Helsinki, 03 September 2020

**Addressees**
Registrants of PFAEO_C16-18_18UNSAT listed in the last Appendix of this decision

**Date of submission for the jointly submitted dossier subject of this decision**
25 June 2018

**Registered substance subject to this decision, hereafter 'the Substance'**
Substance name: 2,2'-(C16-18 (evennumbered, C18 unsaturated) alkyl imino) diethanol
EC number: 620-540-6
CAS number: 1218787-32-6

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

## DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (REACH), ECHA requests that you submit the information listed below by the deadlines provided.

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

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

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

3. Ready biodegradation (Annex VII, Section 9.2.2.1.; test method OECD TG 301B/C/D/F or OECD TG 310) with the Substance;

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

1. Justification for an adaptation of the screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.);

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

### C. Requirements applicable to all the Registrants subject to Annex IX of REACH

1. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method OECD TG 414) in a first species (rat or rabbit), oral route with the Substance;

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

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

### D. Requirements applicable to all the Registrants subject to Annex X of REACH

- Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method OECD TG 414) in a second species (rabbit or rat), oral route with the Substance.

- Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) in rats, oral, with the Substance, specified as follows:
  - Ten weeks premating exposure duration for the parental (P0) generation;
  - Dose level setting shall aim to induce systemic toxicity at the highest dose level;
  - Cohort 1A (Reproductive toxicity);
  - Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation

You must report the study performed according to the above specifications. Any expansion of the study must be scientifically justified.

**Conditions to comply with the requests**

Each addressee of this decision is bound by the requests for information corresponding to the REACH Annexes applicable to their own registered tonnage of the Substance at the time of evaluation of the jointly submitted dossier.
To identify your legal obligations, please refer to the following:

- you have to comply with the requirements of Annex VII of REACH, if you have registered a substance at 1-10 tonnes per annum (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- you have to comply with the requirements of Annexes VII and VIII of REACH, if you have registered a substance at 10-100 tpa;
- you have to comply with the requirements of Annexes VII, VIII and IX of REACH, if you have registered a substance at 100-1000 tpa;
- you have to comply with the requirements of Annexes VII to X of REACH, if you have registered a substance at above 1000 tpa.

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

The Appendix on general considerations addresses issues relevant for several requests while the other Appendices state the reasons for the requests for information to fulfil the requirements set out in the respective Annexes of REACH.

The Appendix entitled Observations and technical guidance addresses the generic approach for the selection and reporting of the test material used to perform the required studies and provides generic recommendations and references to ECHA guidance and other reference documents.

You must submit the information requested in point A.3 above in an updated registration dossier by ***8 June 2021***, and the information requested in all other points above by ***8 June 2023***. You must also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information. The timeline has been set to allow for sequential testing where relevant.

**Appeal**

This decision, 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 general considerations**

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

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

- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)
- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)

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**

In your registration dossier you have formed a group (category) of 'Primary Fatty Amine Ethoxylates' (PFAEO), consisting of the members noted below. You have provided a read-across justification document in IUCLID Section 13.

For the purpose of this decision, the following abbreviations are used for the group members:
[1] Substance A (EC No. 233-520-3), PFAEO C18;
[2] Substance B (EC No. 246-807-3), PFAEO O;
[3] Substance C (EC No. 276-014-8), PFAEO C12-18;
[4] Substance D (EC No. 620-540-6), PFAEO C16-18, 18:1 (the Substance); and
[5] Substance E (EC No. 620-539-0), PFAEO C16-18.

You provide the following reasoning for the grouping of the substances: "*The Primary Fatty Amine Ethoxylates Category are substances derived from Primary Fatty amines, ethoxylated with two mole ethylene oxide to form a tertiary amine structure. The structure varies only with the length of the fatty amine alkyl chain length. The physicochemical, fate and tox-and ecotoxicology properties are expected to vary in a predictable pattern based only on the variation in chain length*".

You define the applicability domain of the category as follows: The boundaries of the category are for the low end an alkyl chain with a majority of C12 alkyl chain length and in the high

end a majority of C18 alkyl chain length. The amount of tertiary amine is [redacted] and residual primary or secondary amine is [redacted] The amount of ethylene oxide in adduct is in average [redacted] moles.

ECHA understands that this is the applicability domain of the grouping and your predictions are assessed on this basis.

## B. Predictions for properties

### a. Prediction for toxicological properties

You have provided the following reasoning for the prediction of toxicological properties: *"read across can be done within the category, taking into account the general trend of properties when the Fatty Alkyl Chain length increases".*

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.

ECHA notes that with regards to prediction(s) of toxicological properties there are shortcoming(s) that are common to all information requirements under consideration and also shortcoming(s) that are specific for these information requirements individually. Altogether they result in a failure to meet the requirement of Annex XI, 1.5. The common shortcoming(s) are set out here, while the specific shortcomings are set out under the information requirement concerned in the Appendices below.

*1. Read-across hypothesis*

According to Annex XI, Section 1.5., two conditions shall be necessarily fulfilled. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group (read-across approach).

A read-across hypothesis needs to be provided, establishing why a prediction for a toxicological or ecotoxicological property is reliable. This hypothesis should be based on recognition of the structural similarities and differences between the source substance(s) and your Substance. It should explain why the differences in the chemical structures should not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern.

According to the information provided in your dossier, you consider that the properties of the Substance can be predicted from information on other category members as a result of similarities in their chemical structures and in their physico-chemical properties.

While structural and physico-chemical similarity is a prerequisite for applying the grouping and read-across approach, it does not necessarily lead to predictable or similar human health properties. You have not provided a well-founded hypothesis to establish a reliable prediction for a toxicological property, based on recognition of the structural similarities and differences between the category members.

### b. Prediction for ecotoxicological properties

I. Predictions within the category

Concerning the predictions of aquatic toxicity properites based on the PFAEO category members, you have provided the following reasoning: "*The toxicity to aquatic organisms is expected to increase with increasing alkyl chain length (..). An introduction of the unsaturation in the alkylchain increases the bioavailability (..)* [and] *this shifts the whole intrinsic toxicity relation with the alkyl chain length to a higher toxicity. (..) Aquatic Aquatic toxicity data for PFAEO O* [Substance B] *have been used to read-across to PFAEO C16-18* [Substance E] *and PFAEO C16-18, 18:1* [Substance D, i.e. the Substance]*, considering this to be a worst-case approach*"

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 a worst-case approach.

ECHA notes that with regards to prediction(s) of ecotoxicological properties there are shortcoming(s) that are common to all aquatic information requirements under consideration and also shortcoming(s) that are specific for these information requirements individually. Altogether they result in a failure to meet the requirement of Annex XI, 1.5. The common shortcoming(s) are set out here, while the specific shortcomings are set out under the information requirement concerned in the Appendices below.

*I.1. Missing information to support the hypothesis*

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*"[2]. The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

Supporting information must include for example bridging studies of comparable design and duration for the Substance and the source substances, information to confirm your claimed worst-case prediction.

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar substances cause the same type of effect(s) and that the source Substance B constitutes a worst case for the prediction of the aquatic property. In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary to confirm that both substance cause the same type of effects.

In order to substantiate your hypothesis of the worst case, you provide QSAR predictions for the aquatic toxicity effect values of some of the individual constituents (C8, C14, C16, C18 and C18 unsaturated), estimated using ECOSAR 1.00 (US EPA). These QSAR predictions indicate that the C18 unsaturated constituent is the most toxic to aquatic organisms, which leads you to conclude that the category member Substance B (i.e. PFAEO O, mono-constituent, C18 unsaturated alkyl chain) constitutes a worst-case for the prediction of the aquatic toxicity of the Substance.

Furthermore, in the technical dossier you have provided aquatic toxicity studies for the category members, as listed under the relevant information requirement sections A.2, B.2 and C.2 below.

[2] ECHA Guidance R.6, Section R.6.2.2.1.f

However, the information you provided cannot be used to support your hypothesis, for the following reasons:

First, regarding the QSAR predictions:

- you have only considered the individual constituents but most of the substances in the category are UVCBs. You do not provide any evidence on why and how data on the individual constituents can adequately characterise the aquatic toxicity of the UVCB category members.
- you do not provide any documentation for the QSAR predictions. Still, ECHA notes that the ECOSAR (US EPA) QSAR model estimates aquatic toxicity effect values based on Log Kow. As noted in ECHA Guidance ECHA R.7b, for surface active substances Log Kow is not a valid descriptor to predict bioaccumulation and toxicity potential. The Substance is surface active (surface tension 30 mN/m).

Consequently, the provided QSAR predictions cannot be used to reliably predict the aquatic toxicity of the individual constituents. You have not provided any other valid justification to support your hypothesis.

Second, there are no aquatic toxicity studies conducted with the Substance. With respect to the source data on the category members, all these studies are considered as not adequate, for the reasons explained in section '*I.2. Adequacy and reliability of source studies*' below and under the relevant information requirements in the Appendices below, with the sole exception of the algae growth inhibition study (ii) with the category member Substance B.

In your comments to the draft decision, you indicated your intention to first address the shortcomings of the existing studies and if the shortcomings cannot be fully addressed, you further proposed to perform new studies. You indicated your intention to have short-term toxicity to *Daphnia* and algae growth inhibition data for all category members as supporting studies and to update the read-across approach. If these supporting studies will confirm the hypothesis of same of type of effects, you proposed to have data for other aquatic toxicity endpoints on few category members that would cover the differences in alkyl chain length and degree of unsaturation: short-term toxicity to fish studies for Substances B and C, and long-term toxicity to Daphnia studies for Substances B, C and E.
ECHA notes the following with regard to your intention of addressing shortcomings and plans for future testing:

- Currently you have not provided information that would remove the deficiencies of the existing studies as described in sections I.2. and II.3 below ('Adequacy and reliability of source studies');
- Lacking the above information or any further data generated on the target and source substances, currently there is no information that could be used to support your hypothesis. Also, the results of any future testing may or may not confirm your hypothesis. Hence, your proposed plan to test only few category members for short-term toxicity to fish and for long-term toxicity to *Daphnia* is not acceptable.

Consequently, since there is only one adequate and reliable study for the aquatic toxicity across the category, no comparison of toxicity can be made. Therefore, you have not established that the category member Substance B constitutes a worst-case for the prediction of the properties under consideration of the Substance.

As explained above, the data set reported in the technical dossier does not include relevant, reliable and adequate information to support your read-across hypothesis.

In the absence of such information, you have not established that the Substance and the source substance(s) are likely to have similar properties.

*I.2. Adequacy and reliability of source studies*

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

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

I.2.1. Test material identity

The Test Methods Regulation (EU) 440/2008, as amended by Regulation (EU) 2016/266, requires that "*if the test method is used for the testing of a [...] UVCB [...] sufficient information on its composition should be made available, as far as possible, e.g. by the chemical identity of its constituents, their quantitative occurrence, and relevant properties of the constituents*". Therefore, the unambiguous characterisation of the composition of the test material used to generate the source data is required to assess whether the test material is representative for the source substance as defined in the read-across justification document and thus relevant to the Substance.

Your read-across justification document contains compositional information for the members of your category in Table 2. It states that the category members are mostly UVCBs with composition varying in the alkyl chain length and in the degree of unsaturation. However, the information on the composition of the test materials of the source data provided in your dossier is limited in general to the generic name of the UVCB substance and/or numerical identifier and it does not contain the chemical identity and quantitative occurrence of its constituents. This issue concerns the following studies:

- studies (i) and (ii), used to cover the requirement for Short-term toxicity testing on fish and listed under that request in the Appendices below.

Due to the above deficiency, ECHA concludes that it is not possible to assess whether the test material is representative for the source substance and thus relevant to the Substance.

In your comments to the draft decision, you indicated your intention to provide data on the test material identity and composition for several studies. Since you did not provide any such data in your comments, you have not demonstrated that test material is representative for the source substance(s).

Therefore, the studies listed above cannot be considered as adequate for the purpose of classification and labelling and/or risk assessment.

I.1.2. Further deficiencies

None of the following studies were performed according to the testing specifications set out in the corresponding OECD TGs (studies listed under the relevant request in the Appendices below):

- study (i), used to cover the requirement for Growth inhibition study aquatic plants;
- studies (ii) and (iv), used to cover the requirement for Short-term toxicity testing on fish;
- study (i), used to cover the requirement for Long-term toxicity testing on aquatic invertebrates.

Therefore, the studies listed above are not adequate for the purpose of classification and labelling and/or risk assessment. The specific reasons are explained further below under the relevant information requirement sections A.2, B.2 and C.2.

For the reasons listed above, the predictions within the category fail.

II. Predictions outside of the category

ECHA notes that the following analogue substances are not referred as category members in your read-across justification document, but source studies performed with these substances are included in the technical dossier for the following ecotoxicological information requirements:

Short-term fish (Annex VIII, Section 9.1.3.):
- EC No 263-177-5, CAS No 61791-44-4

Short-term aquatic invertebrates (Annex VII, Section 9.1.1.):
- EC No 236-062-2, CAS No 13127-82-7

Long-term aquatic invertebrates (Annex IX, Section 9.1.5.) and algae growth inhibition (Annex VII, Section 9.1.2.):
- EC No 291-276-3, CAS No 90367-28-5

Concerning the predictions of ecotoxicological properties based on these substances, ECHA notes the following shortcomings.

*II.1. Lack of documentation*

Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide a justification for the read-across including a hypothesis, explanation of the rationale for the prediction of properties and robust study summary(ies) of the source study(ies).[3]

You have provided studies conducted with analogue substances but not a category member in order to comply with the REACH information requirements. You have not provided documentation, containing the necessary elements as described above, as to why this information is relevant for your Substance.

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

*II.2. Characterisation of the analogue (source) substances*

According to the ECHA Guidance, "*the purity and impurity profiles of the substance and the structural analogue need to be assessed*", and "*the extent to which differences in the purity and impurities are likely to influence the overall toxicity needs to be addressed, and where technically possible, excluded*". The purity profile and composition can influence the overall toxicity/properties of the Substance and of the source substance(s).[4] Therefore, qualitative and quantitative information on the compositions of the Substance and of the source substance(s) should be provided to allow assessment whether the attempted predictions are compromised by the composition and/or impurities.

Furthermore, whenever the Substance and/or the source substance(s) are UVCB (Unknown or Variable composition, Complex reaction products or of Biological materials) substances qualitative compositional information of the individual constituents of the category members

[3] ECHA Guidance R.6, Section R.6.2.6.1
[4] ECHA Guidance R.6, Section R.6.2.3.1

needs to be provided; as well as quantitative characterisation in the form of information on the concentration of the individual constituents of these substances; to the extent that this is measurable.[5]

You do not provide any description of the source substances . Furthermore, for all the studies provided in the technical dossier that were conducted with these substances, as listed above, no information on the composition of the test material used to generate the source data is provided (see Section *II.3.1* below).

In your comments to the draft decision, you indicated that you will update the information on the identity of the analogue substances that are not referred as category members in your current read-across justification document. You specified that the identifiers of these analogues are alternative chemical descriptions for the category members used before REACH registration. You claim that the analogue substances listed above refer to the following category members:

- EC No 263-177-5, CAS No 61791-44-4 corresponds to Substance [D], i.e. the Substance
- EC No 236-062-2, CAS No 13127-82-7 corresponds to Substance [B]
- EC No 291-276-3, CAS No 90367-28-5 corresponds to Substance [E]

However, in your comments you did not provide any data on the qualitative and quantitative description of the composition of the source substance(s) and of the test material to confirm the identity of these analogue substances.

Without this information, no qualitative or quantitative comparative assessment of the compositions of the source substances can be completed. Therefore, ECHA considers that it is not possible to assess whether the attempted predictions are compromised by the composition of the source substance.

*II.3. Adequacy and reliability of source studies*

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

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

II.3.1. Test material identity

As explained in section I.3.1, detailed information on the composition of the test material used to generate the source data is required to to assess whether the test material is representative for the source substance and thus relevant to the Substance.
The information on the composition of the test materials of the source data provided in your dossier is limited to the generic name of the UVCB substance and/or numerical identifier and it does not contain the chemical identity and quantitative occurrence of its constituents. This issue concerns the following studies (studies listed under the relevant request in the Appendices below):

- study (i), used to cover the requirement for Short-term toxicity testing on aquatic invertebrates;
- study (iii), used to cover the requirement for Growth inhibition study aquatic plants;
- study (iii), used to cover the requirement for Short-term toxicity testing on fish;
- study (ii), used to cover the requirement for Long-term toxicity testing on aquatic

[5] ECHA Guidance R.6, Section R.6.2.5.5

invertebrates.

Due to the above deficiency, ECHA concludes that it is not possible to assess whether the test material is representative for the source substance and thus relevant to the Substance.

In your comments to the draft decision, you indicated your intention to provide data on the test material identity and composition for several studies. Since you did not provide any such data in your comments, you have not demonstrated that test material is representative for the source substance(s).

Therefore, the studies listed above are not adequate for the purpose of classification and labelling and/or risk assessment.

II.3.2. Further deficiencies

None of the following studies were performed according to the testing specifications set out in the corresponding OECD TGs (studies listed under the relevant request in the Appendices below):

- study (iii), used to cover the requirement for Growth inhibition study aquatic plants;
- study (iii), used to cover the requirement for Short-term toxicity testing on fish;
- study (ii), used to cover the requirement for Long-term toxicity testing on aquatic invertebrates.

Therefore, the studies listed above are not adequate for the purpose of classification and labelling and/or risk assessment. The specific reasons are explained further below in the relevant information requirement sections A.1, A.2, B.2 and C.2.

For the reasons listed above, the predictions outside the category fail.

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

As explained above, based on the information from the evaluated registration dossier and your comments, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. Therefore, your adaptation is rejected.

Further, specific considerations are addressed under the individual information requirements.

**(ii) Referral of the decision to the Member States Competent Authorities**

In your comments to the draft decision, you request ECHA to postpone the referral of this draft decision to the Member States Competent Authorities by 30 November 2020, so you can address the shortcomings identified and improve the read-across approach in the updated dossier.

As specified in the notification letter accompanying the draft decision, ECHA does not take into account any dossier updates submitted after the date on which you were notified the draft decision in the context of the adoption of the decision according to Article 51. In addition, the new data that you intend to provide and/or generate may or may not confirm your hypothesis. As a consequence, there is no reason to delay the current decision making process.

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

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

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

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

You have adapted this information requirement by using a Grouping of substance and read-across approach under Annex XI, section 1.5. and you have provided in your dossier the following study record flagged as read-across:

i. [redacted] (2009), key study, according to OECD TG 202 with the analogue substance 2,2'-(octadec-9-en-1-ylimino)diethanol (EC No 236-062-2, CAS No 13127-82-7)

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

*A. Predictions outside of the category*

You have provided a study conducted with an analogue substance but not a category member. However, as explained in the Appendix on general considerations your adaptation according to Annex XI, Section 1.5 is rejected.

In your comments to the draft decision, you agree to perform the study with the Substance.

Therefore, the information requirement is not fulfilled.

*Study design*

The Substance is difficult to test due to the adsorptive, ionisable and surface active properties as explained above. OECD TG 202 specifies that for difficult to test substances, the OECD GD 23 is to be followed. To get reliable results, the substance properties need to be considered when performing the test, in particular with regard to the test design; including exposure system, test solution preparation, and sampling. OECD GD 23 (Table 1) describes testing difficulties related to a specific property of the substance. You may use the approaches described in OECD GD 23 or other approaches if more appropriate for your substance. The approach selected must be justified and documented.

Due to the substance properties it may be difficult to achieve and maintain the exposure concentrations. Therefore, you have to demonstrate that the concentration of the substance is stable throughout the test (i.e. measured concentrations remains within 80-120% of the nominal concentration). If it is not possible to demonstrate the stability, you must express the effect concentration based on measured values as described in the applicable test guideline. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the test solution preparation method applied was sufficient to maximise the concentration of the Substance in the test solution. Furthermore, exposure concentrations must be below the critical micelle concentration (CMC). This will ensure that test organisms are exposed to the freely dissolved chemical species and not the micelle which can alter the uptake of the test chemical.

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

Growth inhibition study aquatic plants is a standard information requirement at Annex VII of REACH.

You have adapted this information requirement by using a Grouping of substance and read-across approach under Annex XI, section 1.5. and you have provided in your dossier the following study records flagged as read-across:

i. [redacted](2010a), key study, according to OECD TG 201 with the analogue substance EC No 246-807-3 (Substance B)
ii. [redacted](2014), key study, according to OECD TG 201 with the analogue substance EC No 246-807-3 (Substance B)
iii. [redacted](2010b), key study, according to OECD TG 201 with the analogue substance EC No 291-276-3 (CAS No 90367-28-5)

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

*A. Predictions within the category*

The studies listed in i. and ii. above were conducted with PFAEO category member(s). However, as explained in the Appendix on general considerations your adaptation according to Annex XI, Section 1.5 is rejected.

*B. Predictions outside of the category*

You have provided a study (listed in iii.) conducted with analogue substances but not a category member. However, as explained in the Appendix on general considerations your adaptation according to Annex XI, Section 1.5 is rejected.

*C. Source studies are not adequate and reliable*

To be adequate for the purpose of classification and labelling of the Substance, the source study must be conducted in accordance with the applicable OECD test guidelines or other internationally recognised test methods (Article 13(3) of REACH). For the purpose of classification and labelling, as set out in the CLP Regulation, the study must provide information on intrinsic properties i.e. the basic properties of a substance or mixture as determined in standard tests or by other means designed to identify hazards. This is to be derived without consideration of exposure under realistic environmental conditions.[6]

Similarly, for the purpose of PBT assessment Annex XIII of REACH requires generation of data under 'relevant conditions', i.e. those conditions that allow for an objective assessment of the PBT/vPvB properties of a substance and not the PBT/vPvB properties of a substance in particular environmental conditions.

As a consequence of the above, studies performed with modification to standard tests procedures impacting exposure cannot be considered relevant to derive intrinsic properties.

OECD TG 201 is the preferred guideline to fulfil this information requirement and it requires that you must (among others):

- use two alternative growth media (i.e. the OECD or the AAP medium) and in case a modified test medium is used, this should be described in details and justified in a way

[6] CLP Guidance, Section 1.1.3.

that ensures that the objective of the study is reached;
- describe the analytical monitoring method used, including information on how the test samples were prepared for the quantification of the test substance.

For the studies listed in i. and iii. above, you specify that the test media consist of natural river water with the following characteristics: DOC 3.8 mg/L, TOC 3.7 mg/L and suspended matter 17.6 mg/L. You provide the following justification for the deviation from standard medium: "*The aquatic ecotoxicity tests with ethoxylated primary fatty amines were therefore performed in river water to allow a PECaquatic,bulk/PNECaquatic,bulkapproach and is considered to be conservative but more environmentally realistic than the standard method. [..]. This approach is based on PEC estimations representing 'total aquatic concentrations'. [..] For ecotoxicity tests performed using the bulk approach, however, adsorption to suspended matter and DOC is acceptable. The results of these bulk approach tests are therefore much easier and more realistic, and if compared to PECbulk clearly provide a more appropriate assessment of risks for the environment.*"

For the studies listed in i. and iii. above, exposure concentrations were analytically determined. However, you do not provide information on preparation of test sample for analytical monitoring.

You express the results based on nominal concentrations and you indicate that the effect concentrations are defined as the sum of adsorbed as well as dissolved substance in the volume of the medium tested.

The studies listed in i. and iii. were conducted with non-standard test medium (river water). The test substances are highly adsorptive cationic surfactants and are therefore expected to bind to dissolved organic matter and particulate matter. Since river water differs from standard media with regards to the content of higher organic matter and particulate matter, the use of this modified test medium impacts the exposure to the test substance. Your justification for the use of modified test media only considers the relevance of the study for the risk assessment. However, since the applied modification to standard tests procedures impacts the exposure, studies listed in i. and iii. do not inform on the intrinsic properties and the modification of the test media is not acceptable.

For the studies listed in i. and iii. above, in the absence of sufficient information on how test samples were prepared for the quantification of the test substance, ECHA cannot determine if the truly dissolved test substance concentrations were measured.

Hence, with the exception of study ii., none of the studies provided meets the conditions listed above and therefore these studies are not adequate for the purpose of classification and labelling.

In addition, for studies i. and iii. listed above conducted with deviations from the testing specifications set out in the corresponding OECD TGs (i.e. modification of test media), you indicated that "*we have recognised that the Bulk approach test are less adequate for Classification and labelling purposes as these studies indeed do not allow the quantification of intrinsic toxicity.*" You hence agree that studies i. and iii. listed above are not adequate for the purpose of classification and labelling.

*D. Bias of the prediction*

In order to make an accurate prediction of ecotoxicological and toxicological properties all relevant information must be considered in the prediction. If not all information is considered in the read-across approach, then bias may be introduced in predictions. Bias

may be caused by incorrect/incomplete selection of source substance(s); or due to a particular selection of source study(ies). If all information on all the substances in the category has not been considered, then this may result in an over/under estimation in the prediction[7].

You use the results of the study i. with the category member Substance B (72h-ErC50 = 86.7 µg/L and 72h-ErC10 = 34.1 µg/L) to conclude on this endpoint. The study ii. with Substance B shows a higher concern (72h-ErC50 = 53.8 µg/L and 72h-ErC10 = 15.6 µg/L).

There is data available within the category that give raise to a greater concern (study ii above) than the source studies you use to conclude on this endpoint (i.e. study i.). Therefore, ECHA considers that your predictions are biased and underestimate the hazards of the Substance.

ECHA concludes that not all relevant information within the applicability domain of the category have been provided nor adequately considered in your predictions. Therefore, ECHA considers that there is bias in your predictions.

In your comments to the draft decision, you agree to perform the requested study with the Substance.

Therefore, the information requirement is not fulfilled.

*Study design*

The Substance is difficult to test due to the adsorptive, ionisable and surface active properties as explained above. OECD TG 201 specifies that for difficult to test substances, the OECD GD 23 is to be followed as explained above under request A.1.

### 3. Ready biodegradability (Annex VII, Section 9.2.1.1.)

Ready biodegradability is a standard information requirement at Annex VII of REACH.

You have provided in your dossier the following study records claimed to be conducted with the Substance:

i. [redacted](1990a), key study, according to OECD TG 301D with EC 263-177-5 (CAS No 61791-44-4)
ii. [redacted](1991), according to OECD TG 301D with EC 263-177-5 (CAS No 61791-44-4)

Furthermore, you have adapted this information requirement by using a Grouping of substance and read-across approach under Annex XI, section 1.5. and you have provided in your dossier the following study records flagged as read-across:

iii. [redacted](1990b), key study, according to OECD TG 301D with the analogue substance EC No 246-807-3 (Substance B)
iv. [redacted](2006), key study, according to OECD TG 301B with the analogue substance EC No 246-807-3 (Substance B), test material identified as CAS No 26635-93-8
v. [redacted](2002a), key study, according to OECD TG 301F with the analogue substance EC No 291-276-3 (CAS No 90367-28-5)

[7] RAAF, Section 4.5.1.5.

vi. [redacted](1997a), key study, according to OECD TG 301B with the analogue substance EC No 263-163-9 (CAS No 61791-31-9)
vii. [redacted](1997b), key study, according to OECD TG 301B with the analogue substance EC No 263-177-5 (CAS No 61791-44-4)
viii. [redacted](2005), key study, according to OECD TG 301F with the analogue substance EC No 246-807-3 (Substance B), test material identified as CAS No 13127-82-7
ix. [redacted](2005), according to OECD TG 301B with the analogue substance EC No 276-014-8 (Substance C)
x. [redacted](2002b), according to OECD TG 301F with the analogue substance EC No 263-177-5 (CAS No 61791-44-4)
xi. [redacted](1989), according to OECD TG 301D ("*modified according to the recommendations of* [redacted] *1985*") with the analogue substance EC No 263-163-9 (CAS No 61791-31-9)
xii. [redacted](1996), TG not reported, with the analogue substance fatty amine derivatives
xiii. [redacted](2007), TG not reported, with the analogue substance fatty amine derivatives
xiv. [redacted](1993), TG not reported, with Substance A (EC No 233-520-3)
xv. [redacted](1997), TG not reported, with the analogue substance Alkanolamines
xvi. [redacted](1982), TG not reported, with the analogue substance 2,2'-iminodiethanol (EC No 203-868-0, CAS No 111-42-2)

We have assessed this information and identified the following issues:

**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. Predictions within the category*

You have adapted the standard information requirement in accordance with Annex XI, section 1.5. to REACH by providing in the technical dossier the studies listed in iii., iv., viii., ix. and xiv. above conducted with PFAEO category member(s).

You have described and justified the grouping, as presented in the Appendix on general considerations above.

You have provided a read-across justification document in IUCLID Section 13. You claim that: *"All substances within the group are readily biodegradable."*

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

In your comments to the draft decision, you indicated your intention to provide a more specific read-across hypothesis and a justification explaining the rationale for the prediction. You have also indicated your intention to perform new studies for each category member (if the shortcomings of the existing studies cannot be fully addressed).

ECHA notes that your intentions seem to be contradictory. Also, as explained under section C. below, the information provided in the comments indicates non ready biodegradability as result in some of the studies. This information will have to be considered as it contradicts your current read-across hypothesis.

ECHA notes the following shortcomings with regards to prediction(s) of biodegradation within the category:

*A1. Missing supporting information to compare properties of the substances*

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar substances have similar fate properties. In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance(s).

In your technical dossier you have provided ready biodegradability studies on the category members. You consider that these studies support that the Substance and the source substances are readily biodegradable.

However, as explained under issue A.2. *Adequacy and reliability of the source studies* below, none of these studies are reliable to allow comparison of the ready biodegradability profile. Therefore, the data set reported in the technical dossier does not include such relevant, reliable and adequate information for the Substance and of the source substance(s) to support your read-across hypothesis.

*A2. Adequacy and reliability of the source studies*

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

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

A.2.1. Test material identity

The Test Methods Regulation (EU) 440/2008, as amended by Regulation (EU) 2016/266, requires that "*if the test method is used for the testing of a [...] UVCB [...] sufficient information on its composition should be made available, as far as possible, e.g. by the chemical identity of its constituents, their quantitative occurrence, and relevant properties of the constituents*". Therefore, the unambiguous characterisation of the composition of the test material used to generate the source data is required to assess whether the test material is representative for the source substance as defined in the read-across justification document and thus relevant to the Substance.

Your read-across justification document contains compositional information for the members of your category in Table 2. It states that the category members are mostly

UVCBs with composition varying in the alkyl chain length and in the degree of unsaturation. However, the information on the composition of the test materials of the source data provided in your dossier is limited in general to the generic name of the UVCB substance and/or numerical identifier and it does not contain the chemical identity and quantitative occurrence of its constituents. This issue concerns the following studies:

- studies (iv), (viii), (ix) and (xiv).

Due to the above deficiency, ECHA concludes that it is not possible to assess whether the test material is representative for the source substance and thus relevant to the Substance.

In your comments to the draft decision, you indicated your intention to provide data on the test material identity and composition for several studies. Since you did not provide any such data in your comments, you have not demonstrated that test material is representative for the source substance(s).

Therefore, the studies listed above cannot be considered as adequate for the purpose of classification and labelling and/or risk assessment.

A.2.2. Further deficiencies

None of the following studies were performed according to the testing specifications set out in the corresponding OECD TGs:

- studies (iii), (viii) and (xiv).

Therefore, the studies listed above are not adequate for the purpose of classification and labelling and/or risk assessment. The specific reasons are explained further below under point C.

B. *Predictions outside of the category*

You have provided studies (listed in v., vi., vii., x., xi., xii., xiii., xv, and xvi.) that you indicate were conducted with analogue substances but not a category member.

In addition, you have provided studies listed in i. and ii. claimed to be conducted on the Substance, but the identifiers of the test material (EC No 263-177-5 and CAS No 61791-44-4) do not correspond to those of the Substance. These identifiers also do not correspond to any of the category members. In Section 1.1 of your CSR you indicate that based on the names EC No 263-177-5 correlates to the Substance. However, you have not provided qualitative and quantitative information on the composition to justify why the test materials used to generate the data are consistent with the Substance. Therefore, ECHA considers these studies as also conducted with other substances than your Substance.

ECHA notes the following shortcomings with regards to prediction(s) of biodegradation outside of the category:

*B.1. Lack of documentation*

Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide a justification for the read-across including a hypothesis, explanation of the rationale for

the prediction of properties and robust study summary(ies) of the source study(ies).[8]

You have provided studies conducted with analogue substances but not a category member in order to comply with the REACH information requirements. You have not provided documentation, containing the necessary elements as described above, as to why this information is relevant for your Substance.

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

B.2. *Characterisation of the analogue (source) substances*

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

Furthermore, whenever the Substance and/or the source substance(s) are UVCB (Unknown or Variable composition, Complex reaction products or of Biological materials) substances qualitative compositional information of the individual constituents of the category members needs to be provided; as well as quantitative characterisation in the form of information on the concentration of the individual constituents of these substances; to the extent that this is measurable.[10]

You do not provide any description of the source substances. Furthermore, for all the studies provided in the technical dossier that were conducted with these substances, no information on the composition of the test material used to generate the source data is provided (see Section B.3 below).

In your comments to the draft decision, you indicated that you will update the information on the identity and composition of the analogue substances that are not referred as category members in your current read-across justification document.

In addition, for studies xii., xiii., xv, and xvi., you indicated that these are studies from publications, and you do not intend to use these studies to fulfil the standard information requirement.

For studies v., vi., vii., x. and xi., you specified that the identifiers of the analogues used in these studies are alternative chemical descriptions for the category members used before REACH registration. You claim that these analogue substances refer to the following category members:

- EC No 263-177-5, CAS No 61791-44-4 corresponds to Substance [D], i.e. the Substance
- EC No 236-062-2, CAS No 13127-82-7 corresponds to Substance [B]
- EC No 291-276-3, CAS No 90367-28-5 corresponds to Substance [E]
- EC No 263-163-9 (CAS No 61791-31-9) corresponds to Substance [C]

[8] ECHA Guidance R.6, Section R.6.2.6.1
[9] ECHA Guidance R.6, Section R.6.2.3.1
[10] ECHA Guidance R.6, Section R.6.2.5.5

However, in your comments you did not provide any data on the qualitative and quantitative description of the composition of the source substance(s) and of the test material to confirm the identity of these analogue substances.

Without this information, no qualitative or quantitative comparative assessment of the compositions of the source substances can be completed. Therefore, ECHA considers that it is not possible to assess whether the attempted predictions are compromised by the composition of the source substance.

*B.3. Adequacy and reliability of the source studies*

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

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

B.3.1. Test material identity

As explained in section A.2.1, detailed information on the composition of the test material used to generate the source data is required to to assess whether the test material is representative for the source substance and thus relevant to the Substance.

The information on the composition of the test materials of the source data provided in your dossier is limited to the generic name of the UVCB substance and/or numerical identifier and it does not contain the chemical identity and quantitative occurrence of its constituents. This issue concerns the following studies:
- studies (i), (ii), (v) to (vii), (x) to (xiii), (xv), and (xvi).

Due to the above deficiency, ECHA concludes that it is not possible to assess whether the test material is representative for the source substance and thus relevant to the Substance.

In your comments to the draft decision, you indicated your intention to provide data on the test material identity and composition for several studies wherever possible. Since you did not provide any such data in your comments, you have not demonstrated that test material is representative for the source substance(s).

Therefore, the studies listed above cannot be considered as adequate for the purpose of classification and labelling and/or risk assessment.

B.3.2. Further deficiencies

None of the following studies were performed according to the testing specifications set out in the corresponding OECD TGs:
- studies (i), (ii), (v) to (vii), (x) to (xiii), (xv) and (xvi).

Therefore, the studies listed above are not adequate for the purpose of classification and labelling and/or risk assessment. The specific reasons are explained further below under point C.

C. To be adequate for the purpose of classification and labelling and/or risk assessment of the

Substance, the source study must be conducted in accordance with the applicable OECD test guidelines or other internationally recognised test methods (Article 13(3) of REACH). OECD TG 301 and 310 are the preferred guidelines to fulfil this information requirement. The OECD TG 301 require(s) that you must (among others):

- Apply the test conditions (e.g. inoculum concentration) specified in Table 2 and provide a scientific explanation for any change of procedure.
- Fulfil the validity criteria as set up in the test guideline, among others: the difference of extremes of replicate values of the removal of the test chemical at the plateau, at the end of the test or at the end of the 10-d window, as appropriate, is less than 20%.
- For studies according to OECD TG 301D and 301F with N-containing substances, determine the increase in concentration of nitrite and nitrate over 28d and calculate the correction for the oxygen consumed by nitrification.

For the studies listed in xii. to xvi. above, you have not provided information on test conditions and validity criteria as described above.

For the studies listed in i., ii., iii., v., viii. and x. above, you have not provided information on inoculum concentration.

For the studies listed in i., ii. and iii. above, the following change of procedure was done: ammonium chloride was omitted from the test medium to prevent nitrification.

For the studies listed in i., ii., iii., vi., vii. and xi. above, you have not provided information on results (e.g. data in tabular form and percentage removal at plateau, at end of test, and/or after 10-d window) to allow a verification that the validity criteria of the method were fulfilled.

For the studies listed in i., ii., iii., v., viii., and xi. above, conducted according to OECD TG 301D or OECD TG 301F, you have not determined the increase in concentration of nitrite and nitrate over 28d nor corrected for the oxygen consumed by nitrification.

For the studies listed in xii. to xvi., in the absence of information on test conditions and on results to verify the fulfilment of the validity criteria, it is not possible to verify that the key parameters of OECD TG 301 were met. In your comments to the draft decision, you specified that studies xii. to xvi. are from publications and cannot be used to conclude on the endpoint.

For the studies listed in i., ii., iii., v., viii. and x., in the absence of information on inoculum concentration, it is not possible to verify whether the test conditions set out in OECD TG 301 were met.

For the studies listed in i., ii. and iii., you have not explained the impact of the change of procedure on the test results. In your comments to the draft decision, you justified that the change of procedure did not impact the test results for studies i., ii. and iii.. You stated that ammonium chloride was omitted from test medium to prevent additional oxygen consumption due to nitrification of ammonium. Furthermore you state that omission of ammonium chloride from the medium does not result in nitrogen limitation as demonstrated by the biodegradation of the reference compound. ECHA considers that the information provided in your comments addresses this issue.

For the studies listed in i., ii., iii., vi., vii. and xi. above, in the absence of information on results, it is not possible to verify that the validity criteria of OECD TG 301 were fulfilled.

For the studies listed i., ii., iii., v., viii., and xi. above, since the test substances are N-containing substances and results were not corrected for the oxygen consumed by nitrification, the results are not reliable. In your comments to the draft decision, you stated that for studies listed i., ii., iii., v., viii., and xi. above, the increase in concentration of nitrite and nitrate was only measured for study viii. and no additional nitrification was observed. For these studies, you indicated that in the dossiers the results were not corrected for the oxygen consumed by nitrification. You further indicated that, when the correction is applied, only study v. and viii. fulfil the pass test criteria for ready biodegradability, while studies listed i., ii., iii. and xi are considered as not readily biodegradable. ECHA considers that the information provided in your comments addresses this issue and that the new results and interpretations of the studies must be reported in the dossier.

In addition, in your comments to the draft decision you indicated your intention to provide information on inoculum concentration (for i., ii., iii., v., viii. and x.) and results (for studies i., ii., iii., vi., vii. and xi.). ECHA notes that you did not provide any new information, so currently there is no information that could be used to support the adequacy of these studies.

Overall, based on your comments, some of the deviations can be considered as addressed (but you need to reflect them in the dossier), while other deficiencies still remain.

Hence, none of the studies provided meet the conditions listed above and therefore these studies are not adequate for the purpose of classification and labelling and/or risk assessment.

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

As explained above, based on the information from the evaluated registration dossier and your comments, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and is rejected.

Therefore, the information requirement is not fulfilled.

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

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

1. **Justification for an adaptation of the screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)**

Screening for reproductive/developmental toxicity is a standard information requirement under 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.

In order to fulfil the information requirement, you have provided information from a Combined Repeated Dose Toxicity study with Reproduction/Developmental Toxicity Screening Test in Rats by using the source substance C.

We have assessed this information and identified the following issues.
As explained in the Appendix on general considerations your adaptation is rejected, based also on the following specific shortcoming(s) with regard to your prediction of developmental property:

Absence of information to compare the reproductive toxicity of the substances
The ECHA Guidance[11] indicates that "*it is important to provide supporting information to strengthen the rationale for the read-across*". In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary to confirm 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 Substance and of the source substance(s).

In your technical dossier you have reported the results from a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) conducted with the substance C, (EC 276-014-8). According to the robust study summary provided, "lower litter sizes due to lower numbers of corpora lutea and implantation sites, and higher post implantation losses were evident at 125 mg/kg/day", which is the highest dose tested in this study.

This OECD TG 422 study constitutes the only available source of information on the reproductive toxicity properties of the members of your category, including the Substance, and it raises concerns on the reproductive toxicity.

There is no bridging information addressing reproductive toxicity available within the category.

The comparison of the reproductive toxicity properties of the Substance and of the substance C is not possible. It cannot be therefore confirmed that members of the category, including the Substance, would cause the same type of effects on reproductive toxicity. Also, it cannot be ruled out that the Substance may cause more severe effects on reproductive toxicity than Substance C. A prediction using the data to be generated on Substance C could therefore underestimate the reproductive properties of the Substance.

[11] ECHA Guidance R.6, Section R.6.2.2.1.f

In the absence of additional screening for reproductive/developmental toxicity study and/or bridging information allowing a comparison of the reproductive toxicity of the Substance and of the substance C, the prediction from substance C is not possible. Based on the above, the information you provided do not fulfil the information requirement.

In your comments you acknowledge that "ECHA correctly points at the lack of appropriate bridging studies" and that the available OECD TG 422 conducted with substance C "raised concerns on the reproductive toxicity at the highest dose level tested. Also, the applicants concluded that the available information was too limited for an appropriate and robust evaluation of reproduction toxicity for the members of the category and decided that at least a reproduction screening is necessary to serve as bridging study". You further indicated that you "commissioned an OECD 421 study "with the Substance.".

The present decision requests the registrants concerned to generate and submit an extended one-generation reproductive toxicity study (EOGRTS) with the Substance (see Section D.2). Once an EOGRTS is available, according to Column 2 of Annex VIII, Section 8.7.1. and in order to prevent unnecessary animal testing, a screening for reproductive/developmental toxicity does not therefore need to be conducted. While you still have to comply with the information requirement in Annex VIII, Section 8.7.1., you are requested to submit a justification for the adaptation based on Column 2 of that provision.

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

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

You have adapted this information requirement by using a Grouping of substance and read-across approach under Annex XI, section 1.5. and you have provided in your dossier the following study records (one key study and additional supporting studies) flagged as read-across:

i. [redacted](2009), key study, according to OECD TG 203 with the analogue substance EC No 246-807-3 (Substance B), test material identified as EC No 236-062-2, CAS No 13127-82-7
ii. [redacted](1990), according to OECD TG 203 with the analogue substance EC No 276-014-8 (Substance C)
iii. [redacted](1997), according to OECD TG 203 with the analogue substance EC No 263-177-5 (CAS No 61791-44-4)
iv. [redacted](1990), according to OECD TG 203 with the analogue substance EC No 246-807-3 (Substance B)

We have assessed this information and identified the following issues:

*A. Predictions within the category*

The studies listed in i., ii. and iv. above were conducted with PFAEO category member(s).

However, as explained in the Appendix on general considerations your adaptation according to Annex XI, Section 1.5 is rejected.

*B. Predictions outside of the category*

You have provided a study (listed in iii.) conducted with an analogue substance but not a category member. In Section 1.1 of your CSR you indicate that based on the names EC No 263-177-5 correlates to the Substance. However, you have not provided qualitative

and quantitative information on the composition to justify why the test material used to generate the data is consistent with the Substance. Therefore, ECHA considers this study as conducted with other substances than your Substance.

However, as explained in the Appendix on general considerations your adaptation according to Annex XI, Section 1.5 is rejected.

*C. Source studies are not adequate and reliable*

To be adequate for the purpose of classification and labelling and/or risk assessment of the Substance, the source study must be conducted in accordance with the applicable OECD test guidelines or other internationally recognised test methods (Article 13(3) of REACH). OECD TG 203 is the preferred guideline to fulfil this information requirement. The guideline specifies that for difficult to test substances (such as adsorptive, ionisable and/or surface active substances) the specifications given in the OECD GD 23 must be followed. The OECD TG 203 and the OECD GD 23, require(s) that you must (among others):

- Provide analytical monitoring to verify the initial concentrations and maintenance of the exposure concentrations during the test;
- Provide evidence that exposure concentrations have been maintained throughout the test (within ±20 % of the nominal or initial measured concentration).

The Substance is a 'difficult to test' substance: it is a UVCB, with ionisable hence adsorptive properties and surface active (surface tension 30 mN/m) indicating difficulties for testing based on Table 2 of OECD GD 23.

For the studies listed in ii., iii. and iv. above, you have not carried out any analytical monitoring of the test concentrations nor provided any evidence that the exposure concentrations have been maintained for the test substances during the study period.

For the studies listed in ii., iii. and iv., in the absence of analytical monitoring, you have not demonstrated the maintenance of the exposure concentrations during the test. In your comments to the draft decision, you indicate that these are old studies and analytical monitoring was not performed due to the absence of suitable analytical methods at the time these studies were performed. However, you have not provided any evidence of maintenance of exposure concentrations.

Hence, with the exception of study i., none of the studies provided meet the conditions listed above and therefore these studies are not adequate for the purpose of classification and labelling and/or risk assessment.

In your comments to the draft decision, you confirmed your intention to adapt this information requirement by read-across approach and by future testing on some category members only. However, as explained in the Appendix on general considerations under section *I.1.Missing information to support the hypothesis*, your read-across hypothesis is currently not substantiated and hence the proposed testing strategy is not acceptable.
Therefore, the information requirement is not fulfilled.

*Study design*

The Substance is difficult to test due to the adsorptive, ionisable and surface active properties as explained above. OECD TG 203 specifies that for difficult to test substances, the OECD GD 23 is to be followed as explained above under request A.1.

## Appendix C: Reasons for the requests to comply with Annex IX of REACH

Under Articles 10(a) and 12(1) of REACH, a technical dossier registered at 100 to 1000 tonnes or more per year must contain, as a minimum, the information specified in Annexes VII to IX to REACH.

### 1. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species

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

You have adapted this information requirement by using a Grouping of substance and read-across approach under Annex XI, section 1.5. and you have provided in your dossier:

With the category member Substance B:

- Harlan Laboratories Ltd, (2014), Pre-natal oral developmental toxicity study in the rat.

We have assessed this information and identified the following issues.

As explained in the Appendix on general considerations your adaptation is rejected, based also on the following specific shortcoming(s) with regard to your prediction of pre-natal developmental property:

Differences in the toxicity profiles of category members

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)".The ECHA Guidance[12] indicates that "*it is important to provide supporting information to strengthen the rationale for the read-across*". The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the category members. The observation of differences in the toxicological properties among some members of a category is a warning sign. An explanation for such a difference resulting in a contradiction between the similarities in properties claimed in the read-across hypothesis and the observation of different properties needs to be provided and supported by scientific evidence.

In your technical dossier, you have provided information from a pre-natal developmental toxicity study conducted with the category member Substance B. No effects attributed to the test substance have been detected in that study and a NOAEL of 150 mg/kg/d has been identified.

However, ECHA is aware that there is also a pre-natal developmental toxicity study (OECD TG 414) conducted with the category member C (EC 276-014-8) (Whitehead S., 2018) and this information is disseminated on ECHA's website. In that study, severe treatment-related findings linked to early development of embryos, specifically to neural tube closure and somite development have been observed.
More specifically, on Day 20 of gestation, post-implantation losses were statistically significantly higher compared to the control animals (7.5% to 15.5%) in the Pre-natal developmental toxicity study conducted with the category member Substance C.

[12] ECHA Guidance R.6, Section R.6.2.2.1.f

The fetal development at the high dose 125 mg/kg/day was severely compromised. There were 8 litters with similar major abnormalities, the majority affecting the head, eye and vertebral column (e.g. exencephaly, meningoencephalocele, acephalostomia, cleft lip, anophthalmia, microphthalmia, absent eyes, exoccipital partially fused to 1st cervical arch(es), absent/small/misshapen orbital socket(s), spina bifida, holorachischisis).

Also, at 125 mg/kg/day there was an increased incidence of medially thickened/kinked ribs, short supernumerary cervical ribs, delayed ossification of 5th/6th sternebrae and thoracic/ sacrocaudal vertebral elements and partially undescended lobe(s) of thymus.

Additionally, at 30 mg/kg/day there was an incidence of microphthalmia which although was observed in one fetus in one litter, it was also observed for two fetuses in two litters at 125 mg/kg/day. Therefore, a relationship to treatment at 30 mg/kg/day cannot be ruled out.

In contrast with the absence of effects reported in the source study with the category member Substance B, the study on the category member of Substance C raises serious concerns on the developmental toxicity. You have not provided any justification for not including the information on the category member Substance C in your read-across approach and have not explained why the study on category members raising the highest concern has not been taken into account in predicting the properties of the Substance. You have not demonstrated and justified that the properties of the category members, including the Substance, are likely to be similar despite the observation of these differences. In the absence of such information, the possibility that the prediction underestimates the properties of the Substance cannot be ruled out.

ECHA concludes that the available set of data on the category members shows differences in the pre-natal developmental toxicity property. Therefore you have not demonstrated and justified that the properties of the category members are likely to be similar despite the observation of these differences. Additionally, as not all relevant information within the applicability domain of the category have been provided nor adequately considered in your predictions ECHA considers that there is bias in your predictions.

Therefore, the information you provided do not fulfil the information requirement.

In your comments to the draft decision you indicated that you intend to update the category documentation with better test substance characterisation, additional relevant publicly available data to PFAEO substances which is not included in the category as currently documented in the dossier, and bridging screening studies with the category members and the Substance (see section B.1) which will have been completed when you update the category documentation. You further indicate that this will lead to a better evaluation of the possible hazard for development for each of the members of this category.

ECHA notes that the new data may or may not confirm your hypothesis. As you have not provided in your comments any new scientific information justifying such adaptation or addressing the information requirement other than describing your intentions, the data gap remains.

*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 administration of the Substance.

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

Long-term toxicity testing on aquatic invertebrates is a standard information requirement at Annex IX of REACH.

You have adapted this information requirement by using a Grouping of substance and read-across approach under Annex XI, section 1.5. and you have provided the following study records flagged as read-across:

i. [redacted](2010a), key study, according to OECD TG 211 with the analogue substance EC No 246-807-3 (Substance B)
ii. [redacted](2010b), key study, according to OECD TG 211 with the analogue substance EC No 291-276-3 (CAS NO 90367-28-5)

We have assessed this information and identified the following issues:

*A. Predictions within the category*

The study listed in i. above was conducted with PFAEO category member(s). However, as explained in the Appendix on general considerations your adaptation according to Annex XI, Section 1.5 is rejected.

*B. Predictions outside of the category*

You have provided a study (listed in ii.) conducted with an analogue substance but not a category member. However, as explained in the Appendix on general considerations your adaptation according to Annex XI, Section 1.5 is rejected.

*C. Source studies are not adequate and reliable*

To be adequate for the purpose of classification and labelling of the Substance, the source study must be conducted in accordance with the applicable OECD test guidelines or other internationally recognised test methods (Article 13(3) of REACH). For the purpose of classification and labelling, as set out in the CLP Regulation, the study must provide information on intrinsic properties i.e. the basic properties of a substance or mixture as determined in standard tests or by other means designed to identify hazards. This is to be derived without consideration of exposure under realistic environmental conditions.[13]

Similarly, for the purpose of PBT assessment Annex XIII of REACH requires generation of data under 'relevant conditions', i.e. those conditions that allow for an objective assessment of the PBT/vPvB properties of a substance and not the PBT/vPvB properties of a substance in particular environmental conditions.

As a consequence of the above, studies performed with modification to standard tests procedures impacting exposure cannot be considered relevant to derive intrinsic properties.

OECD TG 211 is the preferred guideline to fulfil this information requirement and it requires that you must (among others):

- use a fully defined medium with TOC below 2 mg/L;
- describe the analytical monitoring method used, including information on how the test samples were prepared for the quantification of the test substance.

For the studies listed in i. and ii. above, you specify that the test media consist of natural river water with the following characteristics: DOC 3.8 mg/L, TOC 3.7 mg/L and suspended

[13] CLP Guidance, Section 1.1.3.

matter 17.6 mg/L. You provide the following justification for the modification to standard tests media: "*The aquatic ecotoxicity tests with ethoxylated primary fatty amines were therefore performed in river water to allow a PECaquatic,bulk/PNECaquatic,bulkapproach and is considered to be conservative but more environmentally realistic than the standard method. [..]. This approach is based on PEC estimations representing 'total aquatic concentrations'. [..] For ecotoxicity tests performed using the bulk approach, however, adsorption to suspended matter and DOC is acceptable. The results of these bulk approach tests are therefore much easier and more realistic, and if compared to PECbulk clearly provide a more appropriate assessment of risks for the environment.*"

For the studies listed in i. and ii. above, exposure concentrations were analytically determined. However, you do not provide information on preparation of test sample for analytical monitoring.

You express the results based on nominal concentrations and you indicate that the effect concentrations are defined as the sum of adsorbed as well as dissolved substance in the volume of the medium tested.

The studies listed in i. and ii. were conducted with non-standard test media (river water) with TOC above 2 mg/L, hence they do not meet the specifications given in OECD TG 211. The test substances are highly adsorptive cationic surfactants and are therefore expected to bind to dissolved organic matter and particulate matter. Since river water differs from standard media with regards to the content of higher organic matter and particulate matter, the use of this modified test medium impacts the exposure to the test substance. Your justification for the use of modified test medium only considers the relevance of the study for the risk assessment. However, since the applied modification to standard tests procedures impacts the exposure, studies listed in i. and ii. do not inform on the intrinsic properties and the modification of the test media is not acceptable.

For the studies listed in i. and ii. above, in the absence of sufficient information on how test samples were prepared for the quantification of the test substance, ECHA cannot determine if the truly dissolved test substance concentrations were measured.

Hence, none of the studies provided meet the conditions listed above and therefore these studies are not adequate for the purpose of classification and labelling.

In your comments to the draft decision, for studies i. and ii. listed above conducted with deviations from the testing specifications set out in the corresponding OECD TGs (i.e. modification of test media), you indicated that "*we have recognised that the Bulk approach test are less adequate for Classification and labelling purposes as these studies indeed do not allow the quantification of intrinsic toxicity.*" You hence agree that studies i. and ii. listed above are not adequate for the purpose of classification and labelling.

In your comments to the draft decision, you confirmed your intention to adapt this information requirement by read-across approach and by future testing on some category members only. However, as explained in the Appendix on general considerations under section *I.1.Missing information to support the hypothesis*, your read-across hypothesis is currently not substantiated and hence the proposed testing strategy is not acceptable.

*Study design*
The Substance is difficult to test due to the adsorptive, ionisable and surface active properties as explained above. OECD TG 211 specifies that for difficult to test substances, the OECD GD 23 is to be followed as explained above under request A.1.

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

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

You have adapted the standard information requirement based on column 2 of Annex IX, Section 9.1. with the following: "*The safety assessment according to Annex 1 does not indicate the need to investigate further the effects on aquatic organisms. Therefore no chronic fish testing is considered to be required*"

As specified in Annex IX, Section 9.1., Column 2, a long-term toxicity study on fish must be performed unless the Chemical Safety Assessment demonstrates that risks towards the aquatic compartment arising from the use of the Substance are controlled (as per Annex I, section 0.1). The justification must be documented in the Chemical Safety Assessment.

In particular, the Chemical Safety Assessment must take into account the following elements to support that long-term toxicity testing is not required:

- all relevant hazard information from your registration dossier.

As specified in requests A.1, A.2, B.2 and C.2, the data on algae growth inhibition, short-term toxicity to *Daphnia* and to fish and the data on long-term toxicity to *Daphnia* are not compliant. Hence, your dossier currently does not include adequate information to characterise the hazardous property of the Substance to aquatic organisms.

In conclusion, in the absence of all this information, your Chemical Safety Assessment does not demonstrate that the risks of the Substance are adequately controlled. As a consequence, your adaptation is rejected as it does not meet the specific rules for adaptation of Annex IX, Section 9.1., Column 2.

In your comments to the draft decision, you confirmed your intention to provide adequate data on algae growth inhibition, short-term toxicity to *Daphnia* and to fish and long-term toxicity to *Daphnia* and update the CSA. If the CSA will indicate the need for further long-term toxicity testing on fish, you proposed to adapt this information requirement by read-across approach and by future testing on some category members only. As regards your plans for selective testing of long-term toxicity to fish ECHA understands that you intend to explore ways to adapt this information requirement. However, you have not provided in your comments any new scientific information justifying such adaptation or addressing the information requirement. Therefore, the data gap remains.

Based on the above, the information requirement is not fulfilled.

*Study design*
The Substance is difficult to test due to the adsorptive, ionisable and surface active properties as explained above. OECD TG 210 specifies that for difficult to test substances, the OECD GD 23 is to be followed as explained above under request A.1.

**Appendix D: Reasons for the requests to comply with Annex X of REACH**

Under Articles 10(a) and 12(1) of REACH, a technical dossier at a tonnage abve 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to REACH.

1. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2.) in a second species**

Pre-natal developmental toxicity (PNDT) studies (OECD TG 414) in two species is a standard information requirement under Annex X to REACH.

You have not provided information on a second species. In order to be compliant and enable concluding if the Substance is a developmental toxicant, information provided has to meet the requirements of OECD TG 414 in two species.

In your comments to the draft decision you indicated that you intend to update the category documentation with better test substance characterisation, additional relevant publicly available data to PFAEO substances that were earlier not in the category, and bridging screening studies with the category members and the Substance (see section B.1) which will have been completed by then. You further indicate that you will then update the dossier with an improved waiving for the pre-natal developmental toxicity study in a second species.

ECHA understands that you intend to explore ways to adapt this information requirement. However, you have not provided in your comments any new scientific information justifying such adaptation or addressing the information requirement other than describing your intentions. Therefore, the data gap remains.

A PNDT study according to the OECD TG 414 study should be performed in rabbit or rat as the preferred second species, depending on the species tested in the first PNDT study (requested in this decision). The study shall be performed with oral administration of the Substance.

2. **Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.)**

The basic test design of an Extended one-generation reproductive toxicity (EOGRT) study (OECD TG 443) is a standard information requirement under Annex X to REACH. Furthermore Column 2 of Section 8.7.3. defines when the study design needs to be expanded.

You have adapted the standard information requirement in accordance with Annex XI, section 1.5. to REACH by providing the justification discussed in the Appendix on general considerations above. In your technical dossier you have provided a reference to a testing proposal for an extended one-generation reproductive toxicity study submitted in the registration dossier for substance B. You expressed your intention to use information from that study in the future in order to predict the reproductive toxicity properties of the Substance.

To support your adaptation you have also reported information from a combined repeat dose toxicity study with reproduction/developmental toxicity study (OECD TG 422) in the rat with the substance C.

We have assessed this information and identified the following issues.

As explained in the Appendix on general considerations your adaptation is rejected, based

also on the following specific shortcoming(s) with regard to your prediction of reproductive property:

Availability of the source study

Under Article 10(a)(vii) of the REACH Regulation, a technical dossier must include "*robust study summaries of the information derived from the application of Annexes VII to XI, if required under Annex I*". Annex I, Section 1.1.4 of REACH states that robust study summaries are "*required of all key data used in the hazard assessment*". When properties of a substance are read-across from a source study conducted with an analogue substance to fulfil an information requirement, this source study provides key data for the hazard assessment. Therefore a robust study summary providing information allowing to make an independent assessment of the study must be provided for each source study used in read-across approaches.

In your technical dossier you have identified an extended one-generation reproductive toxicity study with the substance B which is yet to be conducted as your proposed source study.

You have not provided a robust study summary for the source study that you identified in your documentation of the adaptation. In the absence of such information, ECHA cannot assess the reliability of the information used to predict the properties of the Substance.

Absence of information to compare the reproductive toxicity of the substances

The ECHA Guidance[14] indicates that "*it is important to provide supporting information to strengthen the rationale for the read-across*". In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary to confirm 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 Substance and of the source substance(s).

In your technical dossier you have reported the results from a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) conducted with substance C. According to the robust study summary provided, "*lower litter sizes due to lower numbers of corpora lutea and implantation sites, and higher post implantation losses were evident at 125 mg/kg/day*", which is the highest dose tested in this study.

In addition you noted your intention to use in the future information currently being generated in an extended-one generation reproductive toxicity study on the substance B (EC 246-807-3) in order to predict the reproductive toxicity properties of the Substance.

This OECD TG 422 study constitutes the only available source of information on the reproductive toxicity properties of the members of your category and it raises concerns on the reproductive toxicity.

As there is no other study available within the category, the comparison of the reproductive toxicity properties of the Substance and of the substance C, nor substance B - which you intend to use as a source for this information requirement, is not possible. It cannot be therefore confirmed that members of the category, including the Substance, would cause the same type of effects on reproductive toxicity. Also, it cannot be ruled out that the Substance may cause more severe effects on reproductive toxicity. Also, it cannot be ruled out that the Substance may cause more severe effects on reproductive toxicity than Substance C or B.

[14] ECHA Guidance R.6, Section R.6.2.2.1.f

The prediction using the data to be generated on Substance B could therefore underestimate the reproductive properties of the Substance.

In the absence of bridging information allowing a comparison of the reproductive toxicity of the category members, the prediction from Substance B is not possible.

In your comments to the draft decision you have not provided any new data to support your hypothesis, but you acknowledge that "ECHA correctly points at the lack of appropriate bridging studies" and that the available OECD TG 422 conducted with substance C "raised concerns on the reproductive toxicity at the highest dose level tested. Also, the applicants concluded that the available information was too limited for an appropriate and robust evaluation of reproduction toxicity for the members of the category". You further indicated that you intend to update the category documentation with better test substance characterisation, additional relevant publicly available data to PFAEO substances which is not included in the category as currently documented in the dossier and bridging screening studies with the category members and the Substance (see section B.1) which will have been completed when you update the category documentation, as well as, EOGRTS results from substance B after the completion of that study.

ECHA understands that you intend to explore ways to adapt this information requirement. However, you have not provided in your comments any new scientific information justifying such adaptation or addressing the information requirement other than describing your intentions. Therefore, the data gap remains.

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

The specifications for the study design

*Premating exposure duration and dose-level setting*

The length of premating exposure period must be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

Ten weeks premating exposure duration is required to obtain results adequate for classification and labelling and /or risk assessment. There is no substance specific information in the dossier supporting shorter premating exposure duration.

In order to be compliant and not to be rejected due to too low dose levels, the highest dose level shall aim to induce systemic toxicity, but not death or severe suffering of the animals, to allow comparison of reproductive toxicity and systemic toxicity. The dose level selection should be based upon the fertility effects. A descending sequence of dose levels should be selected in order to demonstrate any dose-related effect and to establish NOAELs.

If there is no relevant data to be used for dose level setting, it is recommended that range-finding results are reported with the main study.

You have to provide a justification with your study results that demonstrates that the dose level selection meets the conditions described above.

*Cohorts 1A and 1B*

Cohorts 1A and 1B belong to the basic study design and must be included.

*Species and route selection*

The study must be performed in rats with oral[15] administration.

*Further expansion of the study design*

The conditions to include the extension of Cohort 1B are currently not met. Furthermore, no triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and/or Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B, Cohorts 2A and 2B and/or Cohort 3 if relevant information becomes available from other studies or during the conduct of this study. Inclusion is justified if the available information meets the criteria and conditions which are described in Column 2, Section 8.7.3., Annex X. You may also expand the study due to other scientific reasons in order to avoid a conduct of a new study. The study design, including any added expansions, must be fully justified and documented. Further detailed guidance on study design and triggers is provided in ECHA Guidance[16].

[15] ECHA Guidance R.7a, Section R.7.6.2.3.2.
[16] ECHA Guidance R.7a, Section R.7.6.

## Appendix E: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of registration dossiers after the date on which you were notified the draft decision according to Article 50(1) of REACH.

The compliance check was initiated on 27 June 2019.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

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

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

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 F: Observations and technical guidance

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

2. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of the Member States.

3. Test guidelines, GLP requirements and reporting

   Under Article 13(3) of REACH, all new data generated as a result of this decision needs to be conducted according to the test methods laid down in a European Commission Regulation or according to international test methods recognised by the Commission or ECHA as being appropriate.

   Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses shall be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

   Under Article 10 (a) (vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide: 'How to report robust study summaries'[17].

4. Test material

   *Selection of the test material(s) for UVCB substances*

   The registrants of the Substance are responsible for agreeing on the composition of the test material to be selected for carrying out the tests required by the present decision. The test material selected must be relevant for all the registrants of the Substance, i.e. it takes into account the variation in compositions reported by all members of the joint submission. The composition of the test material(s) must fall within the boundary composition(s) of the Substance.

   While selecting the test material you must take into account the impact of each constituent/impurity on the test results for the endpoint to be assessed. For example, if a constituent/impurity of the Substance is known to have an impact on (eco)toxicity, the selected test material must contain that constituent/impurity. Any constituents that have harmonised classification and labelling according to the CLP Regulation (Regulation (EC) No 1272/2008) must be identified and quantified using the appropriate analytical methods.

   The OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring, Number 11 [ENV/MC/CHEM(98)16] requires a careful identification of the test material and description of its characteristics. In addition, the Test Methods Regulation (EU) 440/2008, as amended by Regulation (EU) 2016/266, requires that "*if the test method is used for the testing of a* [...] *UVCB* [...] *sufficient information on its composition should be made available, as far as possible, e.g. by the chemical identity of its constituents, their quantitative occurrence, and relevant properties of the constituents*".

   In order to meet this requirement, all the constituents of the test material used for each

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

test must be identified as far as possible. For each constituent the concentration value in the test material must be reported in the Test material section of the endpoint study record.

*Technical Reporting of the test material for UVCB substances*

The composition of the selected test material must be reported in the respective endpoint study record, under the Test material section. The composition must include all constituents of the test material and their concentration values. Without such detailed reporting, ECHA may not be able to confirm that the test material is relevant for the Substance and to all the registrants of the Substance.

Technical instructions are available in the manual "How to prepare registration and PPORD dossiers" on the ECHA website[18].

5. Testing strategy for aquatic toxicity testing

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

6. List of references of the ECHA Guidance and other guidance/ reference documents[19]

Evaluation of available information
Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 in this decision.

QSARs, read-across and grouping
Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 in this decision.

ECHA Read-across assessment framework (RAAF, March 2017)[20]

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.

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

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

OECD Guidance documents[21]
Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD23.
Guidance Document on Mammalian Reproductive Toxicity Testing and Assessment – No 43, referred to as OECD GD43.

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

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

| Registrant Name | Registration number | (Highest) Data requirements to be fufilled |
|---|---|---|
| [redacted] | [redacted] | [redacted] |

Note: where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas the decision is sent to the actual registrant.