~~Confidential~~

Helsinki, 08 June 2022

Addressees
Registrant(s) of JS_[redacted] as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
17/05/2013

Registered substance subject to this decision ("the Substance")
Substance name: Docosanamide
EC number: 221-304-1

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 ***17 March 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. Skin sensitisation (Annex VII, Section 8.3.)

   i. *in vitro/in chemico* skin sensitisation information on molecular interactions with skin proteins (OECD TG 442C), inflammatory response in keratinocytes (OECD TG 442D) and activation of dendritic cells (EU B.71/OECD TG 442E)(Annex VII, Section 8.3.1.); and
   ii. Only if the *in vitro/in chemico* test methods specified under point 1.i are not applicable for the Substance or the results obtained are not adequate for classification and risk assessment, *in vivo* skin sensitisation (Annex VII, Section 8.3.2.; test method: EU B.42./OECD TG 429);

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

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

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

5. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: OECD TG 301B/C/D/F or OECD TG 310)

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

1. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.; test method: OECD TG 473) or In vitro micronucleus study (Annex VIII, Section 8.4.2.; test method: OECD TG 487)

2. If negative results are obtained in tests performed for the information requirement of Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. then: In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)

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

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

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

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

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

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

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

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

5. Long-term toxicity testing on terrestrial invertebrates (triggered by Annex IX, Section 9.4.1., column 2, test method: EU C.33/OECD TG 222 or EU C.32/OECD TG 220)

6. Effects on soil micro-organisms (Annex IX, Section 9.4.2.; test method: EU C.21./OECD TG 216)

7. Long-term toxicity to terrestrial plants (triggered by Annex IX, Section 9.4.3., column 2, test method: EU C.35/OECD TG 225 or EU C.40/OECD TG 233 using spiked sediment)

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

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

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH:

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

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

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

How to comply with your information requirements

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

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

Appeal

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

Failure to comply

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

Authorised[1] under the authority of 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:

- Skin sensitisation study (Annex VII, Section 8.3.)
- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Ready biodegradability (Annex VII, Section 9.2.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)
- Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

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 (eco)toxicological and fate properties

You have provided a read-across justification document in IUCLID Section 13 ("[redacted]").

You read-across between the structurally similar substances

- Erucamide ((Z)-docos-13-enamide), EC No. 204-009-2, CAS No. 112-84-5, and
- Amides, C16-18 (even numbered) with no EC No. or CAS. No. provided

as source substances and the Substance as target substance.

You have provided the following reasoning for the prediction of (eco)toxicological and fate properties:

- *"On the basis of all evaluated data, the similarity of the analogue and source substances as listed in Table 1 is justified on the basis of the physico-chemical*

[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, toxicological profiles and supported by various QSAR methods. There is convincing evidence that these chemicals possess an overall common profile, respectively and therefore are suitable for a read across approach. All substances are not classified in accordance with Directive 67/548/EEC and Regulation (EC) No. 1272/2008";

- *"The target substance and the source substances belong to the chemical class of Amides of Saturated and Unsaturated Fatty Acids. More specifically each of the substances is a primary amide of saturated or unsaturated fatty acids, containing only one or no double bonds. Their structures contain a linear carbon chain (i.e. not branched) and the number of carbon atoms generally fall within the range of > C14 and < C24"*;
- *"The target and source substances share the physical similarities in terms of physical state (solid), melting points of > 60°C, high boiling points (> 250°C), similar densities (0.9 – 1.0g/cm3), high Log Kow values (>5) and low water solubility (< 0.1 g/cm3)"*;
- You consider that the target and source substance have similar environmental fate properties (the substances are according to you readily biodegradable, have a high potential to adsorb to soil and sediment and have a low potential for bioaccumulation);
- You consider that the target and source substance show a similar lack of toxicity towards aquatic organisms;
- *"The toxicological properties show that the target substance docosanamide (CAS 3061-75-4) and the source substance (Z)-docos-13-enamide (Erucamide, CAS 112-84-5) have similar toxicokinetic behaviour, including low bioavailability of the parent substance, but anticipated hydrolysis of the amide bond followed by absorption, distribution, metabolism and excretion of the breakdown products ammonia as well as the structurally closely related long-chain fatty acids behenic acid (C22) and erucic acid (C22:1ω9), which only differ in the saturation of the C22 fatty acid. Based on the common metabolic fate, which is irrespective of the degree of fatty acid saturation, the target and source substance show no acute oral, dermal or inhalative toxicity, no potential for skin and eye irritation and no skin sensitisation properties. Furthermore, they are neither mutagenic nor clastogenic, and indicate no potential for systemic toxicity after repeated oral exposure"*;
- *"Therefore, in a worst case approach, the target substance docosanamide (CAS 3061-75-4) is anticipated to be enzymatically hydrolysed to the long-chain saturated C22 fatty acid docosanoic acid (behenic acid) as well as ammonia. Read-across from the source substance (Z)-docos-13-enamide (CAS 112-84-5), which has been demonstrated to be hydrolysed by FAAH, may rather reflect an overestimation of possible health hazards caused by docosanamide (CAS 3061-75-4), especially with respect to the possible adverse effects reported for its hydrolysis product (Z)-docos-13-enoic acid (erucic acid) (Food Standards Australia New Zealand, 2003)".*

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted based on a worst-case approach in case of Erucamide (EC No. 204-009-2) as a source substance and to be quantitatively equal to those of the source substance Amides, C16-18 (even numbered) (EC No. 931-695-7) (Stearamide, EC No. 204-693-2).

ECHA notes the following shortcomings with regards to predictions of (eco)toxicological and fate properties:

a) *Characterisation of the source substance*

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 (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 must be provided to allow assessing whether the attempted predictions are compromised by the composition and/or impurities.

In your read-across justification document, you state that "*The concept of impurities does not apply to the source substance Amides, C16-18 (even numbered), which is a UVCB substance. The target substance and the source substance (Z)-docos-13-enamide (Erucamide, CAS 112-84-5) are mono-constituent substances with a purity of more than 80% and do not include any impurities or other constituents which could have an effect on classification and labelling.*".
Based on GC, the C20 constituent was determined to amount for c.a. [redacted]% (w/w) of the Substance (Test material: Benehamide, Batch No. 303252). The remaining fraction corresponds to:

- C16 and C26 primary aliphatic amides with a saturated carbon chain length (C16 = [redacted]% (w/w), C18 = [redacted]% (w/w), C20 = [redacted]% (w/w), C24 = [redacted]% (w/w), C26 = [redacted]% (w/w));
- some undefined fatty nitriles typically present at [redacted]% (w/w);
- undefined impurities.

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) 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.

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 is necessary to confirm that both substances cause the same type of effects.

i. Predictions of toxicological endpoints

Supporting information must include bridging studies to compare properties of the Substance and source substances.

In the registration dossier, you have provided *in vivo* skin sensitisation study, *in vitro gene mutation study in bacteria, in vitro* gene mutation studies in mammalian cells, and a 28-d repeated dose toxicity study with the main source substance, Erucamide (EC No. 204-009-2). You have not provided any further endpoint-specific supporting information for the toxicological information requirements listed above. In addition, ECHA notes that your dossier does not contain any studies on either the target or source substances for sub-chronic (90 days) repeated-dose toxicity, screening for reproductive/developmental toxicity or pre-natal developmental toxicity.

Furthermore, your read-across rely on common metabolic pathways of long fatty acid amides including the Substance and source substances 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 "*In summary, for the in vivo situation, it cannot be directly ruled out if the parent substance or a fraction of it may be absorbed unchanged by micellar solubilisation and be hydrolysed within the body. Therefore, in a worst case approach, the target substance docosanamide (CAS 3061-75-4) is anticipated to be enzymatically hydrolysed to the long-chain saturated C22 fatty acid docosanoic acid (behenic acid) as well as ammonia. Read-across from the source substance (Z)-docos-13-enamide (CAS 112-84-5), which has been demonstrated to be hydrolysed by FAAH, may rather reflect an overestimation of possible health hazards caused by docosanamide (CAS 3061-75-4), especially with respect to the possible adverse effects reported for its hydrolysis product (Z)-docos-13-enoic acid (erucic acid) (Food Standards Australia New Zealand, 2003)*". 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(s) to support your read-across hypothesis and to confirm a conservative prediction of the properties of the Substance from data on Erucamide (EC No. 204-009-2).

ii. Prediction of aquatic toxicity

Supporting information must include bridging studies to compare properties of the Substance and source substances.

For the predictions of growth inhibition on algae, long term toxicity to aquatic invertebrates and long term toxicity to fish, you provide the studies used in the prediction in the registration dossier. You have not provided any further supporting information.

Your read-across justification or the registration dossier does not include any robust study summaries or descriptions of data for the source substance that would confirm that both substances cause the same type of effects.

iii. Prediction of ready biodegradability

For ready biodegradability support information could be information to confirm similar bioavailability and similar degradation rates under relevant conditions between the Substance and the source substance.

For the source substance, you provide the study used in the prediction in the registration dossier. Apart from that study, your read-across justification or the registration dossier does not include any supporting information that would confirm similar bioavailability of similar degradation rates under relevant conditions.

In the absence of the above information, you have not established that the Substance and the source substance(s) are likely to have similar properties. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

c) *Adequacy and reliability of source studies*

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

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

Specific reasons why the studies on the source substance do not meet these criteria are explained further below under the applicable information requirement sections A.3., B.2., B.3. Therefore, no reliable predictions can be made for these information requirements.

In addition, you have not provided any studies on the source substance(s) for the following endpoints:

- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

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. Skin sensitisation

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

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

i. a key study according to OECD TG 429 with an analogue substance Erucamide, EC No. 204-009-2 (CAS No. 112-84-5)

We have assessed this information and identified the following issues:

A) Assessment whether the Substance causes skin sensitisation

A. Read-across rejection

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

Therefore study (i) cannot be taken into account in the assessment of whether the Substance causes skin sensitisation.

In addition, the following endpoint-specific deficiency has been identified in your read-across adaptation:

B. Non-compliant study on the source substance

As explained in the Appendix on Reasons common to several requests, the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case OECD TG 429. Therefore, the following specifications must be met:

- highest concentration is the highest technically possible concentration that maximises exposure while avoiding systemic toxicity and/or excessive local skin irritation (OECD TG 429, paragraph 18)
- Justification for the choice of vehicle, if another than the recommended vehicle is used (OECD TG 429, paragraph 19)

In the provided study:

- No dose level selection rationale was provided for selecting the highest dose of 25%.
- No justification was provided for the use of tetrahydrofuran as a vehicle, which is not a recommended vehicle.

Therefore the study (i) does not fulfil cover the specifications required by the EU method B.42/OECD TG 429 and cannot be taken into account in the assessment of whether the Substance causes skin sensitisation.

Based on the above, the information submitted does not enable to conclude whether the

Substance causes skin sensitisation.

B) Assessment whether the Substance can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A)

No assessment of potency

To be considered compliant and enable concluding whether the Substance causes skin sensitisation, in case the substance is considered to cause skin sensitisation the information provided must allow a conclusion whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

As the currently available data does not allow to conclude whether the Substance causes skin sensitisation (see section A. above), this condition cannot be assessed.

On this basis, the information requirement is not fulfilled.

Study design

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

2. In vitro gene mutation study in bacteria

An *in vitro* gene mutation study in bacteria is an information requirement under Annex VII to REACH (Section 8.4.1.).

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

i. A study according to OECD TG 471, with an analogue substance Erucamide, EC No. 204-009-2 (CAS No. 112-84-5)

We have assessed this information and identified the following issues:

A. Read-across rejection

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

Therefore study (i) cannot be taken into account in the assessment of whether the Substance causes genetic toxicity.

In addition, the following endpoint-specific deficiency has been identified in your read-across adaptation:

B. Non-compliant study on the source substance

As explained in the Appendix on Reasons common to several requests, the results to be read across must have an adequate and reliable coverage of the key parameters

addressed in the corresponding test method referred to in Article 13(3), in this case OECD TG 407. Therefore, the following specifications must be met:

a) The test must be performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101)

However, the reported data for the study (i) you have provided did not include:

a) the required fifth strain, *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).

The information provided does not cover one of the key parameters required by OECD TG 471.

On this basis, the information requirement is not fulfilled.

Study design

To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471) is considered suitable.

3. 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 column elution method), the saturation concentration of the Substance in water was below the limit of detection of the analytical method (*i.e.* 0.05 mg/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.

4. 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 also provided an adaptation under Annex XI, Section 1.5. ('Grouping of substances and read-across approach'). In support of your adaptation you provided the following information:

i. a growth inhibition study on algae according to OECD TG 201 with the source substance Amides, C16-C18 (even numbered) (No EC No. or CAS No. provided)
ii. a growth inhibition study on algae according to OECD TG 201 with the source substance Erucamide with EC No. 204-009-2 (CAS No. 112-84-5)

We have assessed this information and identified the following issues:

A. *The identity of the test material cannot be verified*

Under Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must be adequate for the purpose of classification and labelling and/or risk assessment.

In order to predict the properties of the Substance, the test material used in the study on the source substance must be representative for the source substance (Article 10 and Recital 19 of REACH; ECHA Guidance R.4.1.). Therefore, the unambiguous characterisation of the composition of the test material used to generate the source data is required to assess whether the test material is representative for the source substance.

For study i. above, you have identified the test material as "Amides, C16-C18 (even numbered)", without further information, including composition.

In the absence of composition information on the test material, the identity of the test material and its impurities cannot be assessed, and you have not demonstrated that the test material is representative for the substance that was intended to be tested. Therefore, the information provided is rejected.

B. *The provided studies are not reliable*

As explained in the Appendix on Reasons common to several requests, the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case OECD TG 201 and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test. 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;

For study i., you report that "*an amount of test item (550 mg) was dispersed in 11 litres of culture medium with the aid of propeller stirring at approximately 1500 rpm for 24 hours.* […] *undissolved test item was removed by centrifugation at 10000 gte give a saturated solution with a 0-Hour measured concentration of 0.17 mg/L*". However, you have provided no information to support that this approach allows reaching saturation. Also, the substance is a UVCB and you have not provided any information on what constituent(s) was(were) measured

For study ii., you have not provided an estimate of the maximum dissolved concentration that can be achieved in the specific test solution under the conditions of this test

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) information on the saturation concentrations of the test material in water and in the test solution, and
3) a description of the method used to prepare the test solution, and
4) 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;

The test material used in study i. and ii. have low water solubility (< 0.102 mg/L and < 0.1 mg/L, respectively, as reported in your read-across justification document) and you provide information indicating that you intended to test these test materials at their respective saturation concentration. However, for these studies have provided none of the information listed above to support that saturation was achieved.

Characterisation of exposure

c) the test media prepared specifically for analysis of exposure concentrations during the test is treated identically to those used for testing (*i.e.* inoculated with algae and incubated under identical conditions);

For study ii., you report that "*duplicate samples were taken from the test media of all test concentrations at the start of the test (without algae) and at the end of the test (containing algae)*". Therefore, the measurements at the start of the test were not conducted under identical conditions to those used for testing as the test solutions were not inoculated with algae.

d) the concentrations of the test material are measured at least at the beginning and end of the test:
1) at the highest, and
2) at the lowest test concentration, and
3) at a concentration around the expected EC_{50}.

For volatile, unstable or strongly adsorbing test substances, additional samplings for analysis at 24 hour intervals is required;

The test material used in study i. and ii. have low water solubility (log Kow >6.5 and 8, respectively, as reported in your read-across justification document) and have not conducted determination of exposure concentrations at 24h intervals;

Reporting of the methodology and results

e) the test conditions are reported (*e.g.*, composition of the test medium, biomass density at the beginning of the test);

For study ii., you have not reported the test conditions adequately. In particular, no information is available on the composition of the test medium and on biomass density at the beginning of the test.

f) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form;

For studies i. and ii., the results of algal biomass determined in each flask at least daily during the test period is not provided.

g) 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;

For studies i. and ii., 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 test materials used in studies i. and ii. are difficult to test (low water solubility and high adsorptive properties) and there are critical methodological deficiencies resulting in the rejection of the results of these studies. More specifically, you have not provided adequate information on the saturation concentration of the test materials in the test medium used to conduct testing (also taking into account the UVCB nature of the source substance Amides, C16-C18 (even numbered)). In addition, you have not provided any information to support that the test procedure was adequate to maximize exposure to the test materials used in these studies. Finally, the analytical determination of exposure concentrations was not adequate as the frequency of analytical determinations was too low;
- independent of the above issue, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, you have not provided adequate information on the test procedure for study ii. Also, no information is provided on the performance parameters of the analytical method and the reporting of measured test material concentrations is unclear for studies i. and ii. Finally, as you have not provided the results of algal biomass determined in each flask at least daily during the test period, it is not possible to make an independent assessment of whether or not the studies i. and ii. met the validity criteria specified in the OECD TG 201.

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 < 0.05 mg/L based on EU Method A.6) and high adsorptive properties (log Kow > 5.7 based on the HPLC method described in EU Method A.8). 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.

5. Ready biodegradability

Ready biodegradability is an information requirement in Annex VII to REACH (Section 9.2.1.1.).

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

i. a ready biodegradability study according to OECD TG 301B with the source substance Amides, C16-C18 (even numbered) (No EC No. or CAS No. provided) (2001)
ii. a ready biodegradability study according to OECD TG 301B with the source substance Erucamide, EC No. 204-009-2 (CAS No. 112-84-5) (2001);
iii. a ready biodegradability study according to OECD TG 301B with the source substance Erucamide, EC No. 204-009-2 (CAS No. 112-84-5) (1991).

You also provided an adaptation under Annex XI, Section 1.3. ('(Q)SAR'). In support of your adaptation you provided the following information:

iv. Predictions from BIOWIN v4.10 for the C18 constituent of the Substance.

We have assessed this information and identified the following issues:

A. Read-across rejection

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

Therefore, studies i. and ii. cannot be taken into account in the assessment of whether the Substance is readily biodegradable.

In addition, the following endpoint-specific deficiency has been identified in your read-across adaptation:

B. The study i. and iii. above are not reliable

As explained in the Appendix on Reasons common to several requests, the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case

OECD TG 301 or 310 (Article 13(3) of REACH). Therefore, for a study according to OECD TG 301B, the following specifications must be met:

Validity criteria

a) The degradation of the reference compound has reached the pass level by day 14;
b) The difference of extremes of replicate values of the removal of the test material at the plateau, at the end of the test or, if appropriate, at the end of the 10-d window is ≤ 20%;
c) The inorganic carbon content (IC) of the test material suspension in the mineral medium at the beginning of the test is < 5% of the total carbon (TC);
d) The total CO_2 evolution in the inoculum blank at the end of the test does not normally exceed 40 mg CO_2/L;

Technical specifications impacting the sensitivity/reliability of the test

e) The concentration of the inoculum is set to reach a bacterial cell density of 10^7 to 10^8 cells/L in the test vessel. The suspended solid concentration is ≤ 30 mg/L.

Reporting of the methodology and results

f) The source of the inoculum, its concentration in the test and any pre-conditioning treatment are reported;
g) The calculation of the $ThCO_2$ is described and justified;
h) The inorganic carbon content (IC) and total carbon content (TC) of the test material suspension in the mineral medium at the beginning of the test is reported;
i) The results of measurements at each sampling point in each replicate is reported in a tabular form.

Your registration dossier provides an OECD TG 301B on Amides, C16-C18 (even numbered) (study i.) showing the following:

Reporting of the methodology and results

f) You report that the suspended solid concentration was 30 mg/L. However, you have not provided information on inoculum density in cells/mL;
g) the calculation of the $ThCO_2$ is not described;
h) the inorganic carbon content (IC) and total carbon content (TC) of the test material suspension in the mineral medium at the beginning of the test is not reported;
i) the results of measurements at each sampling point in each replicate is not reported.

Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, as you have not provided adequate information on inoculum density (see point e) above) it is not possible to verify whether the test was conducted in compliance with the technical specifications of OECD TG 301B (see point d) above). Then, you have not provided an adequate reporting of the study results (in particular see point g) and h)) and it is not possible to verify that the validity criteria specified under points a) to c) above were met. Finally, since you have not described how the $ThCO_2$ was determined and you have not provided the raw data obtained in the test, it is not possible to verify the validity of the interpretation of the results.

Your registration dossier provides an OECD TG 301B on Erucamide (study iii.) showing the following:

Validity criteria

a) The degradation of the reference substance (i.e. sodium acetate) did not reach 60% within 14 days.

Based on the above, the study does not meet the validity criteria of OECD TG 301B as degradation of the reference substance was too slow.

Therefore, study i. and iii. do not have adequate and reliable coverage of the key parameters of OECD TG 301B.

On this basis, the information requirement is not fulfilled.

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

1. In vitro cytogenicity study in mammalian cells or In vitro micronucleus study

An *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study is an information requirement under Annex VIII to REACH (Section 8.4.2.).

You have adapted this information requirement under Annex XI, Section 1.5. ('Grouping of substance and read-across'). In support of your adaptation, you have provided a key study in your dossier:

i. *in vitro* mammalian chromosome aberration test according to OECD TG 473 with an 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

To fulfil the information requirement for the Substance, either *in vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) or *in vitro* micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) are considered suitable.

2. In vitro gene mutation study in mammalian cells

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

i. Triggering of the study

Your dossier contains an adaptation for an *in vitro* gene mutation study in bacteria, and an adaptation for an *in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study.

The information for the *in vitro* gene mutation study in bacteria and for the *in vitro* cytogenicity study in mammalian cells provided in the dossier are rejected for the reasons provided in Section A.2 and in Section B.1.

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

ii. Assessment of information provided

You have adapted this information requirement under Annex XI, Section 1.5. ('Grouping of substance and read-across'). In support of you adaptation, you have provided a key study in your dossier:

i. A key study according to OECD TG 476 with an analogue substance Erucamide (EC No. 204-009-2, CAS No. 112-84-5)

We have assessed this information and identified the following issues:

A. *Read-across rejection*

For the reasons explained in the Appendix on Reasons common to several requests your read-across adaptation is rejected.

In addition, the following endpoint-specific deficiency has been identified in your read-across adaptation:

B. *Non-compliant study on the source substance*

As explained in the Appendix of Reasons common to several requests, the results to be read across must provide adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case OECD TG 476. Therefore, the following specifications must be met:

a) The maximum concentration tested must induce 80-90% of cytotoxicity compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test concentration must correspond to 10 mM, 2 mg/mL or 2 µL/mL, whichever is the lowest.
b) At least 4 concentrations must be evaluated, in each test condition. In case of poorly soluble substances OECD TG 476 states "*the highest concentration analysed should produce turbidity or a precipitate*".
c) The response for the concurrent negative control must be inside the historical control range of the laboratory.
d) Data on the cytotoxicity and the mutation frequency for the treated and control cultures must be reported.

In the provided study:

a) The concentrations tested in the definitive test were 4.7, 9.4, 18.8, 37.5, 75 and 150 µg/ml. You specified that "precipitation was observed at concentrations of 18.8 µg/ml and above".
b) In the definitive test, only two concentrations did not cause precipitation.
c) You have not provided any information on historical control and whether the concurrent controls were inside the historical control range of the laboratory.
d) You reported the mutation frequencies as a range. Especially, the information on mutation frequency per treated cultures is missing.

The information provided does not cover the specifications required by the OECD TG 476.

On this basis, the provided study is not regarded as providing reliable information to inform on the properties of the Substance. Therefore, the information requirement is not fulfilled.

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

Study design

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

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

A Short-term repeated dose toxicity study (28 days) is an information requirement under Annex VIII to REACH (Section 8.6.1.). This information may take the form of a study record or a valid adaptation in accordance with either a specific adaptation rule under Column 2 of Annex VIII or a general adaptation rule under Annex XI.

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

i. A non-guideline 28-day repeated dose toxicity study via oral route in male rats with an analogue substance Erucamide, EC No. 204-009-2 (CAS No. 112-84-5)

We have assessed this information and identified the following issues:

A. Read-across rejection

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

In addition, the following endpoint-specific deficiency has been identified in your read-across adaptation:

B. Non-compliant study on the source substance

As explained in the Appendix on Reasons common to several requests, the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case OECD TG 407. Therefore, the following specifications must be met:

a) Testing of at least three dose levels and a concurrent control
b) 5 female and 5 male animals should be used at each dose level (including control group)
c) Examination of the animals for weight and histopathology (including weight and histopathology of the thyroid gland, thyroid hormone measurements, organ weight measurements, body weight measurements, examination of the clinical signs, examination of the animals for gross pathology of organs and tissues)

You have provided a study showing the following:

a) The study you have provided was conducted with only one dose level.
b) The study you have provided was conducted with only 5 male animals per test dose group.
c) The following key parameters are missing: weight and histopathology of the thyroid gland has not been measured, thyroid hormone measurements have not been conducted, the organs weights have not been measured, the body weight has not been reported, the clinical signs have not been reported, gross pathology of organs and tissues has not been reported.

Therefore, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the key parameters of the corresponding OECD TG.

On this basis, the information requirement is not fulfilled.

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

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

Because you still must comply with the information requirement in Annex VIII, Section 8.6.1., you are requested to submit a justification for the adaptation provided in Column 2 of that provision.

4. Screening for reproductive/developmental toxicity

A Screening for reproductive/developmental toxicity study (test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) is an information requirement under Annex VIII to REACH (Section 8.7.1.), 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 under Column 2 (Annex VIII, Section 8.7.) and under Annex XI, Section 1.5. ('Grouping of substance and read-across'). In support of your adaptation, you have provided the following statement: "*According to Regulation (EC) No 1907/2006, Annex VIII, column 2, testing for effects on fertility by a screening test is not required as a test for prenatal developmental toxicity (Annex IX, 8.7.2) is proposed for a structurally related substance (Z)-Docos-13-enamide (CAS 112-84-5), which will be used for read-across in accordance with the criteria set out in Annex XI, article 1.5.*"

We have assessed this information and identified the following issues:

A. Read-across rejection

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

In addition, the following endpoint-specific deficiency has been identified in your read-across adaptation:

B. Rejection of Column 2 adaptation

According to Annex VIII, Section 8.7., Column 2, first paragraph, fourth indent, the study does not need to be conducted if a pre-natal developmental toxicity study (OECD TG 414) is already available.

You justified the adaptation by stating that a prenatal developmental toxicity study "*is proposed for a structurally related substance (Z)-Docos-13-enamide (CAS 112-84-5), which will be used for read-across*" and, therefore an EU B.63/OECD TG 421 or EU B.64/OECD TG 422 study does not need to be conducted. However, no prenatal developmental toxicity study is provided in your dossier.

Therefore, your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

Study design

A study according to the test method EU B.63/OECD TG 421 or EU B.64/OECD TG 422 must be performed in rats with oral administration of the Substance (ECHA Guidance R.7.6.2.3.2).

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 column elution method), the saturation concentration of the Substance in water was below the limit of detection of the analytical method (*i.e.* 0.05 mg/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.

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 substance and read-across'). In support of your adaptation, you have provided the following information:

i. A statement "*A repeated dose toxicity study via the oral route according to OECD Guideline 408 for the structurally related substance erucamide (CAS 112-84-5) is proposed and the generated data will comply with the criteria for read-across according to Annex XI, article 1.5.*"
ii. A non-guideline 28-day repeated dose toxicity study via oral route in male rats with an analogue substance Erucamide (EC No. 204-009-2, CAS No. 112-84-5)

You have also provided an adaptation which ECHA understands is based on Annex IX, Section 8.6.2., Column 2.

We have assessed this information and identified the following issues:

A. Read-across rejection

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

In addition, the following endpoint-specific deficiency has been identified in your read-across adaptation:

B. Non-compliant analogue study

You have not provided a Sub-chronic toxicity study (90 day) (OECD TG 408) in your registration dossier nor a testing proposal in accordance with Articles 10(a)(ix) and the format set under 111 of REACH, but only an intention to submit a future study on an analogue substance.

C. Failed Column 2 adaptation

As provided in Annex IX, Section 8.6.2, Column 2, you may adapt the information requirement, provided you fulfil one of the following criterion, including:

(1) The Substance is unreactive, insoluble and not inhalable and there is no evidence of absorption/ of toxicity in a 28-day 'limit test', particularly if it is coupled with limited human exposure .

You stated that *"In addition, data are available for the oral subacute (28-day) toxicity of the erucamide (CAS 112-84-5) in male rats, showing no mortalities and no adverse effects up to a dietary dose of ca. 10000 mg/kg bw/day, which is well above the currently applied limit dose of 1000 mg/kg bw/day. Thus, it may be assumed that erucamide (CAS 112-84-5) is rather unlikely to exert adverse effects after subchronic toxicity testing."*.
You have provided no justification to address the reactivity, solubility, inhalability, absorption and human exposure to the Substance.

As explained in Section B.3 above, the 28-day study provided is rejected. Further, you have not demonstrated that Substance is unreactive, insoluble, not inhalable, that there is no evidence of absorption, and that there is limited human exposure. Therefore, your adaptation 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 vapor pressure of the Substance is less than 0.092 Pa at 20°C and the proportion of inhalable solid is not significant (0.14% under 500 µm).

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 provided the following adaptation according to Annex XI, section 1.5. "*A pre-natal developmental toxicity study via the oral route according to OECD Guideline 414 for the structurally related substance (Z)-Docos-13-enamide (CAS 112-84-5) is proposed and the generated data will comply with the criteria for read-across according to Annex XI, article 1.5. The results of the study will be used to determine the following steps in the testing regime.*".

We have assessed this information and identified the following issues:

A. Read-across rejection

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

In addition, the following endpoint-specific deficiency has been identified in your read-across adaptation:

B. Non-compliant study

You have not provided a Pre-natal developmental toxicity (PNDT) study (OECD TG 414) in your registration dossier nor a testing proposal in accordance with Articles 10(a)(ix) and the format set under 111 of REACH but only an intention to submit a future study on an analogue substance.

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

i. a long-term toxicity study on aquatic invertebrates according to OECD TG 202 (1984) with the source 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.

Therefore study i. cannot be taken into account in the assessment of long-term toxicity on aquatic invertebrates.

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.5.

4. Long-term toxicity testing on fish

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

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

i. a fish, juvenile growth test according to OECD TG 215 with the source Erucamide, EC No. 204-009-2 (CAS No. 112-84-5).

We have assessed this information and identified the following issues:

A. Read-across rejection

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

Therefore study i. cannot be taken into account in the assessment of long-term toxicity on fish.

B. The study on the source substance is not reliable

As explained in the Appendix on Reasons common to several request, under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

The Fish Early Life Stage (FELS) toxicity test (test method: OECD TG 210) is the most suitable test guideline for addressing long-term toxicity on fish for most substances

(ECHA Guidance R.7.8.2.). As specified in ECHA Guidance R.7.8.2., the Fish, Juvenile Growth Test (test method: OECD TG 215) is only considered as an acceptable test method if the following cumulative conditions are met:

a) a well-founded justification is provided to support that growth inhibition is the most relevant effect in fish, and
b) the substance has a log Kow < 5.

Otherwise, OECD TG 215 could underestimate long-term toxicity in fish and not achieve the REACH objective of protection of the environment nor would the study be appropriate for classification and labelling and risk assessment.

You have provided no justification as to why growth inhibition is the most relevant effect in fish for the selected source substance. Further, in your read-across justification document, you report that the log Kow of the source substance is 8.

Therefore, the OECD TG 215 is not regarded as an acceptable test method for the source substance and a Fish Early Life Stage (FELS) toxicity test (test method: OECD TG 210) would need to be provided instead.

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.5.

5. Long-term toxicity on terrestrial invertebrates

Short-term toxicity to invertebrates is an information requirement under Annex IX to REACH (Section 9.4.1). Long-term toxicity testing must be considered (Section 9.4., column 2) if the substance has a high potential to adsorb to soil or is very persistent.

Based on the information from your registration dossier:

- the Substance is considered to have high adsorption potential to soil as you report a log Kow of > 5.7 (EU Method A.8) and a log Koc of 5.7 (Based on QSAR predictions).

On this basis information on long-term toxicity on terrestrial invertebrates must be provided.

We understand that you have adapted this information Under Annex IX, Section 9.4., Column 2 with the following justification: "*Terrestrial data of docosanamide (CAS No. 3061-75-4) are not available but due to the properties of docosanamide (CAS No. 3061-75-4) a hazard to soil organisms is assumed to be low. In accordance with column 2 of EC 1970/2006 Annex IX the effects of terrestrial organisms need not to be tested if a direct and indirect exposure to the soil compartment is unlikely. As the analogue members are readily biodegradable an indirect exposure of soil organisms through sludge application can be ruled out. Regarding the very low water solubility (< 0.05 mg/L) it is not likely that the test substances can be found in the aquatic environment in high concentrations and therefore an application due to floods and irrigation can be ruled out. Data from acute and chronic studies afford that there is no toxicity in the range of water solubility for aquatic organisms. Moreover, chronic and acute studies for mammals result in no toxic effects as well. The test substance is not classified and considering that the test substance is readily biodegradable, has very low water solubility (< 0.05 mg/L),*

is not toxic to aquatic species and mammalians and an indirect application to soil via sludge can be ruled out, no soil toxicity data should be generated".

We have assessed this information and identified the following issue:

> Under Annex IX, Section 9.4, Column 2, the study may be omitted if direct and indirect exposure of the soil compartment is unlikely. ECHA Guidance R.11.2.1. specifies that, in general, it is assumed that soil exposure will occur unless:
> 1) it can be shown that there is no sludge application to land from exposed STPs and,
> 2) aerial deposition is negligible and,
> 3) the relevance of other exposure pathways such as irrigation and/or contact with contaminated waste is unlikely.
>
> In the case of readily biodegradable substances which are not directly applied to soil it is generally assumed that the substance will not enter the terrestrial environment and as such there is no need for testing of soil organisms is required.
>
> In Section 3 of your dossier, you report, for instance, widespread outdoor consumer uses in adhesives and sealants (ERC 8d), widespread outdoor professional uses in Washing and cleaning products and as processing aid (ERC 8d), and widespread outdoor consumer use with high intended release in tyres (ERC 10b). These uses indicate that direct exposure to soil may occur. Also, you have not provided any justification as to why no sludge application to land from exposed STPs would occur and therefore indirect exposure to soil may occur. You also report a high number of consumer and professional uses that may be leading to indirect release to soil.
>
> The reported uses in your dossier indicates that direct exposure to soil may occur. You also have not provided any justification for point 1) and 2) above. In addition for the reasons explained under Appendix A.5., you have not demonstrated that the Substance is readily biodegradable. Therefore, you have not demonstrated that indirect exposure to soil is unlikely. Therefore, your adaptation is rejected. In any case the information provided on most of the elements of your justification are rejected for the reasons already described in the corresponding Appendix sections.

On this basis, the information requirement is not fulfilled.

Study design

ECHA Guidance R.7.11.3.1. specifies that the earthworm reproduction test (OECD TG 222), the Enchytraeid reproduction test (OECD TG 220), and the Collembolan reproduction test (OECD TG 232) are appropriate to cover the information requirement for long-term toxicity testing on terrestrial invertebrates. ECHA is not in a position to determine the most appropriate test protocol since this decision is dependent upon species sensitivity and substance properties. However, when log Kow >5 and log Koc >4, as in this case, the test OECD 232 is not appropriate as the dominant route of exposure for Collembolans is via pore water.

6. Effects on soil micro-organisms

Effects on soil microorganisms is an information requirement under Annex IX to REACH (Section 9.4.2).

You have adapted this information Under Annex IX, Section 9.4., Column 2 with the same justification as already described under Appendix C.5.

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

On this basis, the information requirement is not fulfilled.

Study design

ECHA Guidance R.7.11.3.1. specifies that Soil Microorganisms: Nitrogen Transformation Test (EU C.21/OECD TG 216) is considered suitable for assessing long-term adverse effects on soil microorganisms for most non-agrochemicals.

7. Long-term toxicity on terrestrial plants

Short-term toxicity to terrestrial plants is an information requirement under Annex IX to REACH (Section 9.4.3). Long-term toxicity testing must be considered (Section 9.4., column 2) if the substance has a high potential to adsorb to soil or is very persistent.

Based on the information from your registration dossier:

- the Substance is considered to have high adsorption potential to soil as you report a log Kow of > 5.7 (EU Method A.8) and a log Koc of 5.7 (Based on QSAR predictions).

On this basis information on long-term toxicity on terrestrial plants must be provided.

You have adapted this information Under Annex IX, Section 9.4., Column 2 with the same justification as already described under Appendix C.5.

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

On this basis, the information requirement is not fulfilled.

Study design

The Terrestrial Plant Test (test method: OECD TG 208) is appropriate to cover the information requirement for long-term toxicity on terrestrial plants.

The OECD TG 208 considers the need to select the number of test species according to relevant regulatory requirements, and the need for a reasonably broad selection of species to account for interspecies sensitivity distribution. For long-term toxicity testing, ECHA considers six species as the minimum to achieve a reasonably broad selection. Testing must be conducted with species from different families, as a minimum with two monocotyledonous species and four dicotyledonous species, selected according to the criteria indicated in the OECD TG 208.

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

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

1. Selection of the Test material(s)

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

2. Information on the Test Material needed in the updated dossier
   - You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
   - The reported composition must include all constituents of each Test Material and their concentration values and other parameters relevant for the property to be tested.

This information is needed to assess whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

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

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

Appendix E. 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.

ECHA took into account your comments and did not amend the requests.

In your comments on the draft decision, you requested an extension of the deadline to provide information from 24 to 38 months from the date of adoption of the decision.

You justified the request by additional time required to for the study design and development of analytical methods due to poor water solubility of the Substance. In addition, you provide a letter to justify the request of an extension of the deadline due to limited testing capacities of laboratories

You have only provided a statement from a single laboratory to justify the limited capacity and reporting time was already included in the original deadline. However, ECHA acknowledges the difficulties in conducting the test with your Substance.

Finally, you indicate the timelines for the contracting phase (2 months), the pre-study chemistry (6 months), the 90-day repeated dose toxicity study (12 months) and the pre-natal developmental toxicity study (12 months).

You do not justify the need for sequentiliaty of the 90-day repeated dose toxicity study and the pre-natal developmental toxicity study. The timeline set in this decision allows for generating the required data on the Substance.

On this basis, ECHA has partially agreed with the request and extended the deadline to 30 months.

In your comments on the draft decision, you do not provide any endpoint-specific comments. 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 stated "*Nevertheless, 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 refine the testing strategy, we note that the deadline in the adopted decision 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 F. 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 G. 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]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

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