Helsinki, 30 June 2020

Addressee
Registrant listed in the last Appendix of this decision

Date of submission for the dossier subject of this decision
22/03/2018

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: 2-[(2-hydroxypropyl)(C16-18 sat. C18 unsat. alkyl)amino]propan-1-ol
EC number: 695-977-9
CAS number: 1309955-79-0

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

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (REACH), ECHA requests that you submit the information listed below by the deadline of ***6 January 2023***.

A. Requirements applicable to the Registrant subject to Annex VII of REACH

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

2. Robust study summary for "[redacted]" (Annex VII, Section 9.2.1.1. in conjunction with Annex I, Section 3.1.5.) OR Ready biodegradation (Annex VII, Section 9.2.2.1.; test method OECD TG 301A/B/C/D/E/F or OECD TG 310) with the Substance

B. Requirements applicable to the Registrant subject to Annex VIII of REACH

1. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method OECD 421/422) in rats, oral route with the Substance

C. Requirements applicable to the Registrant subject to Annex IX of REACH

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

2. 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

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

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

Conditions to comply with the requests

You are bound by the requests for information corresponding to the REACH Annexes applicable to your own registered tonnage of the Substance at the time of evaluation.
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.

The Appendix on general considerations addresses common arguments that are applicable throughout the present decision 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 testing material used to perform the required studies must be selected and reported in accordance with the specifications prescribed in Appendix entitled Observations and technical guidance.

You must submit the information requested in this decision by the deadline indicated above in an updated registration dossier and also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information. The timeline has been set to allow for sequential testing where relevant.

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

Authorised[1] under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix on general considerations

The ECHA Guidance documents referred to in this decision are listed in Appendix entitled Observations and technical guidance.

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

You have adapted the following standard information requirements by applying (a) read-across approach(es) 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.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- 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 read-across approach(es) in general before assessing the specific standard information requirements in the following appendices.

Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. 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 related documents.

A. Predictions for toxicological and ecotoxicological properties

You have provided a read-across justification document in IUCLID Section 13.

You read across to your Substance **PFAPO C16-18, 18:1** [Propanol, iminobis-, N-C16-C18 (evennumbered), C18 unsatd. alkyl) derivs] from the substances of the category 'Primary Fatty Amines Ethoxylated' (source substances):

- **PFAEO C12-18**: 2,2'-(C12-18 evennumbered alkyl imino) diethanol; CAS 71786-60-2; EC No 276-014-8
- **PFAEO C16-18, 18:1**: 2,2'-[C16-18 (evennumbered, C18 unsaturated) alkyl imino] diethanol; CAS 1218787-32-6; EC 620-540-6
- **PFAEO O**: Bis(2-hydroxyethyl)oleyl amine; CAS 25307-17-9; EC No 246-807-3;
- **PFAEO C16-18**: 2,2'-(C16-18 evennumbered alkyl imino) diethanol; CAS 1218787-30-4; EC No 620-539-0

You have provided the following reasoning for the prediction of toxicological and ecotoxicological properties: "*Read across justification for Primary Fatty Amine Propoxylate (PFAPO) is based upon the following:*·

- *Common functional groups, structural similarity*
- *Common breakdown products, metabolic pathway*
- *Toxicokinetics (Bioavailability)"*

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

a) Insufficient 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[2]. 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.

Your read-across hypothesis is that the similarity in chemical structure, common breakdown products, toxicokinetics and in some of the physico-chemical properties between the source substances and your Substance is a sufficient basis for predicting the properties of your Substance.

You have not provided an explanation of how the differences in the chemical structures (for instance, ethoxylated as opposed to propoxylated) may affect the prediction of the properties of your Substance for the relevant endpoints.

You stated that there is a difference in water solubility and logKow between the Substance and the source substances, but you consider the difference minimal for the toxicokinetic behavior of the chemicals. You have not provided evidence supporting that the differences in physico-chemical properties, for example water solubility and log Kow, do not affect the toxicokinetic behavior/bioavailability and the prediction of the properties of your Substance specifically for the relevant environmental endpoints.

You further provided a statement regarding breakdown pathways (common breakdown products) of the source substances and the Substance concerning biodegradation of at least two species of microrganisms. You have not explained how the information you provided on breakdown pathways is relevant for the predicted properties of the Substance and source substances. Furthermore, you did not provide any information characterising the breakdown products, rate and extent of biodegradation of the source substances and your Substance.

Similarity in chemical structure, common breakdown products, toxicokinetics and the differences in some of the physico-chemical properties does not necessarily lead to predictable or similar human health and environmental properties. You have not provided a well-founded hypothesis to establish a reliable prediction for a toxicological or ecotoxicological property,

[2] ECHA Guidance R.6

based on recognition of the structural similarities and differences between the source substance(s) and your Substance.

In the absence of this information, ECHA cannot verify that the properties of the Substance can be predicted from the data on the source substance for the relevant endpoints.

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

b) Missing bridging study to compare (eco)toxicological properties

Annex XI, Section 1.5 of the REACH Regulation states that "*adequate and reliable documentation of the applied method shall be provided*". Within this documentation "*it is important to provide supporting information to strengthen the rationale for the read-across*"[3]. 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). "*Adequate and reliable documentation*" must include *bridging studies to compare properties of the target and source substances.*

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar target and source substances cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the target and source substance 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 the source substances.

River water samples from different locations were used for the aquatic toxicity studies with the source substance and the Substance and these different studies show varying toxicities. No bridging studies on aquatic toxicity and human health properties, such as an OECD TG 422, were provided to demonstrate similarity in toxicity.

In your comments to the draft decision you have proposed to conduct OECD 422 and OECD 414 studies as bridging studies, and to reconsider the adaption of the information for an OECD 408 study based on these study outcomes.

In addition, in your comments to the draft decision, you stated that the studies on the source substance (PFAEO O) on algae and long-term daphnia were provided as bridging studies to support the read-across of the short-term fish endpoint.

The aquatic toxicity studies are rejected for the reasons discussed below (section c)-(i)). As stated therein, short-term studies are not adequate for concluding on the aquatic toxicity of the Substance as it is poorly water soluble. Hence availability of adequate short-term fish study would not be a valid reason for adapting the long-term fish request. In any case, it is not possible to compare the results of aquatic toxicity studies directly because of the different river water samples used. Indeed, the differences in the toxicities may be attributed to differences in substance properties, as well as the differences in the characteristics of test medium(s) used (e.g. pH, DOC/TOC content, presence of other cations).

Because of this, and the absence of bridging studies for the endpoints covered, you have not established that the Substance and the source substances are likely to have similar properties. In this respect, the proposed OECD 422 and OECD 414 studies are not available and, therefore, cannot be taken into account.

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

Therefore, you have not provided sufficient supporting information to strengthen the rationale for the read-across.

ECHA notes the following additional shortcoming with regards to prediction of aquatic toxicity, only:

c) *Adequacy and reliability of ecotoxicity source study*

According to Annex XI, Section 1.5., in all cases the results to be read across should:
- be adequate for the purpose of classification and labelling and/or risk assessment;
- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3);

c)-(i) *Testing for pooly water soluble substances*
Poorly water soluble substances require longer time to reach steady-state conditions. Hence, the short-term tests may not give a true measure of toxicity (irrespective of whether analytical monitoring was performed or not) for this type of substances and the long-term test would be needed.

You have provided:
- Two short-term studies on fish conducted according to OECD TG 203; and
- Data on water solubility 0.2 mg/L indicating that the Substance is poorly water soluble.

Hence OECD TG 203 study is not adequate for the Substance and long-term studies are needed.

c)-(ii) *Long-term studies*
The studies on long-term invertebrates & algae with the source substance are not adequate for concluding on the aquatic toxicity of the Substance because:

- the studies were conducted with non-standard test medium (river water) without proper characterisation.

For highly adsorptive ionic substances, (1) totally dissolved concentration of the substance must be measured and reported, (2) medium used must be characterised and (3) its characteristics, in particular DOC content, must remain between defined limits specified by the applicable OECD TG, or deviations from standard medium must be justified (OECD TG 201/210/211 and GD 23).

The Substance is a cationic surfactant and highly adsorptive and hence such substances are expected to bind to dissolved organic matter and particulate matters.

In the technical dossier for the long-term aquatic toxicity endpoints you have provided one study each for algae and daphnia with the source substance, PFAEO O (EC number 246-807-3; CAS number 25307-17-9) and provided following information:

(i) Both studies were performed with river water the test medium contains high DO; high PM (DOC 3.8 mg/L, TOC 3.7 mg/L and suspended matter 17.6 mg/L).
(ii) Exposure concentrations were determined as the sum of the adsorbed and dissolved substance.

In your comments to the draft decision, you provided following;
a) A table (Table 2) with four parameters (pH, DOC, suspended matter, and hardness)

of river water used in the aquatic toxicity studies.

b) Your intention to include a robust summary of a scientific publication ([redacted] 2013) to your dossier and its conclusion to the updated read-across justification document. You outlined that this scientific publication showed that "*sorption of cationic substances is governed cationic exchange processes at negatively charged surface groups by ionic interaction and to a lesser extent by hydrophobic interaction*", and "*pH and electrostatic effects are also of importance but significantly less under ambient conditions*". It is in your discretion to generate and provide the necessary supporting information in order to justify your read-across adaptation.

c) The justification for deviations from standard medium (i.e. river water) and the use of "bulk approach" as follows;

   a. You claim that a risk assessment according to the bulk approach for the Substance is considered justified as it is a cationic surfactant and hence the results from the standard guideline studies are very difficult to interpret. You explain the sorption of cationic surfactants and state that "*the Koc alone does not adequately represent the partitioning of cationic surfactants between water and soil/sediment, because the sorption to soil and sediment is not only related to the organic carbon fraction in the sorbent but also the negatively charged sites in the inorganic fraction*". Hence the EPM, which is based on sorption to organic matter, "*cannot be reliably be used to predict the hazards for the benthic and terrestrial compartment but consequently also not for the calculation of the dissolved concentration ($PEC_{dissolved}$) from the total concentration (PEC_{total}) in the final calculation steps of the exposure assessment*". As a consequence, you believe the used of the "bulk approach" was justified for both the exposure and effect assessment.

   b. You provide the explanation of 'bulk approach' which "is based on PEC estimations representing 'total aquatic concentrations'". You state that "*for ecotoxicity tests performed using the bulk approach, adsorption to suspended matter and DOC is acceptable and only adsorption to glassware should be accounted for. For a valid bulk approach test concentration-effect relationship should thus be based on the sum of adsorbed and dissolved substance*". You explained that the use of river water with high suspended matter and DOC is in perfect alignment with the risk assessment method, as the concentration of suspended matter in surface water is considered to be 15 mg/Lin CHESAR III for risk assessment. You claim that the test organism were fully exposed to bulk concentration test substance during the test.

   c. Additionally, you provided information on the DODMAC and the primary alkyl amines in order to justify why you believe a revision of PNEC values as requested in this decision is not necessary. In your opinion, the 'bulk approach' has been endorsed by EU member States under EU-RAR in the past (e.g. DODMAC (2002) and primary alkyl amines (2008) and thus you believe that ECHA cannot renege a method due to the principle of legitimate expectations.

   d. Furthermore, you state that "*For classification and labelling (PBT and CLP) the available (bulk) effect data are currently as a worst-case divided by a factor of 10 which practically means that it is assumed that 90% was sorbed where EUSES calculates that only 12% is sorbed using the Kd of 4526L/kg. With the availability of the algae and long term daphnia results based the measured concentrations, these values were used for C&L*

together with the other results from non-bulk approach tests. Considering the conservative approach followed for C&L based on bulk approach data no significant changes in the classification are anticipated".

e. You concluded that you consider *'the bulk approach' to be both conservative and more environmentally realistic than the standard method, thus a study performed with such approach to be a higher tier study. You states that the use of 'bulk approach' for the fresh water aquatic risk assessment be justified for the reasons summarised above.*

d) You stated that it is not clear why the sorption to glassware was so high in the algae study with the Substance. You have explained that normally the adsorption to glassware should be much lower as large extent of the substance is sorbed to suspended matter, algae and DOC. You do not provide explanation on the difference in recovery range of the Substance between the different tests (algae and long-term daphnia). However, you agreed to include the loss due to sorption to glassware in the calculation of effect concentrations of the algae studies and you have submitted revised values taking into account a glassware sorbed fraction for both the Substance and your source substances (outlined in Table 1 of your comments).

First, the effect concentrations are defined as the sum of adsorbed to (suspended matter and DOC) as well as the dissolved concentration.

Hence your analytical monitoring does not allow measuring of totally dissolved concentration and the reported effect concentrations can overestimate the true exposure to the Substance.

Second, in your dossier you have provided limited characterisation of the river water samples used and you have not justified how the variation in the composition and characteristics of river water (both spatial and temporal) may affect the physico-chemical parameters of water and subsequently influence the test results and its interpretation in terms of classification and labelling and/ or risk assessment of the Substance.

The following elements are also missing:

(1) Characteristic of river water and how the composition of river water (e.g. electrolyte composition) and the constituents of water (e.g. contaminants or organic carbon) may have influenced the adsorption behaviour of the Substance (thus affecting the total dissolved concentration) and the growth the test organism, respectively.
(2) Sorption behaviour of the test substance (i.e. contribution of the cations in sorption) and how the results may be translated to the hazard assessment of the Substance.
(3) The explanation for the significant differences in adherence to the glassware and/or recovery range of the Substance between the different tests (e.g. algae test and long-term daphnia).

(1) Characteristic of river water and its influence on adsorption behaviour

In your comments to the draft decision, you provided four parameters of river waters used in the aquatic studies listed in your comments a) above. This information was already available in the dossier. However as pointed out above in point (1), information on the factors/constituents which may have influence, the adsorption behaviour of the test substances (e.g. electrolyte composition) or growth of the test organisms (contaminants) are still missing.

Furthermore, you have provided some explanation on the adsorption behaviour of the cationic substances as listed in your comments b) above. ECHA acknowledge your intention to expand on this aspect in your dossier update.

(2) Sorption behaviour of the test substance and its relation to hazard assessment
In your comments to the draft decision you have provided why you believe the deviation from the TGs (i.e. modification of test medium by using natural river water) is acceptable and thus the studies are adequate for the purpose of hazard assessment, classification and/or risk assessment of the Substance in your comments c) above.

However, the study must provide information on the 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 necessary, in particular, to be adequate for the purpose of classification and labelling. This is to be derived without consideration of exposure under realistic environmental conditions.[4]

Although you claim in your comments listed in c)-b that the test organism were fully exposed to the bulk concentrations test substance during the test, since river water you used for the studies contain high amount of organic matter and particulate matter compared to the standard test medium (e.g. total organic carbon (TOC) < 2 mg/L according to the OECD TG 211), the use of the modified test medium impacts the exposure of the Substance to the organisms. Your justification for the use of the modified test medium only considers the relevance of the study for the risk assessment. However, since the modification to the standard tests procedures ie. the use of river water samples (thus affecting the total dissolved concentration), may have significant impact on the investigation of the intrinsic properties of the Substance, hence it is not adequate, especially if the effect concentrations are not based on measured total dissolved concentrations. Hence ECHA does not agree with you that 'bulk approach' is appropriate for deriving effect concentrations and for the purpose of hazard assessment and classification.

Regarding your comments listed in c) above, the EU RAR reports cited by you did not conclude that classification and labelling can be based on effect values based on 'bulk' concentrations (i) the EU RAR on DODMAC (EC Number 203-508-2) does not discuss the classification of this substance and (ii) the Draft EU RAR on Primary Alkyl Amines has not been endorsed by the European Commission (as clearly specified in the foreword section of the document). On the latter, ECHA points out that adopted RAC Opinions are available on the individual substances originally included in the Draft EU RAR on Primary Alkyl Amines (i.e. EC No. 204-015-5, EC No. 204-695-3, EC No. 262-977-1, EC No. 263-125-1, EC No. 262-976-6). RAC concluded that, for studies conducted with a dilution water containing a high level of suspended matter and humic acid, nominal concentrations do not represent the total dissolved concentrations and that such study has limited usefulness for the purposes of classification.

Regarding your comments listed in d) above ECHA notes that there is currently no scientific justification that the proposed correction factor of 10 may be considered as a realistic worst case to correct effect values based on 'bulk' concentrations. In addition, although you anticipate "*no significant changes in the classification*", ECHA points out that of the Substance may be subject to stricter classification depending on the outcome of the ready biodegradability study as requested under A.2, as well as, the aquatic toxicity effect concentrations based on the total dissolved concentrations of the Substance.

(3) Adhesion of the Substance to the glassware and/or recovery range of the Substance

[4] CLP Guidance, Section 1.1.3.

between the different tests

ECHA notes you have now addressed this significant loss due to adsorption to glassware in the calculation of the effect concentrations as listed in your comments d) above.

Taking into account your comments on the draft decision, the following elements are still missing:

- Characteristic of river water and how the composition of river water (e.g. electrolyte composition) and the constituents of water (e.g. contaminants or organic carbon) may have influenced the adsorption behaviour of the Substance (thus affecting the total dissolved concentration) and the growth the test organism, respectively.
- Sorption behaviour of the test substance (i.e. contribution of the cations in sorption) and how the results may be translated to the hazard assessment of the Substance.

Therefore this study does not provide information on the intrinsic properties of the Substance and it is not adequate for the purpose of hazard assessment, classification and labelling and/or risk assessment.

Consequently there are no aquatic toxicity studies available which are considered adequate and reliable as source studies.

B. Conclusions on the read-across approach

As explained above, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. Therefore, your adaptation is it is rejected and it is necessary to perform testing on your Substance.

In your comments on the draft decision, you have indicated your intention to update the read-across justification according to the read-across assessment framework (RAAF) requirements in order to fulfil the information requirements for the algae and long-term daphnia endpoints.

It is in your discretion to generate and provide the necessary supporting information in order to justify your read-across adaptation. If you do so, you are responsible for demonstrating the fulfilment of the requirements of Section 1.5 of Annex XI to REACH. If it fails and the resulting data does not support, or even contradict, your read-across hypothesis, you remain responsible for complying with this decision by the set deadline.

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

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, 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 the REACH Regulation.

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

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

You have provided two key studies in your dossier:

- An OECD TG 201 study (2012) with the Substance;
- An OECD TG 201 study (2010) with an analogue substance.

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

A. As already explained in the Appendix on general considerations your adaptation according to Annex XI, Section 1.5 is rejected. Therefore, the study (2010) does not fulfil the information requirement.

B. Further, both studies are performed with river water samples without characterization of medium and dissolved concentration and are therefore rejected for the same reasons as explained under the Appendix on general considerations, section (i) A. c)-(ii).

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

The OECD TG 201 is preferred to cover this information requirement. The key parameter(s) of this test guideline include,

i. Fulfilment of validity criteria as set up in the test guideline: The mean coefficient of variation for section-by-section specific growth rates (days 0-1, 1-2 and 2-3, for 72-hour tests) in the control cultures must not exceed 35%.
ii. Appropriate reporting of the test results. If the test concentrations are not maintained within the required 20 % of the measured initial concentrations throughout testing, the effect concentrations based on the measured values must be reported (see ECHA Guidance R7B (section R.7.8.4.1).

In the provided study (2012), raw data to assess whether the validity criteria of test guideline OECD TG 201 are met were not provided.

In addition, you have reported that up to 20 % adhesion to the glass was observed, however, this loss has not been taken into account in the estimation of effect concentrations as results are reported as initial nominal concentration.

In your comments on the draft decision, you provided the following:

i. The raw data for the calculation of the validity criteria (Table II). In addition, you indicate that you intend to update the technical dossier to include this data.
ii. You agreed to include the loss due to adhesion to the glassware as discussed under in the Appendix on general considerations (i) A. c)-(ii)(3) above and you provided the revised aquatic PNEC value with the adjusted algae results. You state that the

recoveries in the fresh media were in the range of 57-80% of the nominal values". You provided explanation of the loss as the instant sorption of the test substances to the river water constituents. You agreed to provide raw data on the measured concentrations in the update. However, you stated that you do not agree that the results should be based on measured concentrations as the studies were performed by using "bulk approach". Instead you stated that you believe that the concentration-effect relationship should be based on the sum of adsorbed and dissolved substance.

ECHA notes that:

i. You have now addressed C. i. above. As you remain responsible for complying with this decision by the set deadline, you need to provide the raw data in your updated dossier.

ii. Based on the available information on the reported nominal and measured concentrations, the exposure concentrations were not adequatelty maintained throughout the experiment. As already explained in the Appendix on general considerations (i) A. c)-(ii)(3) above your justification for using the "bulk approach" for the purpose of hazard assessment, classification and labelling and/or risk assessment is rejected.

Hence for both studies (2012) and (2010), the reported effect concentrations are not compliant with the requirements of OECD TG 201. As indicated there, you need to report the effect concentrations based on measured concentrations especially when the test concentrations are not maintained within the required 20 % of the measured initial concentrations throughout testing (see ECHA Guidance R.7b, section R.7.8.4.1).

Based on the above studies (2012) and (2010), the information you provided does not fulfil the information requirement , and the information provided in your comments do not change this conclusion.

2. Ready biodegradability (Annex VII, Section 9.2.1.1.);

Ready biodegradability is a standard information requirement in Annex VII to REACH.

You provided study summaries for the following studies with the Substance

- key study: OECD TG 301D ([redacted], 2009)
- supporting study: OECD TG 301D ([redacted] 2009)

Furthermore, you have provided seven supporting studies on analogue substances.

We have assessed this information and identified the following issues:

A. Key study

A robust study summary must be provided for the sole study available or, if more than one is available, for the study/ies giving rise to the highest concern for the information set out in Annexes VII- to XI (Articles 3(28) and 10(a)(vii) and Annex I, Section 3.1.5, to REACH).

It must include a detailed summary of objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study. Robust study summary for OECD TG 301D study must include following elements (among others):

- Data on the inoculum (concentration and inoculum blank),
- Data on the difference between the extremes of replicate values during the study,
- Justification on the deviation from the test guideline
- Sufficient information on the characteristics of the water used as test media as defined in paragraph 14. of the OECD TG 301 and paragraph 25. of TG 301D.

In your dossier:

1. You have not provided information on inoculum concentration, inoculum blank and difference between replicates
2. The deviation from the test guideline by omitting ammonium chloride from the medium, its effects on nitrification, and impacts on results interpretation (i.e. correction for uptake of oxygen by nitrification if necessary) is not justified.
3. The deviation from the test guideline by using river water as a non-standard test medium is not justified.

In your comments on the draft decision, you provided the following:

1. Regarding the point 1 above: you state that information on the inoculum concentration and inoculum blank can be found in IUCLID under the study design and you re-state the source and pre-conditioning of inoculum which is already provided in the technical dossier.
2. Regarding the point 2 above: you state that ammonium chloride was not added to prevent additional oxygen consumption due to oxidation of ammonium and to reduce endogenous respiration. You justify that the correction for uptake of oxygen by nitrification is not necessary because ammonium is also not added to the control bottles. 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.
3. Regarding the point 3 above: you state that the test substance is the major source of carbon for the energy and growth in the test. You justified this statement by providing new information on the endogenous respiration in the blank control bottles at day 28 (1.1 mg/L), which is below 1.5 mg/L as defined as a validity criterion of the TG.
4. You state that the differences of the replicate values at day 28 were less than 20% and you provide data on the dissolved oxygen concentrations (Table I). You indicate that the table will be included in the technical dossier.

However, ECHA notes that:

1. Information on the inoculum in the dossier and in your comment does not allow for the verification of an adequate inoculum density (concentration of inoculum) as defined in the Table 2 of OECD TG 301.
2. The impact on results interpretation (i.e. correction for uptake of oxygen by nitrification if necessary) is not justified as you did not demonstrate that nitrification was indeed absent during the study (*e.g.* by monitoring changes in concentrations in nitrite and nitrate). The biodegradation of the reference compound does not demonstrate the absence of nitrification. Additionally, it cannot be excluded that ammonia was present in the river water which was used both inoculum and water/medium in your study. Currently, based on the available information, it is not clear to ECHA, 1) how the % degradation is calculated with the modified procedure for N-containing UVCB Substance in particular considering the reported % biodegradation of 62% is very close to the pass-level (i.e. 60%), and 2) whether the nitrification can indeed be considered absent during the study. Hence, it is not possible to evaluate the acceptability of the modified procedure.
3. and 4. The information provided in your comments addressed these specific issues.

The provided study summary for the OECD TG 301D: key study ([redacted] 2009) does not provide all the information required to enable independent assessment of the study adequacy and reliability. Therefore, it is not possible to assess the reliability of the study, its results and its relevance for hazard assessment and the information provided in your comments do not change this conclusion.

B. Supporting study with the Substance

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

The OECD TG 301/310 are preferred to cover this information requirement. The key parameter(s) of this test guideline include,

- fulfilment of validity criteria as set up in the test guideline

In your comments to the draft decision, you provide explanation that this supporting study was performed prior to the key study to assess the toxicity of the Substance and its effect on biodegradability. You explain that based on the outcome of the study, it was decided to use silica gel in the key study in order to mitigate the toxicity of the Substance to the microorganisms. You agree that the validity criteria were not reported nor assessed in the supporting study. However, you believe that the supporting study is reliable because the results were reproducable in the key study.

The provided supporting study ([redacted] 2009) does not comply with the OECD TG 301D because, as you indicated, the validity criteria were not evaluated.

ECHA acknowledges the information provided in your comments, however, ECHA reiterates that the currently available information on this study does not allow for verifying that all the validity criteria of OECD TG 301D were fulfilled. The mere reproducibility of the results in another study does not, by itself, result in the reliability of a study not meeting validity criteria in particular when the other study itself is rejected as is the case here.

Therefore, the validity and reliability of the study cannot be evaluated and the provided study does not fulfil the information requirement.

C. Supporting studies with analogue substances

Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided.

You have provided studies conducted with other substances than your Substance in order to comply with the REACH information requirements. You have not provided documentation as to why this information is relevant for your Substance.

In 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). In any case, no robust study summary was provided for any supporting study to allow for an independent assessment of their validity.

Therefore, the information provided on analogue substances and the supporting study on the Substance is not appropriate to conclude on the ready biodegradability of the Substance and it does not fulfil the information requirement.

In your comments to the draft decision, you state that the supporting studies on analogue substances were intended for grouping and read-across on ready biodegradability test results. You agree that these studies are not adequate and relevant and you indicate you will remove these study records from the technical dossier

To allow assessment of the key study, you need to provide a complete robust study summary with the above missing elements for the key study.

Alternatively, if you cannot submit a complete RSS or the RSS indicates that the key study is not reliable or adequate to fulfil the information requirement, you need to submit the following study for the Substance: Ready biodegradation, OECD TG 301 B, C, D, F or 310.

Appropriate test guidelines are selected based on the applicability domain of the test guidelines and properties of the substance (ECHA Guidance R.7b, Section 7.9. and OECD TG 301 and OECD TG 310). For poorly soluble substances the test guidelines OECD TG 301 B, C, D and F, as well as OECD TG 310 apply.

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

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, 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 the REACH Regulation.

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

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

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5., by providing a study based on OECD TG 422 with an analogue substance.

As explained in the Appendix on general considerations your adaptation is rejected. Therefore, the information requirement is not fulfilled.

In your comments to the draft decision you agree to perform an OECD TG 422 study.

A study according to the test method OECD TG 421 or 422 should be performed in rats with oral[5] administration of the Substance.

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

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

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

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.)

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

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5., by providing 90-day toxicity studies with an analogue substance.

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

Therefore, the information requirement is not fulfilled.

Following the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity[6]. The sub-chronic toxicity study must be performed according to the OECD TG 408, in rats and with oral administration of the Substance, because the Substance is a liquid of very low vapour pressure and no uses with spray application are reported that could potentially lead to aerosols of inhalable size.

2. 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 in Annex IX to REACH.

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5., by providing a study based on OECD TG 422 with an analogue substance and a study based on OECD TG 414 with another analogue substance.

As explained in the Appendix on general considerations your adaptation is rejected. In addition, the following endpoint-specific deficiency has been identified in your read-across adaptation:

To be considered compliant and enable assessing if the Substance is a developmental toxicant, the information you provide has to meet the requirements of OECD TG 414 in one species.

You have provided a study according to OECD TG 422 with an analogue substance. In this study, structural malformations and variations are not investigated as required in the PNDT study (OECD TG 414).

Therefore, the information requirement is not fulfilled.

In your comments to the draft decision you agree to perform an OECD TG 414 study.

[6] ECHA Guidance R.7a, Section R.7.5.4.3.

A PNDT study according to the test method OECD TG 414 should be performed in rat or rabbit as preferred species with oral[7] administration of the Substance.

3. 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 in Annex IX to REACH.

You have provided two key studies in your dossier:

- An OECD TG 211 study (2012) with the Substance;
- An OECD TG 211 study (2010) with an analogue substance.

We have assessed this information and your comments on the draft decision and identified the same deficiencies as for the algae endpoint (request A.1), except the deficiency related to the fulfilment of validity criteria.

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

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

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

You have provided an adaptation based on the alleged lack of indication of the need for further investigation in the CSA.

In order to adapt the information requirement for long-term toxicity to fish based on Annex IX, Section 9.1, Column 2, the Chemical Safety Assessment (CSA) needs to demonstrate that risks towards the aquatic compartment arising from the use of the Substance are controlled (Annex I, section 0.1). The Chemical Safety Assessment (CSA) needs to assess and document that risks arising from the Substance are controlled and demonstrate that there is no need to conduct further testing (Annex I, Section 0.1; Annex IX, Section 9.1, Column 2).

You did not submit in your dossier any specific justification as to why the risks of the substance are controlled. However, to reach the conclusion that the risks are controlled, we understand that you rely on the availability of valid studies on short-term fish and algae and long-term daphnia as well as the PNEC derived from these studies.

In your comments to the draft decision, you have revised your $PNEC_{aquatic}$ to the value of 2.7 µg/L. You have explained that the highest RCR of 0.02 derived by using the bulk approach does not indicate the need to investigate further the effect on aquatic organisms. Therefore you consider long term fish testing is not necessary.

Furthermore, you argue that based on the short-term fish study, you consider fish to be comparable or slightly less sensitive to the source substance (PFAEO O) when compared to algae and daphnia. In addition, you believe that the read-across of the acute fish study is considered to be justified as it is a realistic-worst case approach as 1) the source substance can be considered more toxic than the Substance and 2) in your understanding of the "Bulk approach", a short-term fish study performed with natural river water (i.e. bulk approach)

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

would have yielded a higher LC50 than the currently reported value of 0.1 mg/L (used standard test medium).

As specified in the Appendix on general considerations and request(s) in Appendices A and C, the data on short-term fish, algae and long-term daphnia is not compliant. Hence your dossier currently does not include adequate information to characterize the hazard property of the Substance. The same applies to the first point in your comment.

Regarding the second point in your comment, as already explained above in Appendix on general considerations (i) A. c)-(i), short-term studies may not give a true measure of toxicity for poorly soluble substances such as the Substance. Hence 1) the results of acute toxicity studies cannot be used to demonstrate a species sensitivity and 2) long-term study is needed for such substances like the Substance.

In addition, as explained in the Appendix on general considerations (i) A. c)-(ii), your justification for using the "bulk approach" for the purpose of hazrad assessment, classification and labelling and/or is rejected.

Therefore 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 9.1.5., Column 2.

Appendix D: 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 the REACH Regulation.

The compliance check was initiated on 24 July 2018.

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 took the decision according to Article 51(3) of the REACH Regulation.

Appendix E: 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.

4. 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[8]'.

5. Test material

   Selection of the test material(s)

   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) (constituents and concentration values) 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".

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

In order to meet this requirement, all the constituents of the test material used for each test must be identified as far as possible. For each constituent the concentration value in the test material must be reported in the Test material section of the endpoint study record.

Technical reporting of the test material

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"[9].

6. List of references of the ECHA Guidance documents[10]

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)[11]

Physical-chemical properties
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

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

Environmental toxicology and fate
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

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

PBT assessment

[9] https://echa.europa.eu/manuals
[10] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[11] 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.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.

Appendix F: 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]

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