~~Confidential~~

Helsinki, 08 June 2022

Addressee
Registrant of JS_9427735_FEUC as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
20/12/2018

Registered substance subject to this decision ("the Substance")
Substance name: Amides, C18, branched and linear
List number: 942-773-5

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***15 December 2025***.

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

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

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

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

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

1. In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)

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

3. Simulation testing on ultimate degradation in surface water also requested below (triggered by Annex VIII, Section 9.2.)

4. Soil simulation testing also requested below (triggered by Annex VIII, Section 9.2.)

5. Sediment simulation testing also requested below (triggered by Annex VIII, Section 9.2.)

6. Identification of degradation products also requested below (triggered by Annex VIII, Section 9.2.)

7. Bioaccumulation in aquatic species also requested below (triggered by Annex I, Sections 0.6.1. and 4; Annex XIII, Section 2.1.)

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

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

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

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

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

5. Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.; test method: EU C.25./OECD TG 309) at a temperature of 12°C. Non-extractable residues (NER) must be quantified and a scientific justification of the selected extraction procedures and solvents must be provided.

6. Soil simulation testing (Annex IX, Section 9.2.1.3.; test method: EU C.23./OECD TG 307) at a temperature of 12°C. Non-extractable residues (NER) must be quantified and a scientific justification of the selected extraction procedures and solvents must be provided.

7. Sediment simulation testing (Annex IX, Section 9.2.1.4.; test method: EU C.24./OECD TG 308) at a temperature of 12°C. Non-extractable residues (NER) must be quantified and a scientific justification of the selected extraction procedures and solvents must be provided.

8. Identification of degradation products (Annex IX, 9.2.3.; test method: using an appropriate test method)

9. Bioaccumulation in aquatic species (Annex IX, Section 9.3.2; test method: OECD TG 305)

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

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

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH, the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa.

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

How to comply with your information requirements

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

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

The studies relating to biodegradation and bioaccumulation are necessary for the PBT assessment. However, to determine the testing needed to reach the conclusion on the persistency and bioaccumulation of the Substance you should consider the sequence in which these tests are performed and other conditions described in Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes".

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 Mike Rasenberg, Director of Hazard Assessment

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

Appendix on Reasons common to several requests

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

You seek to adapt the following standard information requirements by applying (a) read-across approach(es) in accordance with Annex XI, Section 1.5:

- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

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 documents[2,3].

A. **Predictions for toxicological properties**

You have provided a read-across justification document "[redacted]" in IUCLID Section 13.2.

You read-across between the structurally similar substances, Erucamide ((Z)-docos-13-enamide), EC No. 204-009-2 (CAS No. 112-84-5) as source substance and the Substance as target substance.

You have provided the following reasoning for the prediction of toxicological properties:

- "*The target substance and the source substance are amides of fatty acids, saturated (target substance) and unsaturated (source substance)"*
- "*They demonstrate physico-chemical characteristics in a comparable range of magnitude*"
- "*Amides of long-chain fatty acids follow the same metabolic pathways after systemic uptake*"
- "*Considering the presence of effective metabolic pathways, the function of the metabolites aseducts for the most effective processes of energy production, storage and signal transduction, and the abundant endogenous availability of the metabolites even in the human body, adverse effects after application of Amides, C18, branched and linear are not to be expected*"

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

[2] Read-Across Assessment Framework (RAAF). 2017 (March) ECHA, Helsinki. 60 pp. Available online: Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across)

[3] Read-across assessment framework (RAAF) - considerations on multi-constituent substances and UVCBs. 2017 (March) ECHA, Helsinki. 40 pp. Available online: https://doi.org/10.2823/794394

properties of your Substance are predicted to be quantitatively equal to those of the source substance.

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

a) *Characterisation of the source substances*

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

According to the Guidance on IRs and CSA, Section R.6, "*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) (Guidance on IRs and CSA R.6, Section R.6.2.3.1). Therefore, qualitative and quantitative information on the compositions of the Substance and of the source substance(s) must be provided to allow assessing 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 (Guidance on IRs and CSA, Section R.6.2.5.5.).

In your read-across justification document, you state that "*The concept of impurities does not apply to the target substance, which is a UVCB substance*. *The source chemical* [i.e. Erucamide] *is a mono-constituent substance with a purity of more than* [redacted]*% and it does not contain any impurities which could have an effect on classification and labelling.*". The Substance is a UVCB and in Section 1.4 of your registration dossier you report compositional information based on gas chromatography. The sum of the branched C18 primary aliphatic amide ([redacted]% w/w) and linear C18 ([redacted]% w/w) primary aliphatic amide is 93.2% (w/w). The remaining fraction corresponds to:

- [redacted]% (w/w) of linear C16 aliphatic amide (i.e. hexadecanamide)
- [redacted]% (w/w) of branched C16 aliphatic amide (i.e. isohexadecanamide)
- [redacted]% (w/w) of unidentified constituents

For the source substance you have provided limited information in your justification document, including a general statement on purity. For some of the source studies, you have provided some description of the test material. However, this information is not provided for all sources studies and lacks either the distribution of C-chain length of the test material or information on impurities (in particular on the presence of fatty nitriles).

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

b) *Read-across hypothesis contradicted by existing data*

Annex XI, Section 1.5. provides that "*substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances*". The Guidance on IRs and CSA, Section R.6.2.2.1.f. 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 source substance.

The observation of differences in the toxicological properties between the source substance and the Substance would contradict the hypothesis that the properties of the Substance can be predicted from the data on the source substances. An explanation why such differences do not affect the read-across hypothesis must be provided and supported by scientific evidence.

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

However, the results in repeated dose toxicity studies obtained with the Substance and the source substance vary. Specifically, a dose-dependent reduction in spleen weight, both absolute and relative to terminal body weight, was observed in males and females in 28-d study via oral route in rats with the Substance. The effect was statistically significant only at the highest dose level (1000 mg/kg bw/d). At this dose level, a decrease in the amount of haematopoiesis in the spleen of females was observed in the histopathological examination. You consider these findings are not adverse but "*represent an adaptive response to treatment*". Although no other immune-system related effects (except reduction of eosinophils in females) were observed in the 28-d study with the Substance, the spleen effects can be an indication of alteration in the immune system and potentially a sign of immunotoxicity. Similar findings were not observed in 90-d study via oral route in rats with the source substance.

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

c) Supporting information

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*" (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.). 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).

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar substances cause the same type of effect(s). 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 the registration dossier, you have provided a sub-chronic (90-d) repeated dose toxicity and prenatal developmental toxicity studies with the source substance. You have not provided

any further endpoint-specific supporting information for the toxicological information requirements listed above. On the contrary, the existing data contradict your read-across hypothesis as explained above under "*Read-across hypothesis contradicted by existing data*".

Furthermore, your read-across rely on common metabolic pathways of long fatty acid amides including the Substance and source substance after systemic uptake. The first step in the metabolism is the hydrolysis of the fatty acid amides by FAAH (fatty acid amide hydrolase) to corresponding fatty acid. In the next step, the free fatty acids are subjected to beta oxidation and energy production. You conclude that "*[c]onsidering the presence of effective metabolic pathways, the function of the metabolites as educts for the most effective processes of energy production, storage and signal transduction, and the abundant endogenous availability of the metabolites even in the human body, adverse effects after application of Amides, C18, branched and linear are not to be expected.*". However, your dossier does not include supporting information to compare overall systemic uptake, and toxicokinetics and toxicodynamics of the target and source substances. Based on the information you have provided, systemic exposure to parent compounds and differences in toxicity cannot be excluded for the target and source substances.

On this basis, the data set reported in the technical dossier does not include relevant, reliable and adequate information for the Substance and of the source substance to support your read-across hypothesis and to confirm similar properties of the Substance and source substance.

B. Conclusions on the read-across approach

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

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

1. Long-term toxicity testing on aquatic invertebrates

Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII to REACH (Section 9.1.1.). Long-term toxicity testing on aquatic invertebrates must be considered (Section 9.1.1., Column 2) if the substance is poorly water soluble.

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

In an EU Method A.6 study (based on the shake flask method), the saturation concentration in water of the Substance was determined to be 19.1 µg/L.

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

The examination of the information provided, as well as the selection of the requested test and the test design are addressed under Appendix C.3.

2. Growth inhibition study aquatic plants

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

You have provided the following information:

i. a growth inhibition study on algae according to OECD TG 201 on the Substance

We have assessed this information and identified the following issues:

To fulfil the information requirement, a study must comply with OECD TG 201 and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

Additional requirements applicable to difficult to test substances

a) if the test material is poorly water soluble, the maximum dissolved concentration that can be achieved in the specific test solution under the test conditions is determined;
b) if the test material is tested at the saturation concentration, evidence must be provided that all reasonable efforts have been taken to achieve a saturation concentration, which include:
    1) an analytical method validation report demonstrating that the analytical method is appropriate, and
    2) a description of the method used to prepare the test solution, and
    3) the results of a preliminary experiment demonstrating that the test solution preparation method is adequate to maximize the concentration of the test material in solution;

Characterisation of exposure

c) a reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (*i.e.* detection and quantification) and working range must be available. Alternatively, a justification why the analytical monitoring of exposure concentrations is not technically feasible must be provided;

Reporting of the methodology and results

d) adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations is provided.

Your registration dossier provides an OECD TG 201 showing the following:

Additional requirements applicable to difficult to test substances

a) the test material is poorly water soluble (water solubility determined to be 19.1 µg/L based EU Method A.6 using the shake flask method). You have provided an estimate of the maximum dissolved concentration (i.e. 5.6 µg/L) that can be achieved in the specific test solution under the test conditions. However, you have provided no description on how this value was obtained;

b) you report that the test was conducted at 0.10, 1.0, 10 and 100% v/v saturated solution which indicates that you intended to test the test material at its saturation concentration. However, you have provided none of the information listed under point b) above to support that saturation was achieved;

Characterisation of exposure

c) you report that the limit of quantification (LOQ) of the analytical method was 10 µg/L while you also report that the saturation concentration of the test material under the conditions of this test was 5.6 µg/L. Therefore, the analytical method used to conduct the monitoring of exposure concentrations had insufficient sensitivity. You have not provided any justification as to why a method with a greater sensitivity could not be developed;

Reporting of the methodology and results

d) you have provided no information on the analytical method (including performance parameters of the method). In addition, the results of the analytical determination of exposure concentration is not reported in an unambiguous way (i.e. table showing measured values in each replicate and each interval of sampling).

Based on the above,

- the Substance is difficult to test (low water solubility and high adsorptive properties) and there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, you have not provided adequate information on the saturation concentration of the test material in the test medium used to conduct testing also taking into account the UVCB nature of the Substance. In addition, you have not provided any information to support that the test procedure was adequate to maximize exposure to the test material.
- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, no information is provided to support that the test procedure was adequate to maximize exposure to the test material. Also no information is provided on the performance parameters of the analytical method and the results of the analytical determinations of exposure concentrations is not

described clearly.

Therefore, this study does not meet the requirements of OECD TG 201 in conjunction with OECD GD 23.

On this basis, the information requirement is not fulfilled.

Study design

The Substance is difficult to test due to its low water solubility (19.1 µg/L based EU Method A.6 using the shake flask method) and high adsorptive properties (log Kow = 6.6 based on QSAR prediction using KOWWIN v1.68). OECD TG 201 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 201. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

For multi-constituents/UVCBs, the analytical method must be adequate to monitor qualitative and quantitative changes in exposure to the dissolved fraction of the test material during the test (e.g. by comparing mass spectral full-scan GC or HPLC chromatogram peak areas or by using targeted measures of key constituents or groups of constituents).

If you decide to use the Water Accommodated Fraction (WAF) approach, in addition to the above, you must:

- use loading rates that are sufficiently low to be in the solubility range of most constituents (or that are consistent with the PEC value). This condition is mandatory to provide relevant information for the hazard and risk assessment (ECHA Guidance, Appendix R.7.8.1-1, Table R.7.8-3);
- provide a full description of the method used to prepare the WAF (including, among others, loading rates, details on the mixing procedure, method to separate any remaining non-dissolved test material including a justification for the separation technique);
- prepare WAFs separately for each dose level (i.e. loading rate) and in a consistent manner.

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

1. In vitro gene mutation study in mammalian cells

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

i. Triggering of the study

Your dossier contains negative results for both an Ames test and an *in vitro* cytogenicity study. In addition, you have provided also an adequate *in vivo* cytogenicity study with a negative result. Therefore, the information requirement is triggered.

ii. Assessment of information provided

Your dossier does not contain any study or adaptation in accordance with column 2 of Annex VIII, Section 8.4.3. or with the general rules of Annex XI for this standard information requirement.

Study design

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

2. Long-term toxicity testing on fish

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

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

In an EU Method A.6 study (based on the shake flask method), the saturation concentration in water of the Substance was determined to be 19.1 µg/L.

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

The examination of the information provided, as well as the selection of the requested test and the test design are addressed under Appendix C.4.

3. Simulation testing on ultimate degradation in surface water

Further degradation testing must be considered if the chemical safety assessment (CSA) according to Annex I indicates the need to investigate further the degradation of the substance (Annex VIII, Section 9.2., Column 2).

This information requirement is triggered in case the chemical safety assessment (CSA) indicates the need for further degradation investigation (Annex I, Section 4; Annex XIII, Section 2.1), such as if the substance is a potential PBT/vPvB substance (ECHA Guidance R.11.4.). This is the case if the Substance itself or any of its constituent or impurity present in concentration ≥ 0.1% (w/w) or relevant transformation/degradation product meets the following criteria:

- it is potentially persistent or very persistent (P/vP) as it is not readily biodegradable (*i.e.* <60% degradation in an OECD 301B);
- it is potentially bioaccumulative or very bioaccumulative (B/vB) as it has a high potential to partition to lipid storage (*e.g.* log K_{ow} > 4.5);
- it meets the T criteria set in Annex XIII: NOEC or EC_{10} < 0.01 mg/L or classification as carc. 1A or 1B, muta. 1A or 1B, repro. 1A, 1B or 2, or STOT RE 1 or 2.

Your registration dossier provides the following:

- The Substance is not readily biodegradable (52% degradation after 28 days in OECD TG 301B);
- The Substance has a high potential to partition to lipid storage (predicted Log K_{ow} ranging from 6.6 based BIOWWIN v1.68).

Furthermore, the information in your dossier is currently incomplete and therefore:

- it is not possible to conclude on bioaccumulation potential of the Substance (see Appendices C.9. of this decision).
- it is not possible to conclude on the toxicity of the Substance (see Appendices C.1-4. of this decision).

Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation.

The examination of the available information or adaptations, as well as the selection of the requested test and the test design are addressed respectively in Appendix C.5.

4. Soil simulation testing

Further degradation testing must be considered if the chemical safety assessment (CSA) according to Annex I indicates the need to investigate further the degradation of the substance (Annex VIII, Section 9.2., Column 2).

As already explained in Appendix B.3., the Substance is a potential PBT/vPvB substance. The Substance has low water solubility (19.1 µg/L based on EU Method A.6. (shake flask)), high partition coefficient (log Kow predicted to be 6.6) and high adsorption coefficient (log K_{oc} predicted to range from 4.59 to 4.67 using the MCI method and 4.58 to 4.63 using the log Kow method), indicating high potential to adsorb to soil.

Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation. Based on the adsorptive properties of the Substance, soil represents a relevant environmental compartment.

The examination of the available information or adaptations, as well as the selection of the requested test and the test design are addressed in Appendix C.6.

5. Sediment simulation testing

Further degradation testing must be considered if the chemical safety assessment (CSA) according to Annex I indicates the need to investigate further the degradation of the substance (Annex VIII, Section 9.2., Column 2).

As already explained in Appendix B.3., the Substance is a potential PBT/vPvB substance. The Substance has low water solubility (19.1 µg/L based on EU Method A.6. (shake flask)), high partition coefficient (log Kow predicted to be 6.6) and high adsorption coefficient (log K_{oc} predicted to range from 4.59 to 4.67 using the MCI method and 4.58 to 4.63 using the log Kow method), indicating high potential to adsorb to sediment.

Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation. Based on the adsorptive properties of the Substance, sediment represents a relevant environmental compartment.

The examination of the available information or adaptations, as well as the selection of the requested test and the test design are addressed respectively in Appendix C.7.

6. Identification of degradation products

Further degradation testing must be considered if the chemical safety assessment (CSA) according to Annex I indicates the need to investigate further the degradation of the substance (Annex VIII, Section 9.2., Column 2).

As already explained under Section B.3., the Substance is a potential PBT/vPvB substance. Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation.

The examination of the available information or adaptations, as well as further information on the selection of the approach to generate this information are addressed in Appendix C.8.

7. Bioaccumulation in aquatic species

Bioaccumulation in aquatic species is required for the purpose of PBT/vPvB assessment (Annex I, Sections 0.6.1 and 4 to REACH).

As already explained under Section B.3., the Substance is a potential PBT/vPvB substance. Therefore, the chemical safety assessment (CSA) indicates the need for further investigation on bioaccumulation in aquatic species.

The examination of the available information or adaptations, as well as further information on the selection of the approach to generate this information are addressed in Appendix C.9.

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

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

A Sub-chronic toxicity study (90 day) is an information requirement under Annex IX to REACH (Section 8.6.2.).

You have adapted this information requirement under Annex XI, Section 1.5. ('Grouping of substances and read-across'). In support of your adaptation, you provided the following information:

i. A key study according to OECD TG 408 via oral route in rats with the analogue substance Erucamide (EC No. 204-009-2, CAS No. 112-84-5)

We have assessed this information and identified the following issue:

As explained in the Appendix on Reasons common to several requests, your read-across adaptation under Annex XI, Section 1.5. is rejected.

On this basis, the information requirement is not fulfilled.

Study design

Referring to the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity, because the Substance is reported to occur as a waxy solid without particles of inhalable size.

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

2. Pre-natal developmental toxicity study in one species

A Pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is an information requirement under Annex IX to REACH (Section 8.7.2.).

You have adapted this information requirement under Annex XI, Section 1.5. ('Grouping of substances and read-across'). In support of your adaptation, you provided the following information:

i. A key study according to OECD TG 414 via oral route in rats with the analogue substance Erucamide (EC No. 204-009-2, CAS No. 112-84-5).

We have assessed this information and identified the following issue:

As explained in the Appendix on Reasons common to several requests, your read-across adaptation under Annex XI, Section 1.5. is rejected.

On this basis, the information requirement is not fulfilled.

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 (ECHA Guidance R.7.6.2.3.2) of the Substance.

3. Long-term toxicity testing on aquatic invertebrates

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

You have provided the following information:

i. a long-term toxicity study on aquatic invertebrates according to OECD TG 211 on the Substance

We have assessed this information and identified the following issues:

To fulfil the information requirement, a study must comply with OECD TG 211 and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

Key parameter to be measured

a) the concentrations of the test material leading to no observed effect (NOECs) on the following parameter, among others, are estimated:
   1) the time to production of the first brood.

Additional requirements applicable to difficult to test substances

b) if the test material is poorly water soluble, the maximum dissolved concentration that can be achieved in the specific test solution under the test conditions is determined;
c) if the test material is tested at the saturation concentration, evidence must be provided that all reasonable efforts have been taken to achieve a saturation concentration, which include:
   4) an analytical method validation report demonstrating that the analytical method is appropriate, and
   5) a description of the method used to prepare the test solution, and
   6) the results of a preliminary experiment demonstrating that the test solution preparation method is adequate to maximize the concentration of the test material in solution;

Reporting of the methodology and results

d) adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations is provided.
e) the full record of the daily production of living offspring during the test by each parent animal is provided;

Your registration dossier provides an OECD TG 211 showing the following:

Key parameter to be measured

a) You have provided no information on the time needed to produce the first brood in either the control or test conditions;

Additional requirements applicable to difficult to test substances

b) the test material is poorly water soluble (water solubility determined to be 19.1 µg/L based EU Method A.6 using the shake flask method). You have provided an estimate of the maximum dissolved concentration (i.e. 5.6 µg/L) that can be achieved in the specific test solution under the test conditions. However, you have provided no description on how this value was obtained;
c) you report that the test was conducted at 0.10, 1.0, 10 and 100% v/v saturated solution which indicates that you intended to test the test material

at its saturation concentration. However, you have provided none of the information listed under point c) above to support that saturation was achieved;

Reporting of the methodology and results

d) you have provided no information on the analytical method (including performance parameters of the method). In addition, the results of the analytical determination of exposure concentration is not reported in an unambiguous way (i.e. table showing measured values in each replicate and each interval of sampling);
e) the full record of the daily production of living offspring during the test by each parent animal is not provided.

Based on the above,

- the study does not provide an adequate coverage of the key parameters of the OECD TG 211 as you have not provided any information on the time to production of the first brood;
- the Substance is difficult to test (low water solubility and high adsorptive properties) and there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, you have not provided adequate information on the saturation concentration of the test material in the test medium used to conduct testing also taking into account the UVCB nature of the Substance. In addition, you have not provided any information to support that the test procedure was adequate to maximize exposure to the test material.
- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, no information is provided to support that the test procedure was adequate to maximize exposure to the test material. Also no information is provided on the performance parameters of the analytical method and the results of the analytical determinations of exposure concentrations is not described clearly. Finally you have not provided adequate reporting of the study results.

Therefore, this study does not meet the requirements of OECD TG 201 in conjunction with OECD GD 23.

On this basis, the information requirement is not fulfilled.

Study design

OECD TG 211 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix A.2.

4. Long-term toxicity testing on fish

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

You have provided the following information:

i. a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2. In support of your adaptation, you provided the following justification: "*According to the Guidance on information requirements and chemical safety assessment Chapter R.7b: Endpoint specific guidance, R.7.8.5.3 (ECHA, 2014), long-term testing of fish should only be conducted if it represents the most sensitive*

taxonomic group. The guidance states that if aquatic invertebrates are likely to be more sensitive than fish and algae or the relative sensitivity of invertebrates cannot be predicted, long-term testing on Daphnia sp. should be preferred instead of fish. The available acute toxicity test indicates no toxic effects to fish and a long-term toxicity study on Daphnia magna is available. The test according to OECD guideline 211 reported a NOEC ≥ 100 mg/L (nominal). Based on the measured test substance concentration a NOEC ≥ 0.0038 mg/L was determined".

We have assessed this information and identified the following issue:

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

Your adaptation is therefore rejected.

On this basis, the information requirement is not fulfilled.

Study design

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

OECD TG 210 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix A.2.

5. Simulation testing on ultimate degradation in surface water

Simulation testing on ultimate degradation in surface water is an information requirement under Annex IX to REACH (Section 9.2.1.2.).

You have provided an adaptation under Annex IX, Section 9.2., Column 2 with the following justification: "*The substance is not readily biodegradable in water and thus is to be considered as potentially persistent in the environment. However, a low persistency under environmental conditions is anticipated. The substance is furthermore not expected to cause any environmental risks due to the lack of acute or chronic toxicity and the low bioaccumulation potential. Therefore further degradation studies are not proposed*".

We have assessed this information and identified the following issue:

Under Section 9.2., Column 2 of Annex IX to REACH, the study may be omitted if the chemical safety assessment (CSA) does not indicate the need for further biotic degradation testing. The CSA does indicate such need (Annex I, Section 4; Annex XIII, Section 2.1) if, for instance, the substance is a potential PBT/vPvB substance (ECHA Guidance R.11.4). This is the case if the Substance itself or any of its constituent, impurity or transformation/degradation product present in concentration ≥ 0.1% (w/w) meets the criteria already listed in Appendix B.3.

As already explained under Appendix B.3., the Substance is a potential PBT/vPvB substance. Therefore, you have not demonstrated that the CSA does not indicate the need for further biotic degradation testing and your adaption is rejected.

On this basis, the information requirement is not fulfilled.

Study design

Simulation degradation studies must include two types of investigations (ECHA Guidance R.7.9.4.1.):

1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and
2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

You must perform the test, by following the pelagic test option with natural surface water containing approximately 15 mg dw/L of suspended solids (acceptable concentration between 10 and 20 mg dw/L) (ECHA Guidance R.11.4.1.1.3.).

The required test temperature is 12°C, which corresponds to the average environmental temperature for the EU (ECHA Guidance R.16, Table R.16-8) and is in line with the applicable test conditions of the OECD TG 309.

As specified in ECHA Guidance R.7.9.4.1., the organic carbon (OC) concentration in surface water simulation tests is typically 2 to 3 orders of magnitude higher than the test substance concentration and the formation of non-extractable residues (NERs) may be significant in surface water tests. Therefore, non-extractable residues (NER) must be quantified. The reporting of results must include a scientific justification of the used extraction procedures and solvents. By default, total NER is regarded as non-degraded substance. However, if reasonably justified and analytically demonstrated a certain part of NER may be differentiated and quantified as irreversibly bound or as degraded to biogenic NER, such fractions could be regarded as removed when calculating the degradation half-life(s) (ECHA Guidance R.11.4.1.1.3.). Further recommendations may be found in the background note on options to address non-extractable residues in regulatory persistence assessment available on the ECHA website.

Relevant transformation/degradation products are at least those detected at ≥ 10% of the applied dose at any sampling time or those that are continuously increasing during the study even if their concentrations do not exceed 10% of the applied dose, as this may indicate persistence (OECD TG 309; ECHA Guidance R.11.4.1.).

6. Soil simulation testing

Sediment simulation testing is an information requirement under Annex IX to REACH (Section 9.2.1.4.) for substances with a high potential for adsorption to sediment.

The Substance has low water solubility (19.1 µg/L based on EU Method A.6. (shake flask)), high partition coefficient (log Kow predicted to be 6.6) and high adsorption coefficient (log K_{oc} predicted to range from 4.59 to 4.67 using the MCI method and 4.58 to 4.63 using the log Kow method), indicating high potential to adsorb to soil. Consequently, a Soil simulation testing must be provided.

You have provided an adaptation under Annex IX, Section 9.2., Column 2 with the following justification with the same justification as already described under Appendix C.5.

For the reasons, already explained under Appendix C.5., your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

Study design

Simulation degradation studies must include two types of investigations (ECHA Guidance R.7.9.4.1.):

1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and
2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

In accordance with the specifications of OECD TG 308, you must perform the test using two sediments. One sediment should have a high organic carbon content (2.5-7.5%) and a fine texture, the other sediment should have a low organic carbon content (0.5-2.5%) and a coarse texture. If the Substance may also reach marine waters, at least one of the water-sediment systems should be of marine origin.

The required test temperature is 12°C, which corresponds to the average environmental temperature for the EU (ECHA Guidance R.16, Table R.16-8) and is in line with the applicable test conditions of the OECD TG 308.

In accordance with the specifications of OECD TG 308, non-extractable residues (NER) must be quantified. The reporting of results must include a scientific justification of the used extraction procedures and solvents (ECHA Guidance R.7.9.4.1.). By default, total NER is regarded as non-degraded substance. However, if reasonably justified and analytically demonstrated a certain part of NER may be differentiated and quantified as irreversibly bound or as degraded to biogenic NER, such fractions could be regarded as removed when calculating the degradation half-life(s) (ECHA Guidance R.11.4.1.1.3.). Further recommendations may be found in the background note on options to address non-extractable residues in regulatory persistence assessment available on the ECHA website.

Relevant transformation/degradation products are at least those detected at ≥ 10% of the applied dose at any sampling time or those that are continuously increasing during the study even if their concentrations do not exceed 10% of the applied dose, as this may indicate persistence (OECD TG 308; ECHA Guidance R.11.4.1.).

7. Sediment simulation testing

Sediment simulation testing is an information requirement under Annex IX to REACH (Section 9.2.1.4.) for substances with a high potential for adsorption to sediment.

The Substance has low water solubility (19.1 µg/L based on EU Method A.6. (shake flask)), high partition coefficient (log Kow predicted to be 6.6) and high adsorption coefficient (log K_{OC} predicted to range from 4.59 to 4.67 using the MCI method and 4.58 to 4.63 using the log Kow method), indicating high potential to adsorb to sediment. Consequently, a Sediment simulation testing must be provided.

You have provided an adaptation under Annex IX, Section 9.2., Column 2 with the following justification with the same justification as already described under Appendix C.5.

For the reasons, already explained under Appendix C.5., your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

Study design

Simulation degradation studies must include two types of investigations (ECHA Guidance R.7.9.4.1.):

1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and
2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

In accordance with the specifications of OECD TG 308, you must perform the test using two sediments. One sediment should have a high organic carbon content (2.5-7.5%) and a fine texture, the other sediment should have a low organic carbon content (0.5-2.5%) and a coarse texture. If the Substance may also reach marine waters, at least one of the water-sediment systems should be of marine origin.

The required test temperature is 12°C, which corresponds to the average environmental temperature for the EU (ECHA Guidance R.16, Table R.16-8) and is in line with the applicable test conditions of the OECD TG 308.

In accordance with the specifications of OECD TG 308, non-extractable residues (NER) must be quantified. The reporting of results must include a scientific justification of the used extraction procedures and solvents (ECHA Guidance R.7.9.4.1.). By default, total NER is regarded as non-degraded substance. However, if reasonably justified and analytically demonstrated a certain part of NER may be differentiated and quantified as irreversibly bound or as degraded to biogenic NER, such fractions could be regarded as removed when calculating the degradation half-life(s) (ECHA Guidance R.11.4.1.1.3.). Further recommendations may be found in the background note on options to address non-extractable residues in regulatory persistence assessment available on the ECHA website.

Relevant transformation/degradation products are at least those detected at ≥ 10% of the applied dose at any sampling time or those that are continuously increasing during the study even if their concentrations do not exceed 10% of the applied dose, as this may indicate persistence (OECD TG 308; ECHA Guidance R.11.4.1.).

8. Identification of degradation products

Identification of degradation products is an information requirement under Annex IX to REACH (Section 9.2.3.).

The information requirement may be omitted if the substance is readily biodegradable. However, the Substance is not readily biodegradable (52% degradation after 28 days in OECD TG 301B) and you have provided no information on identification of degradation products for the Substance.

On this basis, the information requirement is not fulfilled.

Study design

Regarding the selection of appropriate and suitable test method(s), the method(s) will have to be substance-specific. Identity, stability, behaviour, and molar quantity of the degradation/transformation products relative to the Substance must be evaluated and reported, when analytically possible. In addition, degradation half-life, log K_{ow} and potential toxicity of the transformation/degradation may need to be investigated. You may obtain this information from the degradation studies requested in Appendices C.5. and C.6. or by some other measure. If any other method is used for the identification of the

transformation/degradation products, you must provide a scientifically valid justification for the chosen method.

To determine the degradation rate of the Substance, the requested studies according to OECD TG 308 and 307 (Appendices C.5. and C.6.) must be conducted at 12°C and at test material application rates reflecting realistic assumptions. However, to overcome potential analytical limitations with the identification and quantification of major transformation/degradation products, you may consider running a parallel test at higher temperature (but within the frame provided by the test guideline) and at higher application rate (*e.g.* 10 times).

9. Bioaccumulation in aquatic species

Bioaccumulation in aquatic species is an information requirement under Annex IX to REACH (Section 9.3.2.).

You have adapted this information requirement under Annex XI, Section 1.2. In support of your adaptation, you provided the following information:

i. an adaptation under Annex XI, Section 1.3. ('(Q)SAR') with the following supporting information:
   - Predictions based on BCFBAF v3.01 for the C18 iso component of the Substance (Knoell Consult, 2015);
   - Predictions based on BCFBAF v3.01 for the C18 linear component of the Substance (Knoell Consult, 2015).

We have assessed this information and identified the following issue:

Annex XI, Section 1.2 states that there may be sufficient weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

According to ECHA Guidance R.4.4, a weight of evidence adaptation involves an assessment of the relative values/weights of different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance of the information for the given regulatory information requirement. Subsequently, relevance, reliability, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

Annex XI, section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence approach.

However, for each relevant information requirement, you have not submitted any explanation why the sources of information provide sufficient weight of evidence leading to the conclusion/assumption that the Substance has or has not a particular dangerous property.

In spite of this critical deficiency, ECHA has nevertheless assessed the validity of your adaptation and identified the following issues:

To fulfil the information requirement, normally a study performed according to OECD TG 305 must be provided. OECD TG 305 requires the study to investigate the following key parameters:

1) the uptake rate constant (k_1) and loss rate constants including the depuration rate constant (k_2), and/or
2) the steady-state bioconcentration factor (BCF_{SS}), and/or
3) the kinetic bioconcentration factor (BCF_K), and/or
4) The biomagnification factor (BMF).

The source of information i. above (i.e. QSAR predictions using the BCFBAF model) provides relevant information for this information requirement. However, the reliability of this source of information is significantly affected by the following deficiencies:

A. *Selection of the representative structure(s)*

Under ECHA Guidance R.6.1.7.3. a prediction is adequate for the purpose of classification and labelling and/or risk assessment if the following cumulative conditions is/are met:

- the composition of the substance is clearly defined, and
- representative structure(s) for the assessment are selected.

Your registration dossier provides the following information:

- In Section 1.1 of your technical dossier, you define the Substance as an UVCB;
- In Section 1.2, you indicate the following constituent in the composition of the Substance: Isostearamide: [redacted] % (w/w);
- In Section 1.4., you provide an idealised structure for the branched fraction of the Substance. However, you provide a GC chromatogram indicating that both the C16 and C18 fractions are composed of various isomers which likely include varying degree of branching of the alkyl chain;
- For the assessment, you provided predictions for the following structures:
  i. C18 iso component with the following SMILES notation: CC(C)CCCCCCCCCCCCCC(=O)N
  ii. C18 linear component with the following SMILES notation: CCCCCCCCCCCCCCCCCC(=O)N

You have considered the above structures as representative structures. You failed to justify your selection.

However, ECHA disagrees with the representative structure(s) you selected because the Substance likely includes branched C16 and C18 constituents structural isomers with differences in branching. As you have used only 2 structures for the prediction while the Substance is composed of an undefined number of constituents you have not covered all constituents of the Substance. Metabolic transformation is expected to vary for structural isomers with different degree of branching. As a result, you have not demonstrated that the selected structures are likely to provide conservative predictions for all constituents of the Substance.

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

B. *The prediction is not adequate due to low reliability*

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

- the model predicts well substances that are similar to the substance of interest.

All the structures selected for prediction must fulfil the above condition.

Your registration dossier provides the following information:

- predictions from the BCFBAF model (Arnot-Gobas) using a linear and a branched long-chain primary aliphatic amide structures

The following information is also available for the selected model:

- The training or the validation sets of the model do not include similar structures to the substance of interest (i.e. long-chain primary aliphatic amides). The only similar structure found in the training set is Dodecane-12-lactam with EC No. 213-424-8 (CAS No. 947-04-6).

The predictions for the selected structures used as input are not reliable because neither the training nor validation sets of the model include substances that are similar to the structure of the substance of interest. The only structure with some similarity is Dodecane-12-lactam. However, this substance has a cyclic structure and its relevance to non-cyclic primary aliphatic amides is unclear.

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

C. *Lack of or* ina*dequate documentation of the prediction (QPRF)*

ECHA Guidance R.6.1.6.3 states that the information specified in or equivalent to the (Q)SAR Prediction Reporting Format document (QPRF) must be provided to have adequate and reliable documentation of the applied method. For a QPRF this includes, among others the identities of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

You have not provided any assessment of the similarity between the modelled substance and the close analogues, or about how well the model used predicts the substances.

Independent of the issues identified above, in the absence of such information, ECHA cannot establish that the prediction can be used to meet this information requirement.

As a conclusion, the source of information i. above, provide information on Bioaccumulation in aquatic species. However, the reliability of this source of information is severely affected by the issues identified above. Accordingly, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in an OECD TG 305 study. Therefore, your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

Study design

Bioaccumulation in fish: aqueous and dietary exposure (Method EU C.13 / OECD TG 305) is the preferred test to investigate bioaccumulation (ECHA Guidance R.7.10.3.1.). Exposure via the aqueous route (OECD TG 305-I) must be conducted unless it can be demonstrated that:

- a stable and fully dissolved concentration of the test substance in water cannot be maintained within ± 20% of the mean measured value, and/or
- the highest achievable concentration is less than an order of magnitude above the limit of quantification (LoQ) of a sensitive analytical method.

This test set-up is preferred as it allows for a direct comparison with the B and vB criteria of Annex XIII of REACH.

You may only conduct the study using the dietary exposure route (OECD 305-III) if you justify and document that testing through aquatic exposure is not technically possible as indicated above. You must then estimate the corresponding BCF value from the dietary test data according to Annex 8 of the OECD 305 TG and OECD Guidance Document on Aspects of OECD TG 305 on Fish Bioaccumulation (ENV/JM/MONO(2017)16).

Appendix D: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. Test methods, GLP requirements and reporting

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

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

3. Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[4].

B. Test material

1. Selection of the Test material(s)

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

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

With that detailed information, ECHA can confirm whether the Test Material is relevant for the Substance.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[5].

[4] https://echa.europa.eu/practical-guides
[5] https://echa.europa.eu/manuals

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

A. Strategy for the PBT/vPvB assessment

Under Annex XIII, the information must be based on data obtained under conditions relevant for the PBT/vPvB assessment. You must assess the PBT properties of each relevant constituent of the Substance present in concentrations at or above 0.1% (w/w) and of all relevant transformation/degradation products. Alternatively, you would have to justify why you consider these not relevant for the PBT/vPvB assessment.

You are advised to consult ECHA Guidance R.7b (Section R.7.9.), R.7c (Section R.7.10) and R.11 on PBT assessment to determine the sequence of the tests needed to reach the conclusion on PBT/vPvB. The guidance provides advice on 1) integrated testing strategies (ITS) for the P, B and T assessments and 2) the interpretation of results in concluding whether the Substance fulfils the PBT/vPvB criteria of Annex XIII.

In particular, you are advised to first conclude whether the Substance fulfils the Annex XIII criteria for P and vP, and then continue with the assessment for bioaccumulation. When determining the sequence of simulation degradation testing you are advised to consider the intrinsic properties of the Substance, its identified uses and release patterns as these could significantly influence the environmental fate of the Substance. You must revise your PBT assessment when the new information is available.

B. Environmental testing for substances containing multiple constituents

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

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

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

Appendix F: Procedure

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

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

The compliance check was initiated on 22 March 2021.

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

In the comments on the draft decision, you requested an extension of the deadline from 39 to 42 months from the date of adoption of the decision. You considered that the extension of 3 months is needed for the study design and possible development of quantitative analytical test methods for the aquatic based environmental testing as the Substance is difficult to test due to its poor water solubility.

ECHA acknowledges the difficulties in testing due to poor water solubility and in conducting the test, including the development of analytical methods.

On this basis, ECHA has agreed with your request and extended the deadline to 42 months.

In your comments on the draft decision, you do not provide any comments on the information requested. You agree that some additional toxicology testing is needed to satisfy the data requirements for the Substance and agree to generate further data. You also state "[…] *especially regarding higher tier testing, we are concerned about the significant number of animals required for the requested studies and, in consideration of animal welfare, intend to refine the testing strategy by applying a tiered approach.*".

While ECHA acknowledges your intention to apply a tiered testing approach, we remind you that the deadline to submit the requested information is legally binding.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

Appendix G: List of references - ECHA Guidance[6] and other supporting documents

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

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

Read-across assessment framework (RAAF, March 2017)[7]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[8]

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

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

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

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

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

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

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

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

Data sharing
Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

OECD Guidance documents[9]

[6] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[7] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[8] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[9] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

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

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

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

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

Appendix H: Addressees of this decision and their corresponding information requirements

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

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

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.