concern for systemic toxicity after oral administration (NOAEL = 25 mg/kg bw/d based on maternal toxicity).

Therefore the Combined repeated dose toxicity study with the reproduction/ developmental toxicity screening study must be performed according to the OECD TG 422, in rats and with oral administration of the Substance.

4. Screening for reproductive/developmental toxicity

A Screening for reproductive/developmental toxicity study (test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) is a standard information requirement under Annex VIII to REACH, if there is no evidence from analogue substances, QSAR or *in vitro* methods that the Substance may be a developmental toxicant. There is no information available in your dossier indicating that your Substance may be a developmental toxicant.

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

In support of your adaptation, you have provided the following source of information:

i. OECD TG 422 study (2002) with the source substance [5] docosanoic acid (EC No. 204-010-8).

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

In your comments to the draft decision, you indicate your intention to submit a read-across justification for the reproductive/developmental toxicity endpoints. Please refer to ECHA's reply in the *Appendix on reasons common to several requests*.

Please note that, as indicated in the *Appendix on Reasons common to several requests*, this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation").

[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)

You further refer to animal welfare and the use of the Substance mainly as cosmetics to support your disagreement to perform an OECD TG 421 or OECD TG 422 study. Please refer to ECHA's reply in request B.3 of this appendix. The same considerations apply for the present information requirement.

Therefore, the information requirement is not fulfilled.

You have not provided an adaptation based on Annex VIII, Section 8.7.1, Column 2, even though a pre-natal developmental toxicity study is available with the Substance, which could be used to adapt this information requirement. However, please be aware that this study does not inform on fertility, reproductive performance and post-natal developmental toxicity (see ECHA endpoint specific guidance[13]).

Study design

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 B.3), 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]

Therefore, a study according to the test method EU B.64/OECD TG 422 must be performed in rats with oral[14] administration of the Substance.

5. Short-term toxicity testing on fish

Short-term toxicity testing on fish is an information requirement under Annex VIII to REACH (Section 9.1.3.).

You have provided the following information:

i. Adaptation by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. supported by:
   a. OECD TG 203 supporting study with the analogue substance: lauric acid.
   b. data listed under ii.

ii. Adaptation according to Annex XI, section 1.3. supported by effect concentration predicted by ECOSAR version 1.00.

We have assessed this information and identified the following issues:

Rejection of adaptation according to Annex XI, section 1.5.

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

In your comments to the draft decision, you propose a read-across based on an analogue approach and you intend to predict the short-term toxicity of the Substance from the analogue substance dodecanoic acid (EC 205-582-1). You note that *"a well conducted study"* on this analogue substance is available and that study together with justification of the proposed read-across (analogue) approach will be provided in an update of the registration dossier.

[13] ECHA Guidance R.7a, 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)
[14] ECHA Guidance R.7a, Section R.7.6.2.3.2.

The information in your comments is not sufficient for ECHA to make an assessment of the proposed read-across (analogue) approach, because you have not provided adequate and reliable documentation in support of the proposed approach (further specification of such documentation is explained in the *Appendix on Reasons common to several requests*, Section 1.I.B.b).

Rejection of adaptation according to Annex XI, section 1.3.

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

In your comments to the draft decision, you indicate that for this endpoint ECOSAR-calculation is valid because the substance is in the applicability domain and is not a surfactant. You also state that in an update of the registration dossier you will improve the robust study summary by adding the QMRF and the QPRF.

The information in your comments is not sufficient for ECHA to make an assessment, because you have not provided any details of this new information.

Please note that, as indicated in the *Appendix on Reasons common to several requests*, this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation").

On this basis, the information requirement is not fulfilled.

Study design

OECD TG 203 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix A.2.

Appendix C: 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[15].

B. Test material

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

1. Selection of the Test material(s)

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

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

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

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[16].

[15] https://echa.europa.eu/practical-guides
[16] https://echa.europa.eu/manuals

Appendix D: Procedure

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

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

The compliance check was initiated on 9 June 2020.

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 and the deadline.

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[17] 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)[18]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[18]

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[19]
Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

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

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: Addressees of this decision and their corresponding information requirements

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

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

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