EUROPEAN CHEMICALS AGENCY

~~Confidential~~

Helsinki, 21 May 2021

Addressees
Registrants of 262-992-3 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
15/04/2020

Registered substance subject to this decision ("the Substance")
Substance name: Oils, fish, sulfated, sodium salts
EC number: 262-992-3
CAS number: 61788-64-5

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 ***28 August 2023***.

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. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: EU B.13/14. / OECD TG 471)

2. Long-term toxicity testing on aquatic invertebrates also requested below (triggered by Annex VII, Section 9.1.1., column 2)

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 tests performed for the information requirement of Annex VII, Section 8.4.1. and 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. Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90 days) requested below (Annex VIII, Section 8.6.1.)

4. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) by oral route, in rats

5. Long-term toxicity testing on fish also requested below (Annex VIII, Section 9.1.3., column 2)

C. Information required from all the Registrants subject to Annex IX of REACH

1. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.; test method: OECD TG 408) by oral route, in rats

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit)

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

4. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: OECD TG 210)

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

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

For certain endpoints, ECHA requests the same study from registrants at different tonnages. In such cases, only the reasoning why the information is required at lower tonnages is provided in the corresponding Appendices. For the tonnage where the study is a standard information requirement, the full reasoning for the request including study design is given. Only one study is to be conducted; the registrants concerned must make every effort to reach an agreement as to who is to carry out the study on behalf of the other registrants under Article 53 of REACH.

How to comply with your information requirements

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

You must follow the general testing and reporting requirements provided under the Appendix

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

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

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

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 in the category and applying a read-across approach in accordance with Annex XI, Section 1.5:

- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- 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.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)
- Long-term toxicity testing on fish (Annex IX, Section 9.1.6.)

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.

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.

A. Scope of the grouping

i. Description of the grouping

In your registration dossier you have formed a group (category) of 'Fat Liquors and Lubricants' (FLL). You have provided a read-across justification document in IUCLID Section 13. In your comments on the draft decision you have added Rape oil, sulfated, sodium salt (EC 281-978-8) to the group.

Also, in your comments to the draft decision you provided the following Annexes:
Annex I: Updated data matrix
Annex II: FLLSRC – Similarity study and read-across justification
Annex III: Read-across justification-old version
Annex IV: Original reports for OECD 487
Annex V: Robust study summaries of new studies

For the purpose of this decision, the following abbreviations are used for the group members:

[1] Castor Oil, sulfated, sodium salt (EC 269-123-7);
[2] Oils, lard, oxidized, sulfited, sodium salt (EC No. 297-185-5);
[3] Rape oil, bisulfited, sodium salt (FLL Sample 4)(EC No. 281-975-1);
[4] Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4); and
[5] Rape oil, sulfated, sodium salt (EC 281-978-8)

You provide the following reasoning and supporting information for the grouping of the substances:

- The group members are manufactured by [redacted]
- You provide a table showing the typical concentration of fatty acids in the triglyeride molecules of the raw material. The C-chain length is reported to vary from C12 to C24 and the degree of unsaturation from 0 to 6.
- You further sub-categorize the FFL category into Sulfated Fat Liquors and Sulfited Fat Liquors with the following sub-group descriptions:
  i. Sulfated Fat Liquors: sulfated fatty acids produced [redacted].
  Sulfited Fat Liquors: sulfited fatty acids produced from [redacted]
  This sub-group includes sodium salts.

On the basis of the above, we understand that you define the the structural basis for the grouping as follows: sulfated and sulfited oils or natural origin including fatty acid with C-chain length between C12 and C24 and a degree of unsaturation from 0 to 6. ECHA understands that this is the applicability domain of the grouping and will assess your predictions on this basis.

ii. Assessment of the grouping

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

A. 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*".[2] 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*

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

(sub)category members".[3] 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.

As explained above, you describe the applicability domain of the category as sulfated and sulfited oils of natural origin including fatty acid with C-chain length between C12 and C24 and a degree of unsaturation from 0 to 6.

However, the definition of the applicability domain does not introduce unambiguous inclusion/exclusion criteria because it does not cover:

- The range acceptable number of sulfated and sulfited groups in the reaction product, and
- The range acceptable of unreacted starting material in the composition of the group members.

In your comments on the draft decision you provided information on the degree [redacted], on the unreacted starting materials and the fatty acid composition of the starting materials from which the substances in the category are produced. The information you have provided is considered to provide the necessary clarification to the applicability domain of the category. However, as the information is currently not available in your registration dossier, the issue remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

B. Read-across hypothesis not well founded for Castor Oil, sulfated, sodium salt (EC 269-123-7)

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[4]. It should explain why the differences in the chemical structures should not influence the toxicological and ecotoxicological properties or should do so in a regular pattern.

In your comments on the draft decision, you explain that castor oil, from which the source substance Castor Oil, sulfated, sodium salt (EC 269-123-7) is derived, has a fatty acid distribution containing [redacted] whereas the other oils/fats starting materials for the other members of the category do not contain such constituents.

The [redacted] constituent of the source substance Castor Oil, sulfated, sodium salt (EC 269-123-7) differ from the other fatty acid constituents of category members because they contain a hydroxy moiety whereas the other fatty acids do not, but you have not provided an explanation why this difference in chemical structure should not influence the toxicological/ ecotoxicological properties. Therefore, you have not provided a well-founded hypothesis to justify Castor Oil, sulfated, sodium salt (EC 269-123-7) as a member of the category. Therefore read-across is not reliable from Castor Oil, sulfated, sodium salt (EC 269-123-7).

B. Predictions for properties

a. Prediction for toxicological properties

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

You have provided the following reasoning for the prediction of toxicological properties, additional to the justifications of similarity of structure and similarity in properties discussed above: '*the metabolism of alkyl sulfates and alkane sulfonates is similar*' and '*for human toxicological endpoints, results on sulfited derivatives can be taken as conservative surrogate for sulfated substances*'.

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 Substance from information obtained from the following source substances. Moreover, in your comments on the draft decision you added Rape oil, sulphated, sodium salt (EC 281-978-8) as another source substance.

In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.):
- Castor Oil, sulfated, sodium salt (EC 269-123-7), OECD TG 471, [redacted], (2014);
- Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4), OECD TG 471, [redacted] (2010);
- Rape oil, bisulfited, sodium salt (EC 281-975-1), OECD TG 471, [redacted] (2010);
- Oils, lard, oxidized, sulfited, sodium salt (EC 297-185-5), OECD TG 471, [redacted], (2010).
- Rape oil, sulphated, sodium salt (EC 281-978-8), OECD TG 471, [redacted] (2012).

In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.):
- Castor Oil, sulfated, sodium salt (EC 269-123-7), OECD TG 473, [redacted] (2014);
- Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4), OECD TG 473, [redacted] (2010);
- Rape oil, bisulfited, sodium salt (EC 281-975-1), OECD TG 473, [redacted] (2010).
- Rape oil, sulphated, sodium salt (EC 281-978-8), OECD TG 487, [redacted] (2013).

In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4), OECD TG 476, [redacted] (2010).
- Rape oil, sulphated, sodium salt (EC 281-978-8), OECD 476, [redacted] (2013).

Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Castor Oil, sulfated, sodium salt (EC 269-123-7), OECD TG 422, [redacted] (2014);
- Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4), OECD TG 422, [redacted], (2010);
- Rape oil, bisulfited, sodium salt (EC 281-975-1), OECD TG 422, [redacted] (2010)
- Rape oil, sulphated, sodium salt (EC 281-978-8), OECD TG 422, [redacted] (2013).

Sub-chronic repeated dose toxicity (Annex IX, Section 8.6.2.)
- Castor Oil, sulfated, sodium salt (EC No. 269-123-7), OECD TG 408, [redacted] (2020).

Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Castor Oil, sulfated, sodium salt (EC No. 269-123-7), OECD TG 414, [redacted] (2020)

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

A. Characterisation of the group members/source substance(s)

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

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

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

Your read-across justification document contains compositional information for the members of your category. The category members are UVCBs including sulfated and sulfited fatty acids of various carbon chain lengths. The representative percentages of neutralised free fatty acids, glycerol and free fatty acids and unreacted oil are given.

No information on the number of sulfated groups of the individual constituents of the category members is provided. Furthermore, no further details are provided on how the average fraction of unreacted materials is determined.

Without consideration of the number of sulphated groups amongst constituents with different carbon chain length, no qualitative or quantitative comparative assessment of the compositions of the different category members can be completed. Therefore, ECHA considers that it is not possible to assess whether the attempted predictions are compromised by the composition of the category members.

In your comments on the draft decision you provided information on the composition of the members of the category listed in the 'Description of the grouping' section above. The information you have provided is considered to provide the necessary clarification on the characterisation for the group members

However, as the information is currently not available in your registration dossier, the issue remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

B. Data density

[5] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.4.1
[6] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.5.5

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.*

According to the ECHA Guidance, one of the factors in determining the robustness of a category is the density and distribution of the available data across the category.[7] To identify a regular pattern and/or to derive reliable prediction of the properties of the members of the category, adequate and reliable information covering the range of structural variations identified among the category members needs to be available.

Furthermore in larger categories there may be breaks in trends which could affect the reliability of interpolation.[8] To confirm that there are no such breakpoints, adequate and reliable information needs to cover also substances within a range of homologous series.

i. Studies with source substance Rape oil, sulphated, sodium salt (EC 281-978-8)

You have provided data for *in vitro* gene mutation in bacteria, for *in vitro* cytogenicity in mammalian cells and for *in vitro* gene mutation in mammalian cells, and for Screening for reproductive/developmental toxicity using several source substances, including Rape oil, sulphated, sodium salt (EC 281-978-8) in your comments on the draft decision, as described above in the description of the grouping. Based on the studies provided with Rape oil, sulphated, sodium salt (EC 281-978-8) and the other source substances in the category you claim that the target and source substances have the same behaviour in respect to the *in vitro* mutagenicity and Screening for reproductive/developmental toxicity endpoints.

The information you have provided on the composition of the substances is considered sufficient to establish similar behaviour of the source substance Rape oil, sulphated, sodium salt (EC 281-978-8) and the Substance for *in vitro* mutagenicity and for screening for reproductive/developmental toxicity endpoints. However, as the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

ii. Studies with Oils, lard, oxidized, sulfited, sodium salt (EC 297-185-5, Rape oil, bisulfited, sodium salt (EC 281-975-1 and Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4)

In addition, in your comments on the draft decision you have provided mutagenicity data for *in vitro* gene mutation in bacteria, *in vitro* cytogenicity, and *in vitro* gene mutation in mammalian cells, using other source substances as described above. However, although the new information adds to the data density, it is not possible to conclude on the biological relevance of this new information because you have not explained how the sulphitation versus sulphonation impacts on the toxicological properties of the substances. Therefore, the information provided is not sufficient to conclude that *in vitro* mutagenicity properties are likely to follow a regular pattern.

iii. Studies with source substances Castor Oil, sulfated, sodium salt (EC 269-

[7] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.1.5.
[8] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.2.2.

123-7),

You have provided toxicity data for Sub-chronic repeated dose toxicity and Pre-natal developmental toxicity using data on a single category member i.e. the source substance Castor Oil, sulfated, sodium salt (EC No. 269-123-7). You claim that the target and source substances have the same behaviour in respect to repeated dose toxicity. You have not provided any repeated-dose or developmental toxicity data using the Substance in your registration dossier.

However, information for a single category member is not sufficient to establish a trend across the category. Furthermore, in the absence of information on the substance, it cannot be confirmed that there is no breakpoint in toxicity trend within the given range of chain length and number of sulphated groups. As mentioned in the decision above, you have not provided a well-founded hypothesis to justify Castor Oil, sulfated, sodium salt (EC 269-123-7) as a member of the category. Therefore read-across is not reliable from Castor Oil, sulfated, sodium salt (EC 269-123-7). Therefore, the information provided is not sufficient to conclude that repeated dose toxicity and developmental toxicological properties are likely to follow a regular pattern.

C. 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 toxicokinetic information on the formation of the common compound and 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 effect(s). 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 your comments on the draft decision, you propose to use the screening for reproductive/developmental toxicity requested in this decision as a bridging study to justify read-across from the source substance Castor Oil, sulfated, sodium salt (EC No. 269-123-7) for the Sub-chronic toxicity study (90-day) and Pre-natal developmental toxicity study. However, as mentioned above, you have not provided a well-founded hypothesis to justify Castor Oil, sulfated, sodium salt (EC 269-123-7) as a member of the category. Therefore read-across is not reliable from Castor Oil, sulfated, sodium salt (EC 269-123-7).

You refer to the class of "Fat Liquors and Lubricants" with two sub-categories, namely "Sulfated Fat Liquors" to which the Substance belongs and "Sulfited Fat Liquors" are "*manufactured from the same type of source oil will have similar physicochemical and toxicological properties, and that these properties are also likely to be similar even among different source oils*".

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

However, the data set in your dossier does not include reliable information on the toxicological properties of the Substance. You have not provided any toxicokinetic information for the Fat Liquors and Lubricants substances which is specific to the Substance or to the other category members. Concerning the sulfate and the sulfite groups, there are structural differences that could lead to differences in toxicokinetics and toxicity. As indicated in the read-across justification document, metabolism of alkyl sulfates and alkane sulfonates share some similarities, but are also partly different. You have not provided experimental data to prove that the sulfite and sulfate moieties of the source and target substances follow the same toxicokinetic path. Therefore, differences in metabolism can also be expected for fatty acids sulfated and sulfited. These differences may lead to different dissociation pattern, to different absorption and metabolism, or to differences in toxicodynamics. These dissimilarities have not been addressed in your read-across justification or in your comments on the draft decision

Based on the above, it is not possible to conclude whether there are differences in the toxicokinetic behaviour, in particular the metabolic fate and (bio)transformation of the substances and how these differences may influence the toxicity profile of the target and source substances. Based on the lack of comprehensive toxicokinetic data, there is not an adequate basis for predicting the toxic properties from the data of the source substances.

Therefore, the data set reported in the technical dossier does not include relevant, reliable and adequate information for the category members to support your read-across hypothesis of toxicological properties likely to be similar among different source oils.

In the absence of such information, you have not established that the category members of the 'Sulfited Fat Liquors' subgrouping are likely to have similar properties. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across from the source substances Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4), Rape oil, bisulfited, sodium salt (EC 281-975-1) and Oils, lard, oxidized, sulfited, sodium salt (EC 297-185-5).

b. Predictions for Aquatic toxicity

You have provided the following reasoning for the prediction of aquatic toxicity: "*The structural similarities result in the same mode of ecotoxic action. Within each subcategory the most important parameter influencing ecotoxicity is the varying length of the alkyl chain. Although the counter ion may also influence the physico-chemical behaviour of these chemicals, the chemical reactivity and classification for the purpose of this assessment is not expected to be affected by the difference in counter ion*".

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.

In your comments on the draft decision, you agreed to conduct a growth inhibition study aquatic plants and a long-term toxicity test on fish. You still intend to predict the properties for the Substance from information obtained from the following source substance:

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

- Castor Oil, sulfated, sodium salt (EC 269-123-7), OECD TG 211, [redacted] (2019)

ECHA notes the following shortcomings with regards to predictions of aquatic toxicity:

A. Characterisation of the group members/source substance(s)

The conditions for the characterisation of the group member/source substance(s) explained for toxicological properties (under point a.A. above) apply equally to your read across hypothesis for aquatic toxicity.

Your read-across justification document contains compositional information for the members of your category. The category members are UVCBs including sulphated fatty acids of various carbon chain lengths. The representative percentages of neutralised free fatty acids, glycerol and free fatty acids and unreacted oil are given.

However, no information on the number of sulfated groups of the individual constituents of the category members is provided. Furthermore, no further details are provided on how the average fraction of unreacted materials is determined.

Without consideration of the number of sulphated groups amongst constituents with different carbon chain length, no qualitative or quantitative comparative assessment of the compositions of the different category members can be completed. Therefore, ECHA considers that it is not possible to assess whether the attempted predictions are compromised by the composition of the category members.

As noted above, in your comments on the draft decision you provided information on the composition of the members of the category and this provides the necessary clarification on the characterisation of the group members. However, as the information is currently not available in your registration dossier, the issue remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

B. Data density

The conditions for the density explained for toxicological properties (under point a.B. above) apply equally to your read across hypothesis for aquatic toxicity.

You have provided aquatic toxicity data on a single category member, i.e. Castor Oil, sulfated, sodium salt (EC 269-123-7) for long-term fish toxicity. Based on these studies you claim that there is a trend within the category. You do not specify what this trend should be.

However, information for a single category member is not sufficient to establish a trend across the category. Furthermore, in the absence of information on substances between the upper and lower borders of the category, it cannot be confirmed that there is no breakpoint in toxicity trend within the given range of chain length and number of sulphated groups. Therefore, the information provided is not sufficient to conclude that ecotoxicological properties are likely to follow a regular pattern.

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

As explained above, you have not established that relevant properties of the Substance can be predicted from data on the analogue substances Castor Oil, sulfated, sodium salt (EC 269-123-7), Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4), Rape oil, bisulfited, sodium salt (EC 281-975-1) and Oils, lard, oxidized, sulfited, sodium salt (EC 297-185-5).

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 for these source substances.

Based on your comments on the draft decision, read-across is acceptable from the source substance rape oil, sulphated, sodium salt (EC no. 281-978-8). However, as the information is currently not available in your registration dossier, the data gaps remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

2. Assessment of your weight of evidence adaptation under Annex XI, Section 1.2

You have adapted the following standard information requirements by applying weight of evidence (WoE) adaptation in accordance with Annex XI, section 1.2:

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

Your weight of evidence adaptation raises the same decifiencies irrespective of the information requirement for which it is invoked. Accordingly, ECHA addressed these deficiencies in the present Appendix, before assessing the specific standard information requirements in the following appendices.

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.

However, for each relevant information requirement, you did not submit explanation in the registration dosser why the sources of information provide sufficient weight of evidence leading to the conclusion/assumption that the Substance has or has not a particular dangerous property. Nevertheless, in your comments on the draft decision you provided a discussion for each of the endpoints on reliability of the data, consistency of results, nature and severity of effects and relevance and coverage of effects. This is considered to provide the necessary explanation of why the sources of information provide a sufficient weight of evidence to conclude on the endpoint. However, as the information is currently not available in your registration dossier, the issue remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

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

1. In vitro gene mutation study in bacteria

An *in vitro* gene mutation study in bacteria is an information requirement under Annex VII to REACH.

You have adapted this information requirement by applying weight-of-evidence approach in accordance with Annex XI, Section 1.2.
In support of your adaptation you have provided the following sources of information:

Information provided in the dossier:

i. a key *in vitro* gene mutation study ([redacted], 2014); in bacteria according to OECD TG 471 and GLP with the analogue Castor Oil, sulphated, sodium salt, 75 %, (EC No. 269-123-7; CAS RN 68187-76-8)

ii. an *in vitro* gene mutation study in bacteria ([redacted] 2010) according to OECD TG 471 and GLP with the analogue Oils, lard, oxidized, sulfited, sodium salt Oils, lard, oxidized, sulfited, sodium salt (FLL Sample 6)(EC No. 297-185-5; CAS RN 93348-42-6);

iii. an *in vitro* gene mutation study in bacteria ([redacted], 2010) according to OECD TG 471 and GLP with the analogue Rape oil, bisulfited, sodium salt (FLL Sample 4)(EC No. 281-975-1;CAS RN 84082-27-9);

iv. an *in vitro* gene mutation study in bacteria ([redacted], 2010) according to OECD TG 471 and GLP with the analogue Oils, fish, oxidized, bisulfited, sodium salts (FLL Sample 3)(EC No. 307-037-4; CAS RN 97488-98-7).

Information provided in the comments on the draft decision:

In your comments on the draft decision you have included the following additional sources of information under Annex XI, Section 1.2., supported by documents with robust study summaries:

v. an *in vitro* gene mutation study in bacteria ([redacted], 2012) according to OECD TG 471 with the analogue Rape oil, sulfated, sodium salt (EC 281-978-8);

vi. a non GLP *in vitro* gene mutation study in bacteria screening test in bacteria ([redacted], 2012) in three tester strains (TA98, TA100 and WP2 uvrA) with the Substance.

To fulfil the information requirement, normally a study performed according to OECD TG 471 must be provided. OECD TG 471 investigates gene mutations in bacteria as a key parameter using 5 different bacterial strains.

The sources of information (i.) to (vi.) provide relevant information on *in vitro* gene mutations in bacteria.

However, the reliability of the sources of information (i) to (iv.) is significantly affected by the following deficiencies:

A. Information from source substances can contribute to weight of evidence adaptation only if the read-across is acceptable.
Studies (i.) to (v.) are performed with analogue substances.

However, for the reasons explained under section 2 of the Appendix on Reasons common to several requests, your adaptations according to Annex XI, Section 1.5 is rejected for (i.) to (iv.) and the provided studies performed on source substances cannot be considered reliable source of information that could contribute to the conclusion on the key parameters investigated by the required OECD TG 471.

B. To fulfil the information requirement, the study has to meet the requirements of OECD TG 471[10] (1997). One of the key parameters of this test guideline includes:
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).
However, the source of information (vi.) provides information on 3 strains only.

Taken together, all of the sources of information provide information on gene mutations in bacteria. However, the reliability of the sources of information (i.) to (iv.) is affected so significantly that they cannot be taken into consideration in a weight of evidence approach.

The sources of information (v.) and (vi.) you have provided in your comments addresses the incompliances identified in this decision for this information requirement. However, as the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

Information on the study design

To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471) should be performed.

2. Long-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.). Long-term toxicity testing on aquatic invertebrates must be considered (Section 9.1.1., Column 2) if the substance is poorly water soluble.

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.7b, Section 7.8.5). In section 4.8 of your technical dossier, you provide a study according to OECD TG 105. The saturation concentration of the Substance in water is reported as <0.51mg/L. Therefore, the Substance is poorly water soluble and information on long-term toxicity on aquatic invertebrates must be provided.

You have adapted this information requirement under Section 9.1.1, column 2, second indent of Annex VII with the following justification: "*the study does not need to be conducted because a long-term aquatic toxicity study on invertebrates is available*".

In support of your column 2 adaptation, you have provided an adaptation according to Annex XI, Section 1.5 (Grouping of substances and read-across approach). Under section 6.1.4. of

[10] ECHA Guidance R.7a, Table R.7.7-2, p.557

your technical dossier you have provided the following study:

i. OECD TG 211 on the source substance Castor Oil, sulfated, sodium salt (EC 269-123-7), by the Sulphated Oil Derivatives Consortium (2019).

We have assessed this information and identified the following issues:

A. Under Section 9.1.1, column 2, second indent of Annex VII, the study may be omitted if a long-term study on aquatic invertebrates is available.

As explained above you have provided a long-term study aquatic invertebrates according to OECD TG 211 on the source substance Castor Oil, sulfated, sodium salt (EC 269-123-7).

However, for the reasons explained under the Appendix on general considerations your adaptation according to Annex XI, Section 1.5 is rejected. Therefore, no valid information on long-term toxicity to aquatic inveretbrates is currently available in your dossier and your adaptation under Section 9.1.1, column 2, second indent of Annex VII is rejected.

In your comments on the draft decision, you propose a testing strategy for long-term aquatic organism studies. Based long-term tests in aquatic organisms on the source substance substance Castor Oil, sulfated, sodium salt (EC 269-123-7), you argue that '*it has been evident that fish is a more sensitive species than daphnia in the long term testing and therefore we believe that a correct classification and a correct behaviour for the environmental toxicity can be properly investigated just performing an OECD 210 (FELS) on the fish oil derivative, while daphnia study will not adequately represent the concern for this class of substances and it is evaluated as not necessary*.'

However, your justification to adapt this information requirement does not refer to any legal ground for adaptation.

On this basis, the information requirement is not fulfilled. The examination of the selection of the requested test and the test design are addressed under section C.3.

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 an adaptation according to Annex XI, Section 1.5 (Grouping of substances and read-across approach). Under section 6.1.4. of your technical dossier you have provided the following study:

- OECD TG 201 on the source substance Castor Oil, sulfated, sodium salt (EC 269-123-7), key study by [redacted] (2014).

We have assessed this information and identified the following issue:

For the reasons explained under the Appendix on general considerations your adaptation according to Annex XI, Section 1.5 is rejected.

On this basis, the information requirement is not fulfilled. In your comments on the draft decision you agree to conduct a growth inhibition study in aquatic plants.

Study design

The Substance is difficult to test due to the low water solubility (<0.51 mg/L) and the fact that it is includes ionisable funtionnal groups. OECD TG 201 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 201. 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.

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

An *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study is a standard information requirement in Annex VIII to REACH.

You have adapted this standard information requirements by applying weight-of-evidence approaches in accordance with Annex XI, Section 1.2.

Information provided in the dossier:

In support of your adaptation you have provided the following sources of information with analogue substances:

i. A key study according to OECD Guideline 473 (In Vitro Mammalian Chromosome Aberration Test) ([redacted], 2014) with the analogue Castor Oil, sulphated, sodium salt, 75% (EC No 269-123-7; CAS RN 68187-76-8);

ii. A chromosomal aberration test according to OECD TG 473 ([redacted] 2010) with the analogue Oils, fish, oxidized, bisulfited, sodium salts (FLL Sample 3) (EC No 307-037-4; CAS RN 97488-98-7)

iii. A chromosomal aberration test according to OECD TG 473 ([redacted] 2010) with the analogue Rape oil, bisulfited, sodium salt (FLL Sample 4) (EC No. 281-975-1; CAS RN 84082-27-9)

Information provided in the comments to the draft decision:

In your comments on the draft decision you have included the following additional source of information under Annex XI, Section 1.2., supported by a document with a robust study summary:

iv. an *in vitro* micronucleus study in mammalian cells ([redacted], 2013) according to OECD TG 487 with the analogue Rape oil, sulfated, sodium salt (EC 281-978-8).

To fulfil the information requirement, normally a study performed according to OECD TG 473/487 must be provided. OECD TG 473/487 investigate the following:

- Detection and quantification of structural or numerical chromosomal aberrations in cultured mammalian cells including data on the cytotoxicity and the frequency of cells with chromosomal aberrations or micronuclei.

The sources of information (i.) to (iv.) provide relevant information on structural or numerical chromosomal aberrations in cultured mammalian cells.

However, the reliability of these sources of information is significantly affected by the following deficiencies:

A. Information from source substance(s) can contribute to weight of evidence adaptation only if the read-across is acceptable.
Studies (i), (ii.), (iii.) and (iv.) are performed with analogue substances.
However, for the reasons explained under section 2 of the Appendix on Reasons common to several requests, your adaptations according to Annex XI, Section 1.5 is

rejected for (i.) to (iii.) the provided studies performed on source substances cannot be considered reliable sources of information that could contribute to the conclusion on the key parameters investigated by the required OECD TG 473/487.

In addition, the reliability of the sources of information (i. to iii.) is also affected by the following issues:

B. The specifications of OECD TG 473/487, include the following:

a) At least 300 well-spread metaphases (OECD TG 473) or 2000 cells (OECD TG 487) must be scored per concentration
b) Data on the cytotoxicity and the frequency of cells with structural chromosomal aberrations / micronuclei for the treated and control cultures must be reported.

The reported data for the studies under (ii.) and (iii.) you have provided do not include:
a) the scoring of at least 300 metaphases per concentration (OECD TG 473) and the scoring of at least 2000 cells per concentration (OECD TG 487).
b) data on the cytotoxicity and/or the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures (OECD TG 473) and data on the cytotoxicity and/or the frequency of micronuclei for the treated and control cultures (OECD TG 487).

As indicated in OECD TG 473 this information is required to conclude whether a test chemical is clearly negative. Therefore the acceptability criteria of the OECD TG 473 are not met and the provided studies (i. to iii.) cannot be considered as a reliable source of information that could contribute to the conclusion on this information investigated by the required study.

This being said, the source of information (iv.) you have provided in your comments addresses the incompliances identified in this decision for this information requirement. However, as this information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

Study design

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

2. Only if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. is obtained, In vitro gene mutation study in mammalian cells

An *in vitro* gene mutation study in mammalian cells is an information requirement in Annex VIII to REACH in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

Triggering of the study

Your dossier contains an adaptation (weight-of-evidence) for an *in vitro* gene mutation study in bacteria, and an adaptation (weight-of-evidence) for an *in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study.

The information for the *in vitro* gene mutation study in bacteria and for the *in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study provided in the dossier are rejected for the reasons provided in sections A.2 and B.1 of this draft decision.

The result of the requests for information in A.2 and B.1 of this decision will determine whether the present requirement for an *in vitro* mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

Information in dossier

You have adapted this standard information requirements by applying weight-of-evidence approaches in accordance with Annex XI, Section 1.2. In support of your adaptation you have provided the following source of information with an analogue substance:

i. OECD TG 476 with the analogue Oils, fish, oxidized, bisulfited, sodium salts (FLL Sample 3) (EC No 307-037-4; CAS RN 97488-98-7)([redacted], 2010).

Information provided in the comments to the draft decision:

In your comments on the draft decision you have included the following additional source of information under Annex XI, Section 1.2., supported by a document with a robust study summary:

ii. OECD TG 476 with the analogue Rape oil, sulphated, sodium salt (EC 281-978-8; CAS RN 84020-30-4)([redacted], 2013).

To fulfil the information requirement, the study has to be an *in vitro* gene mutation study conducted in mammalian cells in accordance with OECD TG 476 or OECD TG 490, respectively. OECD TG 476/490 investigate the following:
Detection and quantification of gene mutations (point mutations, frame-shift mutations, small deletions, etc.) in cultured mammalian cells including data on the frequency of mutant colonies.

The sources of information provide relevant information on gene mutation in cultured mammalian cells.

However, the reliability of the sources of information is significantly affected by the following deficiency:

> Information from source substance(s) can contribute to weight of evidence adaptation only if the read-across is acceptable.
> The studies (i.) and (ii.) are performed with an analogue substances. However, for the reasons explained under section 2 of the Appendix on Reasons common to several requests, the provided study performed on a source substance (i.) cannot be considered a reliable source of information that could contribute to the conclusion on the key parameters investigated by the required OECD TG 476/490.

This being said, the source of information (ii.) you have provided in your comments addresses the incompliances identified in this decision for this information requirement. However, as the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

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. Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90 days)

A Short-term repeated dose toxicity study (28 days) is an information requirement in Annex VIII to REACH. This information may take the form of a study record or a valid adaptation in accordance with either a specific adaptation rule under Column 2 of Annex VIII or a general adaptation rule under Annex XI.

You have provided an adaptation according to Annex XI, Section 1.5 (Grouping of substances and read-across approach). In support of your adaptation, you provided the following studies:

Information provided in the dossier:

i. Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test ([redacted], 2010) with the analogue substance Oils, fish, oxidized, bisulfited, sodium salts (FLL Sample 3) (EC no. 307-037-4), according to OECD TG 422.
ii. Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test ([redacted], 2010) with the analogue substance Rape oil, bisulfited, sodium salt (FLL Sample 4) (EC no. 281-975-1), according to OECD TG 422.
iii. Combined Repeated Dose Toxicity key Study with the Reproduction / Developmental Toxicity Screening Test ([redacted], 2014) with the analogue substance Castor Oil, sulphated, sodium salt, 75 % , EC No 269-123-74 according to OECD TG 422.

Information provided in the comments to the draft decision:

In your comments on the draft decision you have included the following additional source of information, supported by a document with a robust study summary:

iv. Combined repeated dose toxicity study with the reproduction / developmental toxicity screening test ([redacted], 2013) with the analogue Rape oil, sulphated, sodium salt (EC 281-978-8; CAS RN 84020-30-4), according to OECD TG 422

We have assessed this information and identified the following issue:

The studies (i.) to (iv.) are performed with analogue substances. For the reasons explained in the "Appendix on Reasons common to several requests", your adaptations according to Annex XI, Section 1.5 is rejected for the source substances for studies (i.) to (iii.) For study (iv.) as explained under section 2 of the Appendix on Reasons common to several requests, your adaptation according to Annex XI, Section 1.5 is plausible.

As regards (iv.), ECHA has assessed the information against the requirements in OECD TG 422. The information you have provided in your comments addresses the incompliances identified in this decision for this information requirement. However, as the information is currently not available in your registration dossier, the data gap remains. You should

therefore submit this information in an updated registration dossier by the deadline set out in the decision.

Therefore, the information requirement is not fulfilled.

Column 2 of Annex VIII, Section 8.6.1. provides that an experimental study for this endpoint is not needed if a reliable sub-chronic (90 days) or chronic toxicity study is available.

The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see Section C.1). According to Column 2 of Annex VIII, Section 8.6.1., and to prevent unnecessary animal testing, a short term toxicity study (28 days) does not therefore need to be conducted.

Because you still must comply with the information requirement in Annex VIII, Section 8.6.1., you were requested to submit a justification for the adaptation provided in Column 2 of that provision. However, as explained above, the information provided in your comments would address this issue by means of a study record once present in the dossier.

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 an 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 provided an adaptation according to Annex XI, Section 1.5 (Grouping of substances and read-across approach). In support of your adaptation, you provided the following studies:

Information provided in the dossier:

i. Combined repeated dose toxicity Key study with the reproduction / developmental toxicity screening test ([redacted], 2010) with the analogue substance Oils, fish, oxidized, bisulfited, sodium salts (FLL Sample 3) (EC no. 307-037-4), according to OECD TG 422 and GLP (reliability 2).
ii. Combined repeated dose toxicity supporting study with the reproduction / developmental toxicity screening test ([redacted], 2010) with the analogue substance Rape oil, bisulfited, sodium salt (FLL Sample 4) (EC no. 281-975-1), according to OECD TG 422 and GLP (reliability 2).
iii. Combined repeated dose toxicity Key study with the reproduction / developmental toxicity screening test ([redacted], 2014) with the analogue substance Castor Oil, sulphated, sodium salt, 75 % , EC No 269-123-74 according to OECD TG 422 and GLP (reliability 2).

Information provided in the comments to the draft decision:

In your comments on the draft decision you have included the following additional source of information supported by a document with a robust study summary:

iv. Combined repeated dose toxicity study with the reproduction / developmental toxicity screening test ([redacted], 2013) with the analogue Rape oil, sulphated, sodium salt (EC 281-978-8; CAS RN 84020-30-4), according to OECD TG 422

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

A. The studies (i.) to (iv.) are performed with analogue substances. For the reasons explained in the "Appendix on Reasons common to several requests", your adaptations according to Annex XI, Section 1.2, and Section 1.5 are rejected for the source substances for studies (i.) to (iii.).

B. To fulfil the information requirement and to generate information concerning the effects of the Substance on male and female reproductive performance as well as specific target organ toxicity, the study has to meet the requirements of EU B.64/OECD TG 422. The key parameter(s) of this test guideline include for example

   1) Dosing of the Substance for a minimum of four weeks for males and approx. 63 days for females to cover premating, conception, pregnancy and at least 13 days of lactation.

   However, in the studies (i.) and (ii.) you have provided the female animals were exposed for 42-47 days. In study (iii.) females were exposed for 41-47 days, i.e. during 2 weeks prior to mating, during mating, during post-coitum, and during at least 4 days of lactation. The studies do not have a required exposure duration according to OECD TG 421/422 because the exposure does not cover two weeks of premating and pregnancy and at least 13 days of lactation. Therefore it does not fulfil the criteria set in EU B.64/OECD TG 422.

This being said, the source of information (iv.) you have provided in your comments addresses the incompliances identified in this decision for this information requirement. However, as the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

Therefore, the information requirement is not fulfilled.

Information on study design

A study according to the test method EU B.63/OECD TG 421 or EU B.64/OECD TG 422 must be performed in rats with oral[11] administration of the Substance.

2. Long-term toxicity testing on fish

Short-term toxicity testing on fish is a standard information requirement in Annex VIII to REACH (Annex VIII, Section 9.1.3). Long-term toxicity testing on fish must be considered (Section 9.1.3., Column 2) if the substance is poorly water soluble.

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.7b, Section 7.8.5). In section 4.8 of your technical dossier, you provide a study according to OECD TG 105. The saturation concentration of the Substance in water is reported as <0.51mg/L. Therefore, the Substance is poorly water soluble and information on long-term toxicity on fish must be provided.

You have adapted this information requirement under Section 9.1.3, column 2, second indent of Annex VIII with the following justification: "*the study does not need to be conducted because a long-term aquatic toxicity study on fish is available*".

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

In support of your column 2 adaptation, you have provided an adaptation according to Annex XI, Section 1.5 (Grouping of substances and read-across approach) and, under section 6.1.2. of your technical dossier, the following study:

- OECD TG 210 on the source substance Castor Oil, sulfated, sodium salt (EC 269-123-7), by [redacted] (2019).

We have assessed this information and identified the following issue:

> Under Section 9.1.3, column 2, second indent of Annex VIII, the study may be omitted if a long-term study on fish is available.
>
> As explained above you have provided a study according to OECD TG 210 on the source substance Castor Oil, sulfated, sodium salt (EC 269-123-7).
>
> However, for the reasons explained under the Appendix on general considerations your adaptation according to Annex XI, Section 1.5 is rejected. Therefore, no valid information on long-term toxicity to aquatic fish is currently available in your dossier and your adaptation under Section 9.1.3, column 2, second indent of Annex VIII is rejected.

On this basis, the information requirement is not fulfilled. In your comments on the draft decision you agree to conduct a long-term toxicity test on fish. The examination of the selection of the requested test and the test design are addressed under section C.4.

Appendix C: Reasons to request information required under Annex IX of REACH

1. Sub-chronic toxicity study (90-day)

A Sub-chronic toxicity study (90 day) is a standard information requirement in Annex IX to REACH.

Information provided in the dossier:

You have provided an adaptation according to Annex XI, Section 1.5 (Grouping of substances and read-across approach). In support of your adaptation, you provided the following studies:

i. Sub-chronic toxicity study ([redacted], 2020) with the analogue Castor Oil, sulfated, sodium salt (EC No. 269-123-7; CAS RN. 68187-76-8), according to OECD TG 408.
ii. Combined repeated dose toxicity study with the reproduction / developmental toxicity screening test ([redacted], 2014) with the analogue substance Castor Oil, sulphated, sodium salt, 75 %, EC No 269-123-74 according to OECD TG 422.
iii. Combined repeated dose toxicity study with the reproduction / developmental toxicity screening test ([redacted], 2010) with the analogue substance Oils, fish, oxidized, bisulfited, sodium salts (FLL Sample 3) (EC no. 307-037-4), according to OECD TG 422.
iv. Combined repeated dose toxicity study with the reproduction / developmental toxicity screening test ([redacted], 2010) with the analogue substance Rape oil, bisulfited, sodium salt (FLL Sample 4) (EC no. 281-975-1), according to OECD TG 422.

Information provided in the comments to the draft decision:

In your comments on the draft decision you have included the following additional source of information:

v. Combined repeated dose toxicity study with the reproduction / developmental toxicity screening test ([redacted], 2013) with the analogue Rape oil, sulphated, sodium salt (EC 281-978-8; CAS RN 84020-30-4), according to OECD TG 422.

We have assessed this information and identified the following issues:

A. The studies (i.) to (v.) are performed with analogue substances. For the reasons explained under the "Appendix on Reasons common to several requests", your adaptation according to Annex XI, Section 1.5 is rejected for the source substances for studies (i.) to (iv.).

B. Moreover, to be considered compliant and enable concluding whether the Substance has dangerous properties and supports the determination of the No-Observed Adverse Effect Level (NOAEL), a study has to meet the requirements of OECD TG 408. The following key parameter(s) of this test guideline include, among others dosing of the Substance daily for a period of 90 days until the scheduled termination of the study.

However, all the Combined repeated dose toxicity studies with the reproduction/developmental toxicity screening test (OECD TG 422) you have submitted in your dossier or in your comments do not have the required exposure duration of 90 days as required in OECD TG 408, because the exposure duration of the screening tests you have provided do not have the required exposure duration of 90 days as required in OECD TG 408, because you indicated an exposure duration of 29 days for males and 41-47 days for females in study (ii.). For studies (iii.) and (iv.) you indicated an exposure duration of 42 days for males and 42-47 days for females.

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

Outcome

Referring to the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity, because the substance is likely to have a low vapour pressure and no uses with spray application are reported that could potentially lead to aerosols of inhalable size.

Therefore the sub-chronic toxicity study must be performed according to the OECD TG 408, in rats and with oral administration of the Substance

2. Pre-natal developmental toxicity study in one species

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

Information provided in the dossier:

You have provided an adaptation according to Annex XI, Section 1.5 (Grouping of substances and read-across approach). In support of your adaptation, you provided the following study:

i. OECD TG 414 study ([redacted], 2020) with the analoge Castor Oil, sulfated, sodium salt (EC No 269-123-7; CAS RN 68187-76-8).

Information provided in the comments to the draft decision:

In your comments on the draft decision you have included the following additional source of information:

ii. OECD TG 422 Combined repeated dose toxicity study with the reproduction / developmental toxicity screening test with the analogue Rape oil, sulphated, sodium salt (EC 281-978-8; CAS RN 84020-30-4)

We have assessed this information and identified the following issues:

A. The studies (i.) an (ii.) are performed with analogue substances. For the reasons explained under the Appendix on general considerations your adaptation according to Annex XI, Section 1.5 is rejected for the source substance for study (i.).

B. The study (ii.) you have provided with your comments on the draft decision was not performed in accordance with OECD TG 414. Instead, you have provided a "combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" (OECD TG 422). However, this study does not inform on skeletal and visceral malformations and variations as required by OECD TG 414.

Therefore, this study does not fulfil the information requirement.

On this basis, the information requirement is not fulfilled.

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[12] administration of the Substance.

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

3. Long-term toxicity testing on aquatic invertebrates

Long-term toxicity testing on aquatic invertebrates is an information requirement under Annex IX to REACH (Section 9.1.5.).

You have provided an adaptation according to Annex XI, Section 1.5 (Grouping of substances and read-across approach). In support of your adaptation, you provided the following study:

i. OECD TG 211 on the source substance Castor Oil, sulfated, sodium salt (EC 269-123-7), key study by [redacted] (2019).

However, for the reasons explained under the Appendix on general considerations your adaptation according to Annex XI, Section 1.5 is rejected.

As discussed in Section A.2, in your comments on the draft decision, you propose a testing strategy for long-term aquatic organism studies. Based long-term tests in aquatic organisms on the source substance substance Castor Oil, sulfated, sodium salt (EC 269-123-7), you argue that '*it has been evident that fish is a more sensitive species than daphnia in the long term testing and therefore we believe that a correct classification and a correct behaviour for the environmental toxicity can be properly investigated just performing an OECD 210 (FELS) on the fish oil derivative, while daphnia study will not adequately represent the concern for this class of substances and it is evaluated as not necessary*.'

However, your justification to adapt this information does not refer to any legal ground for adaptation. In spite of any explicit legal grounds, we have nevertheless considered if this justification would refer to Annex IX, Section 9.1., Column 2.

Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to Daphnia under Column 1. It must be understood as a trigger for providing further information on long-term toxicity to Daphnia if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018). This adaptation is therefore rejected.

On this basis, the information requirement is not fulfilled.

Study design

To fulfil the information requirement for the Substance, Daphnia magna Reproduction Test (OECD TG 211) should be performed.

The Substance is difficult to test due to the low water solubility (<0.51 mg/L). OECD TG 201 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 201. 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.

4. Long-term toxicity testing on fish

Long-term toxicity testing on fish is an information requirement under Annex IX to REACH (Section 9.1.6.).

You have provided an adaptation according to Annex XI, Section 1.5 (Grouping of substances and read-across approach). In support of your adaptation, you provided the following study:

- OECD TG 210 on the source substance Castor Oil, sulfated, sodium salt (EC 269-123-7), key study by [redacted] (2019).

However, for the reasons explained under the Appendix on general considerations your adaptation according to Annex XI, Section 1.5 is rejected.

On this basis, the information requirement is not fulfilled. In your comments on the draft decision you agree to conduct a long-term toxicity test on fish.

Study design

To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (ECHA Guidance R.7.8.2.).

OECD TG 210 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 Section C.3.

Appendix D: 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[13].

B. Test material

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

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

2. *Information on the Test Material needed in the updated dossier*
   a) You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
   b) The reported composition must include the careful identification and description of the characteristics of the Tests Materials in accordance with OECD GLP (ENV/MC/CHEM(98)16) and EU Test Methods Regulation (EU) 440/2008 (Note, Annex), namely all the constituents must be identified as far as possible as well as their concentration. Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods. The reported composition must also include other parameters relevant to the properties to be tested, in this case the distribution of the C-chain length, the degree of unsaturation, the number of sulfated groups in the reacted material and the relative abundance of ureacted material.

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

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[14].

[13] https://echa.europa.eu/practical-guides
[14] https://echa.europa.eu/manuals

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

A. Environmental testing for substances containing multiple constituents

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

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

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

Appendix F: 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 03 May 2019.

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

ECHA took into account your comments and did not amend the request(s).

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 G: List of references - ECHA Guidance[15] 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)[16]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[16]

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.

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

OECD Guidance documents[17]
Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

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

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

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

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

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

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

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