EUROPEAN CHEMICALS AGENCY

~~Confidential~~

Helsinki, 18 May 2021

**Addressees**
Registrant(s) of animal oil sulfonated Na as listed in the last Appendix of this decision

**Date of submission of the dossier subject to this decision**
02/04/2015

**Registered substance subject to this decision ("the Substance")**
Substance name: Oils, animal, sulfonated, sodium salts
EC number: 305-979-0
CAS number: 95371-11-2

**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 ***23 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. Skin sensitisation (Annex VII, Section 8.3.) with the Substance;

   i. *in vitro/in chemico* skin sensitisation information on molecular interactions with skin proteins (OECD TG 442C), inflammatory response in keratinocytes (OECD TG 442D) and activation of dendritic cells (EU B.71/OECD TG 442E) (Annex VII, Section 8.3.1.); and

   ii. Only if the *in vitro/in chemico* test methods specified under point i.) are not applicable for the Substance or the results obtained are not adequate for classification and risk assessment, *in vivo* skin sensitisation (Annex VII, Section 8.3.2.; test method: EU B.42./OECD TG 429)

2. Long-term toxicity testing on aquatic invertebrates (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 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. 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. Long-term toxicity testing on fish (triggered by 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)

**D. Information required from all the Registrants subject to Annex X of REACH**

1. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) by oral route, in a second species (rat/rabbit)

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 X 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;
- the information specified in Annexes VII to X to REACH, for registration at more than 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 information requirements by grouping substances in the category and applying a read-across approach in accordance with Annex XI, Section 1.5:

- Skin sensitisation (Annex VII, Section 8.3.)
- In vitro cytogenicity study in mammalian cells (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.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)

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.

**A. Scope of the grouping**

*i. Description of the grouping*

You have provided a read-across justification document in the CSR. You have formed a group (category) of 'Fat Liquor and Lubricants (FLL)', with the following six members of the sub-category of 'Sulfited Fat Liquors':

a) Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4)
b) Oils, animal, sulfonated, sodium salts (EC 305-979-0)
c) Rape oil, bisulfited, sodium salt (EC 281-975-1)
d) Rape oil, sulfonated, sodium salt (EC 293-618-7)
e) Rape oil oxidized (EC 305-871-3)
f) Oils, lard, oxidized, sulfited, sodium salts (EC 297-185-5)

In your comments on the draft decision, you clarify that:

- (b) and (f) are different names for the same substance
- (c) and (d) are different names for the same substance
- (e) is not a member of the category.

Furthemore, in your comments on the draft decision, you argue that Fat Liquor and Lubricants derived from rape, sunflower and soybean vegetable oils are *'quite undistinguishable from a chemical point of view and their registration falls within the same substance name as "vegetable"'*.

You therefore redefine the Fat Liquor and Lubricants category to consist of only three members:

a) Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4)
b) Oils, animal, sulfonated, sodium salts (EC 305-979-0)
f) Oils, vegetable, sulfonated, sodium (salts EC 307-044-2)

You provide the following reasoning for the grouping of the substances: "*Given the structural similarities of all of the FLL Substances (i.e., they are all triglyceride molecules that have been subjected to a sulfonation process), it is expected that substances 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.*".

You define the structural basis for the grouping as "*triglyceride molecules that have been subjected to a sulfonation process*". 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.

*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 (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.

You describe the applicability domain of the substances covered by the grouping as:"*triglyceride molecules that have been subjected to a sulfonation process*".

This applicability domain does not introduce unambiguous inclusion/exclusion criteria within which reliable estimations can be made for the Substance because it does not cover:

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

In your response to the draft decision you provided information on the sulfited groups in the reaction product and unreacted starting material. You also provided information on 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 data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

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

*Characterisation of the group members*

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

According to the ECHA Guidance, "*in identifying a category, it is important that all potential category members are described as comprehensively as possible*", because the purity profile and composition can influence the overall toxicity/properties of the potential category members.[4] Therefore, qualitative and quantitative information on the compositions of the category members should be provided to confirm the category membership.

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.[5]

You have defined the applicability domain of the category as explained above. Your read-across justification document contains compositional information for the members of your category. The category members are UVCBs sulphonated fatty acids of various carbon chain lengths. The ranges of the sulphonate content and the lipophilic fraction are given.

No information on the number of sulphonated groups of the individual constituents of the category members is provided.

Without consideration of the number of sulphonated (i.e. sulfited) 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, the category membership cannot be confimed.

In your response to the draft decision you provided information on the sulfited groups in the reaction product and information on 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 Characterisation of the group members. 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.

## B. Predictions for properties

### a. Prediction for toxicological properties

You have provided the following reasoning for the prediction of toxicological properties: "*Given the structural similarities of all of the FLL Substances (i.e., they are all triglyceride molecules that have been subjected to a sulfonation process), it is expected that substances 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*".

[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.6.2.5.5

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

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

Skin sensitisation (Annex VII, Section 8.3.)
- Rape oil, bisulfited, sodium salt (EC 281-975-1), OECD TG 429, [redacted] (2010)
- Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4), OECD TG 429, [redacted] (2010).

In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.)
- Rape oil, bisulfited, sodium salt (EC 281-975-1), OECD TG 473, [redacted] (2010)
- Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4), OECD TG 473, [redacted] (2010).

In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Rape oil, bisulfited, sodium salt (EC 281-975-1), OECD TG 476, [redacted] (2010)
- Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4), OECD TG 476, [redacted] (2010).

Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Rape oil, bisulfited, sodium salt (EC 281-975-1), OECD TG 422, [redacted] (2010)
- Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4), OECD TG 422, [redacted] (2010).

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

*Data density*

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.[6] 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.

You have provided data for skin sensitisation, for *in vitro* cytogenicity in mammalian cells, for *in vitro* gene mutation in mammalian cells, screening for reproductive/developmental toxicity and sub-chronic repeated dose toxicity using two category members as described above in the description of the grouping. Based on the studies provided with other category members in the category you claim that the target and category members have the same behaviour in respect to the toxicity endpoints. You have not provided any toxicity data using the Substance in your registration dossier.

However, information for two category members is not sufficient to establish a trend across the category. Furthermore, in the absence of information on the Substance, it cannot be

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

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 toxicological properties are likely to follow a regular pattern.

As noted above, in your comments on the draft decision, you redefine the Fat Liquor and Lubricants category to consist of only three members. The information you have provided is considered to provide the necessary clarification on adequate data density for the category. 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.

*Supporting information*

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*"[7]. The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on 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 substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the category members.

As mentioned above, there is information for two category members and none on the Sustance.

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.

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

In your response to the draft decision you provided information on structural alert profiles for skin sensitisation and mutagenicity for all 3 members of the category . This information is considered to provide the necessary supporting information for the read-across justification for skin sensitisation (Annex VII, Section 8.3.), *in vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.) and *in vitro* gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.). 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.

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

As regards Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.) you indicate in your comments that you intend to provide an OECD 422 study on the Substance. This aspect is addressed in detail under section B.3 below.

**b. Predictions for ecotoxicological properties**

*i. Aquatic toxicity*

You have provided the following reasoning for the prediction of aquatic toxicity: " *Given the structural similarities of all of the FLL Substances (i.e., they are all triglyceride molecules that have been subjected to a sulfonation process), it is expected that substances 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".*

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:

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

- Rape oil, bisulfited, sodium salt (EC 281-975-1), OECD TG 201, [redacted] (2010)
- Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4), OECD TG 201, [redacted] (2010).

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

*Data density*

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

You have provided algal toxicity data on two category members. Based on these studies you claim that there is no toxicity at a WAF loading rate of 100mg/l.

Information for two category members in the sub-category of six 'Sulfited Fat Liquors' is not sufficient to establish a trend across the category. Therefore, the information provided is not sufficient to conclude that ecotoxicological properties are likely to follow a regular pattern.

As explained above, in your comments on the draft decision you have redefined the category to cover 3 substances only. The information on the redefined category is currently not available in your registration dossier and so the issue remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

In addition, as noted below under issue A.3, you have agreed to conduct the requested study on the Substance. ECHA acknowledges your intention to provide information on the substance to strengthen the rationale for read across.

## 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 substance. Therefore, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

Based on your comments on the draft decision, the information detailed above is considered to provide necessary clarification and supporting information for the read-across justification for the prediction of toxicological properties. However, as noted above, the information is currently not available in your registration dossier so 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. Skin sensitisation

Skin sensitisation is an information requirement under Annex VII to REACH (Section 8.3.). Under Section 8.3., Column 1, the registrants must submit information allowing (1) A) a conclusion whether the substance is a skin sensitiser and B) whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A), and (2) risk assessment, where required.

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:

i) OECD TG 429, key study, with the analogue substance Rape oil, bisulfited, sodium salt (EC 281-975-1), [redacted] (2010);
ii) OECD TG 429, supporting study, with the analogue substance Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4), [redacted] (2010);

We have assessed this information and identified the following issue:

As explained in the Appendix on general considerations, your adaptation under Annex XI, Section 1.5 is rejected.

Therefore, the information requirement is not fulfilled.

In your comments on the draft decision, you provided an updated category. You claim that the similarity from the source and the target substances, supported by the modelled characteristics of skin adsorption and protein binding, justify the application of Read Across from the vegetable oil and fish oil derivative as source substances to the animal as target substance ,for skin sensitisation. 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.

*Study design*

To fulfil the information requirement for the Substance for skin sensitisation, *in vitro/in chemico* studies (OECD TG 442C, OECD TG 442D and EU Method B.71/OECD TG 442E) are considered suitable. In case *in vitro/in chemico* methods are not suitable for the Substance or the results cannot be used for classification and risk assessment an *in vivo* skin sensitisation study must be performed and the murine local lymph node assay (LLNA) (EU Method B.42/OEDC TG 429) is considered as the appropriate study.

### 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.

You have provided two Short-term toxicity testing on aquatic invertebrates (test method OECD TG 202) studies on aquatic invertebrates but no information on long-term toxicity on aquatic invertebrates for the Substance.

We have assessed this information and identified the following issue:

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, the water solubility of the substance or its constituents is 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).

You have provided information which indicate that the Substance includes constituents that are poorly water soluble, i.e. the water solubility estimated to be <1mg/l in section 4.8 of your dossier.

Therefore, the Substance is poorly water soluble and information on long-term toxicity on aquatic invertebrates must be provided.

In your comments on the draft decision you agree to conduct this study.

The examination of the information provided, as well as 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 the following information:

- Growth inhibition study aquatic plants (test method OECD TG 201) key study on the source substance Rape oil, bisulfited, sodium salt (EC 281-975-1), OECD TG 201, [redacted] (2010)
- Growth inhibition study aquatic plants (test method OECD TG 201) supporting study on the source substance Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4)

We have assessed this information and identified the following issues:

A. For the reasons explained under the Appendix on general considerations your adaptation according to Annex XI, Section 1.5 is rejected. In addition, the following endpoint-specific deficiency has been identified in your read-across adaptation:

B. According to Annex XI, Section 1.5., the results to be read across should have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case OECD TG 201 and OECD GD 23 (ENV/JM/MONO(2000)6/REV1 as the substance is difficult to test. The required specifications include:

*Reporting of the methodology and results*

- the method for determination of biomass and evidence of correlation between the measured parameter and dry weight are reported;
- the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form;

*Characterisation of exposure*

- a reliable analytical method for the quantification of the test material in the test solutions must be available. Alternatively, a justification why the analytical monitoring of exposure concentrations is not technically feasible must be provided;

*Additional requirements applicable to difficult to test substances*

- if the test material is poorly water soluble, the maximum dissolved concentration that can be achieved in the specific test solution under the test conditions is determined;
- if water-accommodated fractions (WAFs) are used, a preliminary study must be conducted to determine that saturation has been achieved.

Your registration dossier provides two OECD TG 201 studies both showing the following:

*Reporting of the methodology and results*

- the method used to determine algal biomass is not reported;
- tabulated data on the algal biomass determined daily for each treatment group and control are not reported;

*Characterisation of exposure*

- loading levels were analysed by total organic carbon (according to DIN EN 1484) measured as non-purgeable organic carbon, but this method is not specific for the Substance, i.e. it determines the total organic carbon present in the test medium, not only the Substance; neither did you provide a justification why the analytical monitoring of exposure concentrations of the Substance itself is not technically feasible;

*Additional requirements applicable to difficult to test substances*

- the maximum dissolved concentration that can be achieved in the specific test solution under the test conditions has not been determined;
- a preliminary study to determine that saturation has been achieved in the WAFs has not been conducted;

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

- in the absence of a compound-specific analytical method, you have not demonstrated that measured concentrations provide a reliable estimate of exposure to the test material during the test;
- the Substance is difficult to test because it is poorly water soluble and the maximum dissolved concentration in the test solution under the test conditions has not been determined. Furthermore, the saturated concentration in the WAFs used for testing have not been established.
- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, the method to determine algal biomass is not reported. Furthermore, in the absence of tabulated data on the algal biomass, it is not possible to verify whether or not the validity criteria of the OECD TG 201 were met.

Therefore, the requirements of OECD TG 201 are not met for both studies.

On this basis, the information requirement is not fulfilled.

In your comments on the draft decision you have provided information on the key study and supporting study conducted on analogue substances. Nevertheless, you also agree to conduct the study on the substance.

ECHA ackowledges your agreement to conduct the study.

*Study design*

The Substance is difficult to test due to the low water solubility (<1 mg/L). OECD TG 211 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 211. 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 solutions.

## 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 an information requirement under 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. To support your adaptation you have provided the following studies carried out with analogue substances:

i) OECD TG 473, key study, with the analogue substance Rape oil, bisulfited, sodium salt (EC 281-975-1), [redacted] (2010).
ii) OECD TG 473, supporting study, with the analogue substance Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4), [redacted] (2010).

We have assessed this information and identified the following issue:

As explained in the Appendix on general considerations, your adaptation under Annex XI, Section 1.5 is rejected.

In your comments on the draft decision, in order to support the consistency of the category and the expected results on genotoxicity, the representative structures have been proposed and justified in the CSR, combined with a QSAR Toolbox estimation on the three category members.

You state that the three representative structures reflect the difference in fatty acid distribution, which results in slight differences in molecular weight, but it is well described by the Toolbox estimation that the difference in the chain-length distribution has no impact on the genotoxicity endpoint. The same Micronucleous alert by ISS is reported. Experimental data demonstrate that this alert has no relevance for the described substances.

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.

*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

An *in vitro* gene mutation study in mammalian cells is an information requirement under 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.

*i. Triggering of the study*

Your dossier contains an adaptation for an *in vitro* gene mutation study in bacteria, and an adaptation 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.

The result of the requests for information in sections A.2. and B.1. 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.

*ii. Assessment of information provided*

You have adapted this information requirement by using a grouping of substances and read-across approach under Annex XI, Section 1.5. To support your adaptation you have provided the following studies carried out with analogue substances:

i) OECD TG 473, key study, with the analogue substance Rape oil, bisulfited, sodium salt (EC 281-975-1), [redacted] (2010).
ii) OECD TG 473, supporting study, with the analogue substance Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4), [redacted] (2010).

We have assessed this information and identified the following issues:

As explained in the Appendix on general considerations, your adaptation under Annex XI, Section 1.5 is rejected.

In your comments on the draft decision, in order to support the consistency of the category and the expected results on genotoxicity, the representative structures have been proposed and justified in the CSR, combined with a QSAR Toolbox estimation on the three category members.

You state that the three representative structures reflect the difference in fatty acid distribution, which results in slight differences in molecular weight, but it is well described by the Toolbox estimation that the difference in the chain-length distribution has no impact on the genotoxicity endpoint. The same Micronucleous alert by ISS is reported. Experimental data demonstrate that this alert has no relevance for the described substances.

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.

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

*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 under Annex VIII to REACH (Section 8.6.1.). 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 adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. To support your adaptation you have provided the following studies carried out with analogue substances:

i) OECD TG 422, key study, with the analogue substance Rape oil, bisulfited, sodium salt (EC 281-975-1), [redacted] (2010).
ii) OECD TG 422, supporting study, with the analogue substance Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4), [redacted] (2010).

We have assessed this information and identified the following issues:

As explained in the Appendix on general considerations, your adaptation under Annex XI, Section 1.5 is rejected.

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

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.

In your comments on the draft decision, in order to provide supporting information, to verify the crucial aspects of the read-across hypothesis and confirming that the properties of the Substance can be predicted from the data on other category members (bridging anchor point), you propose to perform a Combined repeated dose toxicity study with the Reproduction/developmental toxicity screening test (OECD 422) by oral route in rats on the Substance.

ECHA notes that a reliable OECD 422 study on the substance would also be sufficient to meet this information requirement.

### 4. Long-term toxicity testing on fish

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

You have provided two short-term toxicity testing on fish studies (one using test method OECD TG 203 and the other according to ISO 7346-1), but no information on long-term toxicity on fish for the Substance.

We have assessed this information and identified the following issue:

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, the water solubility of the substance or its constituents is below the detection limit of the analytical method of the test material (ECHA Guidance R.7b, Section 7.8.5).

As already explained under Section A.1, the Substance is poorly water soluble and information on long-term toxicity on fish must be provided.

The examination of the information provided, as well as 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 an information requirement under Annex IX to REACH (Section 8.6.2.).

You have provided a waiver based on results of OECD TG 422: *"Justify based on results of OECD 422 - There was no evidence of toxicity in the 8-week test; however, it is uncertain whether significant absorption occurred. Given the low hazard found for all human toxicology endpoints, it is considered highly unlikely that toxicity would be observed in the 90-d study. Therefore, conducting this test is not considered necessary."*

ECHA understands that you are providing an adaptation according to Annex IX, Section 8.6.2, Column 2.

You have also included the following studies:

i) [redacted] (2010): key study, according to OECD 422 with the analogue EC 281-975-1.
ii) [redacted] (2010): supporting study, according to OECD 422 with the analogue EC 307-037-4.

We have assessed this information and identified the following issues:

Under Annex IX, Section 8.6.2, Column 2, a study may be omitted if, coupled with limited human exposure, and a set of cumulative conditions are met, including the following:

i) there is not evidence of absorption, and
ii) there is no evidence of of toxicity in a 28-day 'limit test'.

However, you did not provide any toxicokinetic data with the Substance to prove that there is no evidence of absorption. Instead you indicate that the following processes with the Substance are important: *"Digestion in digestive tract followed by absorption of unmodified fatty acids and (potentially) absorption of modified fatty acids"*; and *"Absorption through the digestive tract and skin"*. Moreover, in the OECD TG 422 study there were some effects noted in rats (such as increase in thyroid weight and changes in clinical chemistry) which could indicate that the Substance is absorbed. Also, in your waiver you state that *"it is uncertain whether significant absorption occurred"*.

In addition, as regards human exposure, consumer uses are reported in the dossier.

Based on the above, you have neither demonstrated that there is no evidence of absorption/ of toxicity in a 28-day 'limit test' nor that there is limited human exposure.

Therefore, your adaptation is rejected and the information requirement is not fulfilled.

In your comments on the draft decision, you propose to adapt the requested information requirement with the result of the 90 day study which will be performed on the analogue substance Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4) and no further vertebrate testing is needed to be performed on the Substance.

In order to provide supporting information, to verify the crucial aspects of the read-across hypothesis and confirming that the properties of the Substance can be predicted from the data on other category members (bridging anchor point), you propose to perform a Combined repeated dose toxicity study with the Reproduction/developmental toxicity screening test (OECD 422) by oral route in rats on the Substance.

ECHA ackowledges your intention to adapt this information requirement on the basis of studies yet to be conducted.

*Study design*

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 a liquid of very low vapour pressure (25 x $10^{-5}$ Pa at 25°C) 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) in one species is an information requirement under Annex IX to REACH (Section 8.7.2.).

You have provided a waiver based on results of OECD TG 422: *"There was not evidence of systemic or reproductive toxicity in the 8-week combined test. Given the low hazard found for almost all human toxicology endpoints, it is considered highly unlikely that reproductive toxicity would be observed in this study. Therefore, conducting this test is not considered necessary."*

ECHA understands that you have provided an adaptation according to Annex IX, Section 8.7., olumn 2.

We have assessed this information and identified the following issues:

Under Annex IX, Section 8.7., Column 2, third indent, a study may be omitted if the substance is of low toxicological activity. This needs to be demonstrated with three concomitant criteria, two of them being:

- that it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure; and
- that there is no or no significant human exposure.

You have not provided any toxicokinetic data to show that there is no systemic absorption. Furthermore, the uses of the Substance indicate that there is significant human exposure.

Therefore, your adaptation is rejected.

In your comments on the draft decision, you propose to adapt the requested information requirement with the results of PNDT study which will be performed on the analogue substance Oils, fish, oxidized, bisulfited, sodium salts (EC 307-037-4) and no further vertebrate testing is needed to be performed on the Substance.

In order to provide supporting information, to verify the crucial aspects of the read-across hypothesis and confirming that the properties of the Substance can be predicted from the data on other category members (bridging anchor point), you propose to perform a Combined repeated dose toxicity study with the Reproduction/developmental toxicity screening test (OECD 422) by oral route in rats on the Substance.

ECHA ackowledges your intention to adapt this information requirement on the basis of studies yet to be conducted.

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

*Study design*

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[8] administration of the Substance.

### 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 the following information: an adaptation under Annex XI, Section 2 ('Testing is technically not possible') with the following justification: '*Because of the extremely low water solubility of the substances, conventional acute testing was not possible. Long-term testing is not expected to be feasible.*'

We have assessed this information and identified the following issue:

Under Annex XI, Section 2 of REACH, the study may be omitted if it is technically not possible to conduct the study as a consequence of the properties of the substance. The guidance given in the test methods referred to in Article 13(3) and, if applicable, in OECD GD 23, on the technical limitations of the corresponding method must always be respected.

Your dossier does not include documented evidence as to why a study according to OECD TG 211 is not technically feasible.

OECD TG 211 in conjunction with OECD TG 23 provide guidance on how to test poorly soluble substances. In the absence of evidence that the study cannot be conducted your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

In your comments on the draft decision you agree to conduct this study.

*Study design*

OECD TG 211 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 A.3.

### 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.).

In your dossier, you have provided the following information: an adaptation under Annex XI, Section 2 ('Testing is technically not possible') with the following justification: '*Because of the extremely low water solubility of the substances, conventional acute testing was not possible. Long-term testing is not expected to be feasible.*'

In your comments:

i) You propose to waive the study on the grounds that the substance is not available in the water column, because you consider that it is 'highly insoluble' (which you indicate could be a water solublity ≤ 0.001 mg/L).

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

ii) You argue that there is no release to the environment because of complete degradation of residues in effluent in on-site STPs before discharge to drain.
iii) You propose to conduct a quantitative risk assessment for the aquatic compartment using a PNEC derived from the long-term Daphnia study (requested under section A.1 and C.3).

We have assessed this information in your dossier and your comments and identified the following issues:

A. Under Annex XI, Section 2 of REACH, the study may be omitted if it is technically not possible to conduct the study as a consequence of the properties of the substance. The guidance given in the test methods referred to in Article 13(3) and, if applicable, in OECD GD 23, on the technical limitations of the corresponding method must always be respected.

Your dossier does not include documented evidence as to why a study according to OECD TG 210 is not technically feasible. OECD TG 210 in conjunction with OECD TG 23 provide guidance on how to test poorly soluble substances. In the absence of evidence that the study cannot be conducted your adaptation is rejected.

*B. The legal basis for the adaptation in your comments is not clear*

As reiterated by ECHA's Board of Appeal in appeal A-011-2018 (paragraph 35) "*A registrant who submits an adaptation must set out clearly, in the relevant part of its registration dossier, the provision of Annexes VII to XI on which the adaptation is based, the grounds for the adaptation, and the scientific information which substantiates those grounds*".

In your comments on the draft decision you have not identified the provision of Annexes VII-XI on which the adaptation you intend to include in the registration dossier is based.

Consequently, in the absence of a clear reference to a provision, ECHA is not in a position to assess the adaptation referred to in your comments.

On this basis, the information requirement is not fulfilled.

*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 211 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 A.3.

## Appendix D: Reasons to request information required under Annex X of REACH

### 1. Pre-natal developmental toxicity study in a second species

Pre-natal developmental toxicity (PNDT) studies in two species is an information requirement under Annex X to REACH (Section 8.7.2.).

ECHA understands that you have adapted the information requirement according to Annex IX, Section 8.7., Column 2, third indent (low toxicological activity).

As explained under Appendix C.2. your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

In your comments on the draft decision you state your belief that the study can be waived based on the existing information and information to be generated after this decision. You also state that you will assess the need to perform this study after the generation of the above requested information requirements.

You may perform the study sequentially following the 1st PNDT study. However, as stated above, a PNDT study in a 2nd species is a standard information requirement under Annex X and your current adaptation according to Annex IX, Section 8.7., Column 2, third indent (low toxicological activity) is rejected. Therefore, the data gap remains.

*Study design*

A PNDT study according to the OECD TG 414 study should be performed in the rabbit or rat as the preferred second species, depending on the species tested in the first PNDT study (request C.2 in this decision).

The study shall be performed with oral[9] administration of the Substance.

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

## Appendix E: 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[10].

### 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, in this case the distribution of the C-chain length, the degree of unsaturation, the number of sulphonated groups in the reacted material and the relative abundance of unreacted material.

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[11].

[10] https://echa.europa.eu/practical-guides
[11] https://echa.europa.eu/manuals

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

### A. Environmental testing for substances containing multiple constituents

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

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

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

**Appendix G: Procedure**

The information requirement for an Extended one-generation reproductive toxicity study (EOGRTS; Annexes IX or X, Section 8.7.3.) is not addressed in this decision. This may be addressed in a separate decision once the information from the Sub-chronic toxicity study (90-day) requested in the present decision is provided; due to the fact that the results from the 90-day study is needed for the design of the EOGRTS. Similarly the information requirement for a Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.) is not addressed in this decision; as the EOGRTS will cover the same parameters.

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 27 November 2019.

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

ECHA took into account your comments and amended the request(s).

You have provided comments during the decision-making phase which were found to be compliant with the information required in the draft decision for *in vitro* gene mutation study in bacteria. Therefore the original request (A2) was removed.

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 H: List of references - ECHA Guidance[12] 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)[13]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[13]

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[14]
Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

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