~~Confidential~~

Helsinki, 21 October 2020

Addressees
Registrants of JS_943-728-2 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
05/09/2017

Registered substance subject to this decision ("the Substance")
Substance name: Reaction mass of 3,5-dimethylcyclohex-3-ene-1-carbaldehyde and 2,4-dimethylcyclohex-3-ene-1-carbaldehyde
List number: 943-728-2
CAS number: NS

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 ***26 October 2022***.

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

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

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

4. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: OECD TG 301C/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. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: OECD TG 203)

6. Activated sludge respiration inhibition testing (Annex VIII, Section 9.1.4.; test method: EU C.11/ OECD TG 209)

7. The same simulation testing on ultimate degradation in surface water (triggered by Annex VIII, Section 9.2.) requested under Section C.5

8. The same identification of degradation products (triggered by Annex VIII, Section 9.2.) requested under C.6

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

6. Identification of degradation products (Annex IX, 9.2.3.; test method: using the simulation test method requested under Section C.5)

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 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 Christel Schilliger-Musset, Director of Hazard Assessment

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

Appendix on Reasons common to several requests

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

You have adapted the following standard information requirements by applying a read-across approach in accordance with Annex XI, Section 1.5:

- 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 vivo mammalian erythrocyte micronucleus test (Annex IX, Section 8.4., column 2)
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)
- Ready biodegradability (Annex VII, Section 9.2.1.1.)

ECHA has considered the scientific and regulatory validity of your read-across approach in general before assessing the specific standard information requirements in the following appendices.

Grouping of substances and read-across approach

Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. 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[2] and related documents[3, 4].

A. Predictions for toxicological properties

You have provided a read-across justification in the corresponding endpoint summary records in IUCLID and in your CSR.

You read-across between the structurally similar substances:

- Reaction mass of 3-(4-hydroxy-4-methylpentyl)cyclohex-3-ene-1-carbaldehyde and 4-(4-hydroxy-4-methylpentyl)cyclohex-3-ene-1-carbaldehyde or **HMPCC**, EC No. 915-617-9;
- 4-isopropenylcyclohex-1-en-1-ylmethanol or **L-perillyl alcohol**, EC No. 208-639-9;
- 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-264-1

[2] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals. 2008 (May) ECHA, Helsinki. 134. pp. Available online: https://echa.europa.eu/documents/10162/13632/information_requirements_r6_en.pdf/77f49f81-b76d-40ab-8513-4f3a533b6ac9

[3] 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)

[4] 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

as source substances and the Substance as target substance.

You have not provided any reasoning for the prediction of toxicological properties using information from 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-264-1.

For HMPCC and L-perillyl alcohol, you have provided a justification where 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-264-1 is identified as the target substance. You have provided the following reasoning for the predictions of toxicological properties:

a) The Substance and the selected analogues have similar physicochemical properties. You state that "*structural differences in the side chains do not significantly influence the physicochemical properties of both substances, i.e. vapour pressure, partition coefficient and water solubility*";
b) The Substance and the selected analogues have similar toxicokinetic behaviour based on their similar physicochemical properties:
   - the molecular weights, water solubility, neutral form at relevant pH and moderate log Kow values indicate absorption via the oral and dermal routes and wide distribution in the body;
   - the physical forms (liquid) and low vapour pressures indicate low volatility, so respiratory exposure is expected to be low;
   - the Substance and the selected analogues are expected to be metabolized via oxidation of the aldehyde to a carboxylic acid group and conjugated in Phase II reactions to facilitate excretion, mainly in the urine (based on predictions from SMARTCyp, Toxtree v2.5.0);
   - structural differences between Substance and the selected analogues are not expected to have an impact on metabolism routes;
   - the non-common metabolites have low toxicity after oral exposure and occur naturally in a wide variety of foods.
c) The Substance and the selected analogues have similar toxicological properties:
   - they have similar acute oral and dermal toxicity, they induce moderate skin irritation and positive skin sensitization (except for L-perillyl alcohol) and have negative Ames test results
   - the Substance and L-perillyl alcohol are identified as Cramer Class I in the Toxtree v2.5.0 profiler, which you consider supportive of the read-across oral repeated dose toxicity. On the other hand, you also state that in the OECD QSAR Toolbox v3.1, the Substance is identified as Cramer Class II and HMPCC as Cramer Class III.

Your read-across justification is referring to the analogue substance 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-264-1 as target substance. However, considering that this analogue corresponds to the main constituent of the Substance, we assume that you consider the justification to apply also to the Substance.

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

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

A. Read-across hypothesis

According to Annex XI, Section 1.5., two conditions shall be necessarily fulfilled. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it

is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group (read-across approach).
A read-across hypothesis needs to be provided, establishing why a prediction for a toxicological or ecotoxicological property is reliable. This hypothesis should be based on recognition of the structural similarities and differences between the source substance(s) and your Substance[5]. It should explain why the differences in the chemical structures should not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern.

Your read-across hypothesis is that the similarity in chemical structure and in some of the physicochemical and toxicological properties between the source substances and your Substance is a sufficient basis for predicting the properties of your Substance for other endpoints.

Similarity in chemical structure and similarity of some of the physicochemical and toxicological properties does not necessarily lead to predictable or similar human health properties in other endpoints. As described above, a well-founded hypothesis is needed to establish a reliable prediction for a toxicological property, based on recognition of the structural similarities and differences between the source substance(s) and your 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*"[6]. The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

Supporting information must include bridging studies to compare properties of the Substance and source substances and, if relevant, information on the properties of the non-common compound(s).

The data set in your dossier does not include any information on the toxicological properties of the Substance. In addition, for the read-across with 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-264-1, you have not provided any information on the non-common compound (i.e. 3,5-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-263-6).

However, in your comments on the draft decision, you explain that the substance identified as 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-264-1 in your registration dossier is in fact a "*multi-constituent of 3-Cyclohexene-1-carboxaldehyde, 2,4-dimethyl- and 3-Cyclohexene-1-carboxaldehyde, 3,5-dimethyl-, covering possible stereochemistry isomers*" and you consider that "*it is the same as the Substance*". You further explain that "*due to the higher content and contribution to the fragrance, the identifier 2,4-dimethylcyclohex-3-ene-1-carbaldehyde (EC No. 268-264-1) is commonly used within the industry to represent the product, especially before full registration*".

[5] *Guidance on information requirements and chemical safety assessment*, Chapter R.6: QSARs and grouping of chemicals.

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

Finally you explain, that "*for the study reports* [you] *purchased,* [you] *have no right to change the test sample information, in order to match the current identifier*" and that you may consider providing further information to clarify the identity of the test material used to conduct these studies.

We take note of the explanation you provided in your comments on the draft decision and of your intention to provide further information to clarify the identity of the test material used to conduct the corresponding studies. Such information must include a confirmation that the relative concentration of 2,4-dimethylcyclohex-3-ene-1-carbaldehyde and 3,5-dimethylcyclohex-3-ene-1-carbaldehyde is consistent with the substance identity profile of the Substance. In addition, we note that the chemical structure of these two constituents includes 2 chiral centres and that therefore, each of these constituents may have four isomers (2 pairs of enantiomers). Therefore, supporting information to demonstrate a similar isomeric composition of the Substance and the test materials referred to as 2,4-dimethylcyclohex-3-ene-1-carbaldehyde (EC No. 268-264-1) needs to be provided.

For the read-across from HMPCC and L-perillyl alcohol, your technical dossier does not include relevant, reliable and adequate information for the Substance and of the source substances to support your read-across hypothesis. For the studies conducted with test materials referred to as 2,4-dimethylcyclohex-3-ene-1-carbaldehyde (EC No. 268-264-1), your registration dossier currently does not include adequate information to confirm the substance identity of the test material. In the absence of such 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.

B. Predictions for ecotoxicological and environmental fate properties

You have not provided a read-across justification for environmental fate properties.

While you have not claimed a read-across, you have only provided information on the analogue substance 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-264-1.

You have not provided any reasoning for the prediction of ecotoxicological and environmental fate properties using information from 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-264-1. We note that this analogue substance corresponds to the main constituent of the Substance.

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

ECHA notes the following shortcomings with regards to prediction of ecotoxicological and environmental fate properties:

A. Absence of read-across documentation

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

study(ies).[7]

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

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

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

Supporting information must include bridging studies to compare properties of the Substance and source substances and, if relevant, information on the properties of the non-common compound(s).

The data set in you dossier does not include any information on the toxicological properties of the Substance. In addition, you have not provided any information on the non-common compound (i.e. 3,5-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-263-6). Finally, for the reasons explained under the corresponding sections below, some of the studies on the source substance are not adequate to fulfil the corresponding information requirement.

As already explained under Section A. above, in your comments on the draft decision you claim that 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-264-1 is a "*multi-constituent of 3-Cyclohexene-1-carboxaldehyde, 2,4-dimethyl- and 3-Cyclohexene-1-carboxaldehyde, 3,5-dimethyl-, covering possible stereochemistry isomers*" and you consider that "*it is the same as the Substance*". However, as already explained, your registration dossier currently does not include adequate information to confirm the substance identity of the test material. Therefore, your technical dossier currently does not include relevant, reliable and adequate information for the Substance and of the source substance(s) to support your read-across hypothesis. In the absence of such information, you have not established that the Substance and of 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. 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 selected analogue substances. Therefore, your adaptations do not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approaches are rejected.

[7] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.6.1

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

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

1. 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 Section 1.5, Annex XI to REACH using an OECD TG 471 study with the analogue substance 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-264-1.

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

Therefore, the information requirement is not fulfilled.

As explained under Section 1 (Assessment of your read-across approach under Annex XI, Section 1.5.) of the Appendix on Reasons common to several requests, you consider that 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-264-1 and the Substance are identical. However, your registration dossier currently does not include convincing evidence to demonstrate this claim.

Study design

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

2. Short-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.).

You have adapted this information requirement under Section 1.5, Annex XI to REACH using an EU Method C.2 study with the analogue substance 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-264-1.

We have assessed this information and identified the following issues:

A. Annex XI, section 1.5. requires that in all cases results should have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3) of REACH, in this case the OECD TG 202 or the EU Method C.2. Therefore, the following requirements must be met:
   - 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 is available;
   - Adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations are provided.

   In your robust study summary you state that "*Analysis of all test concentrations plus a control at test start and after 48 hours of exposure (in the nominal concentrations 45 mg/l and 90 mg/l after 24 hours of exposure because of early l00% immobilization rates)*". You have not provided any information on the analytical method that was used. You have not reported the results of the analytical determination of exposure

concentrations.

In the absence of this information, you have not demonstrated that a reliable analytical method for the quantification of the test material was available and that the exposure was satisfactorily maintained throughout the exposure period. Therefore, this study does not meet the requirements of a short-term toxicity testing on aquatic invertebrates.

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

Therefore, the information requirement is not fulfilled.

As explained under Section 1 (Assessment of your read-across approach under Annex XI, Section 1.5.) of the Appendix on Reasons common to several requests, you consider that 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-264-1 and the Substance are identical. However, your registration dossier currently does not include convincing evidence to demonstrate this claim. On the deficiencies identified under issue A. above, you have not provided any comments.

Study design

The substance is difficult to test due to its Henry's Law constant of 22.9 Pa.m^3/mole (predicted by HENRYWIN v3.20 in EPI SUITE). OECD TG 202 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 202. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solutions.

3. Growth inhibition study aquatic plants

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

You have adapted this information requirement under Section 1.5, Annex XI to REACH using an OECD TG 201 study with the analogue substance 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-264-1.

We have assessed this information and identified the following issues:

A. Annex XI, section 1.5. requires that in all cases results should have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3) of REACH, in this case the OECD TG 201 or the EU Method C.3. Therefore, the following requirements must be met:
   - 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 is available;

- Adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations are provided.

In your robust study summary you state that "*there was no analytical method available at the time of the study, so there was no analysis of test substance concentrations in the test medium*".

In the absence of the analytical determination of exposure concentrations, you have not demonstrated that exposure was satisfactorily maintained throughout the exposure period. Therefore, this study does not meet the requirements of a growth inhibition study in aquatic plants.

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

Therefore, the information requirement is not fulfilled.

In your comments on the draft decision, you agreed to conduct the requested study.

Study design

As already explained in Section A.2, the substance is difficult to test. 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, as already described under Section A.2.

4. Ready biodegradability

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

You have adapted this information requirement under Section 1.5, Annex XI to REACH using an OECD TG 301C study with the analogue substance 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-264-1.

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

Therefore, the information requirement is not fulfilled.

As explained under Section 1 (Assessment of your read-across approach under Annex XI, Section 1.5.) of the Appendix on Reasons common to several requests, you consider that 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-264-1 and the Substance are identical. However, your registration dossier currently does not include convincing evidence to substantiate this claim.

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 Section 1.5, Annex XI to REACH using an OECD TG 473 study with the analogue substance Reaction mass of 3-(4-hydroxy-4-methylpentyl)cyclohex-3-ene-1-carbaldehyde and 4-(4-hydroxy-4-methylpentyl)cyclohex-3-ene-1-carbaldehyde or HMPCC, EC No. 915-617-9.

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

In your comments to the draft decision you indicate your intention to update the read-across adaptation with an OECD TG 473 study "*using the analogue Reaction mass of 3-(4-hydroxy-4-methylpentyl)cyclohex-3-ene-1-carbaldehyde and 4-(4-hydroxy-4-methylpentyl)cyclohex-3-ene-1-carbaldehyde (HMPCC; EC number 915-617-9) with constituents 4-(4-hydroxy-4-methylpentyl)cyclohex-3-enecarbaldehyde (CAS number 31906-04-4) and 3-(4-hydroxy-4-methylpentyl)cyclohex-3-ene-1-carbaldehyde (CAS number 51414-25-6)*". You also indicate that the decision "*should be paused until the updated read-across adaptation is submitted for re-assessment.*"

ECHA takes notes of your acknowledgement of the deficiency of your read-across adaptation and your intention to update.

Nevertheless the information requirement is not fulfilled.

Study design

To fulfil the information requirement for the Substance, either *in vitro* cytogenicity study in mammalian cells (OECD TG 473) or *in vitro* micronucleus study (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.

You have not provided an *in vitro* gene mutation study in mammalian cells.

Instead you have adapted this information requirement under Section 8.4.3., Column 2, Annex VIII to REACH. In support of your adaptation, you have provided *in vivo* micronucleus assay on the structurally similar substance HMPCC (EC No. 915-617-9).

Triggering of the study

Your dossier contains an adaptation under Annex XI, Section 1.5 for an *in vitro* gene mutation study in bacteria, and an adaptation under Annex XI, Section 1.5 for an *in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study.

However, for the reasons explained in the Appendix on Reasons common to several requests, your read-across adaptations for *in vitro* mutagenicity endpoints are rejected. Hence, this information cannot be used to omit the information requirement for an *in vitro* gene mutation study in mammalian cells.

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

Assessment of your adaptation under Section 8.4.3., Column 2

With regard to your adaptation, we have identified the following issues:

A. Under Section 8.4.3., Column 2, Annex VIII to REACH, the study may be omitted if a reliable *in vivo* mammalian gene mutation test is available. ECHA Guidance R.7.7.3.1. clarifies that the study must be a Transgenic Rodent Somatic and Germ Cell Gene Mutation Assay (OECD TG 488).

   Your dossier contains an *in vivo* micronucleus assay according to OECD TG 474.

   This test is not a Transgenic Rodent Somatic and Germ Cell Gene Mutation Assay.

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

In your comments to the draft decision you indicate your intention to update the read-across adaptation with an OECD TG 474 study "*using the analogue Reaction mass of 3-(4-hydroxy-4-methylpentyl)cyclohex-3-ene-1-carbaldehyde and 4-(4-hydroxy-4-methylpentyl)cyclohex-3-ene-1-carbaldehyde (HMPCC; EC number 915-617-9) with constituents 4-(4-hydroxy-4-methylpentyl)cyclohex-3-enecarbaldehyde (CAS number 31906-04-4) and 3-(4-hydroxy-4-methylpentyl)cyclohex-3-ene-1-carbaldehyde (CAS number 51414-25-6)*". You also indicate that the decision "*should be paused until the updated read-across adaptation is submitted for re-assessment.*"

ECHA takes notes of your acknowledgement of the deficiency of your read-across adaptation and your intention to update.

Nevertheless, the information requirement is not fulfilled.

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.).

You have provided:

i. an OECD TG 407 key study on the analogue substance Reaction mass of 3-(4-hydroxy-4-methylpentyl)cyclohex-3-ene-1-carbaldehyde and 4-(4-hydroxy-4-methylpentyl)

cyclohex-3-ene-1-carbaldehyde or HMPCC, EC No. 915-617-9;

ii. a non-guideline sub-chronic toxicity (oral route) key study on the analogue substance 4-isopropenylcyclohex-1-en-1-ylmethanol or L-perillyl alcohol, EC No. 208-639-9.

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

Therefore, 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).

In your comments to the draft decision you indicate that you will generate and submit an OECD TG 408 oral study with the Substance.

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.

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 with the analogue substance Reaction mass of 3-(4-hydroxy-4-methylpentyl)cyclohex-3-ene-1-carbaldehyde and 4-(4-hydroxy-4-methylpentyl) cyclohex-3-ene-1-carbaldehyde or HMPCC, EC No. 915-617-9 is available and, therefore an EU B.63/OECD TG 421 or EU B.64/OECD TG 422 study does not need to be conducted.

However, for the reasons explained in the Appendix on Reasons common to several requests, your read-across adaptation is rejected. Moreover, as explained under section C.2 of this decision, the study referred to in your adaptation does not provide equivalent information to an OECD TG 414 study.

In your comments to the draft decision you indicate your intention to update the read-across adaptation. Moreover you indicate that if the read-across adaptation is not accepted then an oral OECD TG 414 study will be considered. You refer to the adaptation of Annex VIII, Section 8.7.1, Column 2, first paragraph, fourth indent, where the study does not need to be conducted if a pre-natal developmental toxicity (PNDT) study (OECD TG 414) is already

available.

ECHA takes notes of your acknowledgement of the deficiency of your read-across adaptation and your intention to update. Moreover, we note that, based on the specific rules for adaptation under Annex VIII Section 8.7.1. column 2, fourth indent, this study (OECD TG 421 or 422) does not need to be conducted if you provide a compliant PNDT study. However, currently in your dossier there is no PNDT study according to OECD TG 414 available.

Therefore, based on the above, currently the information you provided does not fulfil the information requirement.

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[9] administration of the Substance.

5. Short-term toxicity testing on fish

Short-term toxicity testing on fish is an information requirement under Annex VIII to REACH (Section 9.1.3).

You have adapted this information requirement under Section 1.5, Annex XI to REACH using an OECD TG 203 study with the analogue substance 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-264-1.

We have assessed this information and identified the following issues:

A. Annex XI, section 1.5. requires that in all cases results should have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3) of REACH, in this case the OECD TG 203 or the EU Method C.1. . Therefore, the following requirements must be met:
   - 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 is available;
   - Adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations are provided.

   In your robust study summary you state that "*Analysis of the test preparations at 0, 24 and 96 hours showed measured test concentrations to range from 85% to 115% of nominal*". You have not provided any information on the analytical method that was used. You have not reported the results of the analytical determination of exposure concentrations.

   In your comments on the drat decision, you state that "*the test item concentration in the test samples was determined by GC using an external standard*". However, you have not provided any information on the performance parameter of the analytical method (i.e. specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range) and you have not reported the results of the analytical determination of exposure concentrations.

   In the absence of this information, you have not demonstrated that a reliable analytical

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

method for the quantification of the test material was available and that the exposure was satisfactorily maintained throughout the exposure period. Therefore, this study does not meet the requirements of a short-term toxicity testing on fish.

B. For the reasons explained in the Appendix on Reasons common to several requests, your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

As explained under Section 1 (Assessment of your read-across approach under Annex XI, Section 1.5.) of the Appendix on Reasons common to several requests, you consider that 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-264-1 and the Substance are identical. However, your registration dossier currently does not include convincing evidence to demonstrate this claim.

Study design

As already explained in Section A.2, the substance is difficult to test. OECD TG 203 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, as already described under Section A.2.

6. Activated sludge respiration inhibition testing

Activated sludge respiration inhibition testing is an information requirement under Annex VIII to REACH (Section 9.1.4).

You have adapted this information requirement under Section 9.1.4., Column 2, third indent with the following justification: "*In accordance with column 2 of REACH Annex VIII, the activated sludge respiration inhibition test does not need to be conducted as the applied test concentrations in ready biodegradability test are in the range of concentrations that can be expected in the influent of a sewage treatment plant*".

We have assessed this information and identified the following issue:

To adapt this information requirement based on column 2, third indent, all the following conditions must be met:
d) the substance is readily biodegradable, and
e) the applied test concentration(s) in the ready biodegradability test(s) are in the range of concentrations that can be expected in the influent of a sewage treatment plant.

For the reasons explained under Section A.4, the information requirement for ready biodegradability is not fulfilled. Therefore, you have not demonstrated that the Substance is readily biodegradable. Furthermore, you have not provided any justification that the test concentrations used in ready biodegradability tests are in the range of concentrations that can be expected in the influent of a sewage treatment plant. Consequently, your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

In your comments on the draft decision, you explain that you intend to use the ready biodegradability study according to OECD TG 301F on 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-264-1 ([redacted], 1995) as key study for this endpoint. According to you, the study is indicative that "*there was no toxic effect on the micro-organisms at the*

test concentration of 100 mg/L" and that according to ECHA Guidance R.7b, this information may be used to adapt the information requirement.

However, for the reasons explained in the Appendix on Reasons common to several requests, you have not demonstrated that 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 268-264-1 is identical to the Substance. Furthermore, you have provided only a statement that no toxicity was observed but without any supporting data (i.e., O_2 consumption measurement in the functional control and the toxicity control) allowing to verify this claim.

7. 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 or vPvB (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 following criteria:

- the Substance is potentially persistent or very persistent (P/vP) if, for instance:
  - it is not readily biodegradable (*i.e.* <60/70% degradation in an OECD 301D),
- the Substance is potentially bioaccumulative or very bioaccumulative (B/vB) if, for instance:
  - it has a high potential for bioaccumulation in air-breathing organisms (log K_{ow} >2 and log K_{oa} >5)
- the Substance is potentially toxic (T) if, for instance:
  - its lowest effect value in short-term aquatic toxicity test (*i.e.* E(L)C_{50}) is < 0.1 mg/L.

The information provided in your dossier indicates that:

- it cannot be excluded that the Substance meets the screening criteria for P as, for the reasons explained under Sections A.4, the information you have provided on ready biodegradability does not fulfil the information requirement. Additionally, we note that information available on the structural analogue suggests very limited biodegradation in ready biodegradability tests;
- the Substance is potentially B/vB in air-breathing organisms since the Log K_{ow} is above the threshold of 2 (Log K_{ow} = 2.7 based on OECD TG 117) and K_{oa} is above the threshold of 5 (Log K_{oa} = 4.734 ± 0.526 as predicted by KOAWIN v1.10 using the water solubility and vapour pressure estimates reported in your dossier). Taking into account the accuracy of the prediction and the intrinsic uncertainties of the experimental water solubility and Log Kow estimates used as input parameters in the model, the K_{oa} threshold of 5 is met;
- it cannot be excluded that the Substance is potentially T as, for the reasons explained under Sections A.2-3 and B.5 the information requirements for short-term toxicity to fish and aquatic invertebrates and for growth inhibition in aquatic plants are not fulfilled.

Based on the above the Substance may have PBT or vPvB properties and therefore further information on biodegradation must be provided.

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

In your comments on the draft decision, you agreed to conduct the requested study.

8. 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.7, 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 the selection of the requested tests and the tests design are addressed in Section C.6.

In your comments on the draft decision, you agreed to provide the requested information.

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 Section 1.5, Annex XI to REACH using a non-guideline sub-chronic toxicity (oral route) key study on the analogue substance 4-isopropenylcyclohex-1-en-1-ylmethanol or L-perillyl alcohol, EC No. 208-639-9.

However, for the reasons explained in the Appendix on Reasons common to several requests, your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

Study design

Following the criteria provided in Annex IX, Section 8.6.2., Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity and the preferred rodent species is rat (ECHA Guidance R7a, Section R.7.5.6.3.2 and Table R.7.5-1). The sub-chronic toxicity study must be performed according to the OECD TG 408, in rats and with oral administration of the Substance.

In your comments to the draft decision, you agreed to provide the requested information.

2. Pre-natal developmental toxicity study in one species

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

You have adapted this information requirement under Section 1.5, Annex XI to REACH using:

i. an OECD TG 415 (One Generation Reproduction Toxicity Study) key study on the analogue substance on the analogue substance Reaction mass of 3-(4-hydroxy-4-methylpentyl)cyclohex-3-ene-1-carbaldehyde and 4-(4-hydroxy-4-methylpentyl) cyclohex-3-ene-1-carbaldehyde or HMPCC, EC No. 915-617-9;
ii. two non-guideline repeated-dose toxicity (oral route) supporting studies on the analogue substance Reaction mass of 3-(4-hydroxy-4-methylpentyl)cyclohex-3-ene-1-carbaldehyde and 4-(4-hydroxy-4-methylpentyl) cyclohex-3-ene-1-carbaldehyde or HMPCC, EC No. 915-617-9.

We have assessed this information and identified the following issues:

A. To fulfil the information requirement, a study must comply with the OECD TG 414 Article 13(3) of REACH). Therefore, the following requirements must be met:
   - 20 female animals with implantation sites for each test and control group;
   - examination of the dams, including histopathology of the thyroid gland and thyroid hormone measurements;
   - examination of the foetuses for each sex, including skeletal and soft tissue alterations (variations and malformations), number of resorptions and or live foetuses and measurement of anogenital distance in live rodent foetuses.

   In the studies listed under ii. above, only 10 females were included per dose group. Only external examinations were conducted on offspring and examination of the dams

did not include histopathology of the thyroid gland and thyroid hormone measurements.

Therefore, none of these studies provide equivalent information to an OECD TG 414 study.

B. For the reasons explained in the Appendix on Reasons common to several requests, your adaptation is rejected.

In your comments to the draft decision you indicate your intention to update the read-across adaptation. ECHA takes notes of your acknowledgement of the deficiency of your read-across adaptation and your intention to update.

Therefore, 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[10] administration of the Substance.

3. Long-term toxicity testing on aquatic invertebrates

and

4. Long-term toxicity testing on fish

Long-term toxicity testing on aquatic invertebrates and on fish are information requirements under Annex IX to REACH (Sections 9.1.5. and 9.1.6.).

You have adapted these information requirements under Annex IX, Section 9.1, Column 2 with the following justification: "*In accordance with column 2 of REACH annex IX, long-term toxicity testing does not need to be conducted as the chemical safety assessment does not indicate a need for further investigation*".

We have assessed this information and identified the following issue:

To adapt this information requirement the Chemical Safety Assessment (CSA) must demonstrate that risks towards the aquatic compartment arising from the manufacture and use of the Substance are controlled (Annex IX, Section 9.1., Column 2; Annex I, Section 0.1). The justification must be documented in the Chemical Safety Report (CSR) and include all of the following elements:

- the predicted no effect concentrations (PNEC) for the aquatic compartment is based on:
  - reliable information on the hazardous properties of the Substance on at least three trophic levels, and
  - an appropriate assessment factor as explained in ECHA Guidance R.10, Section R.10.3), and
- an exposure assessment leading to derivation of predicted environmental concentrations (PECs),
- the outcome of the risk characterisation demonstrating that the risks are adequately controlled (*i.e.* PEC < PNEC).

For the reasons explained under Section A.2-3 and B.4 your technical dossier does not include adequate hazard information for the Substance. Hence, a reliable PNEC cannot be derived.

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

Therefore, your adaptation is rejected.

In your comments on the draft decision, you specify that you intend to "*make section A.2-3 and B.4 comprehensive including three trophic levels by adding relevant information or performing new test*" and that on this basis long-term toxicity testing on aquatic invertebrates and on fish will not be considered. We take note of your comment. However our assessment of your current dossier remains unchanged.

Therefore, the information requirement is not fulfilled.

Study design

As already explained in Section A.2, the substance is difficult to test. OECD TG 210 and 211 specify 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, as already described under Section 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 adapted these information requirements under Annex IX, Section 9.2, Column 2 with the following justification: "*In accordance with column 2 of REACH annex IX, further degradation testing does not need to be conducted as the chemical safety assessment does not indicate a need for further investigation*".

We have assessed this information and identified the following issue:

> This information requirement may be adapted under column 2 if the Chemical Safety Assessment (CSA) demonstrates and documents that risks arising from the Substance are controlled (Annex I, Section 0.1; Annex IX, Section 9.2, Column 2).
>
> To this end, you need to provide a justification as why there is no need to provide any further information for simulation testing on ultimate degradation in water taking into account the PBT/vPvB properties of the Substance itself and of any of its constituent, impurity or transformation/degradation product present in concentration ≥ 0.1% (w/w).
>
> However, if there are indications for potential PBT/vPvB properties (Annex I Section 4; Annex XIII, Section 2.1) further testing on degradation is required.
>
> As already explained under Section B.6. the Substance may have PBT or vPvB properties and therefore your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

In your comments on the draft decision, you agreed to conduct the requested study.

Study design

Under Annex XIII, the information must be based on data obtained under conditions relevant for the PBT/vPvB assessment. Therefore:

- You must perform the OECD TG 309 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).

- The required temperature of 12 °C is the average environmental temperature for the EU (ECHA Guidance R.16, Table R.16-8). Performing the tests at this temperature 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 NERs may be significant in surface water tests also. Therefore, as for soil and sediments simulation tests, the NERs should be quantified and the extraction procedure and solvent used should be explained and scientifically justified. Non-extractable residues (NER) must be quantified in all simulation studies. 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 Chapter R.11).

6. Identification of degradation products

Identification of the degradation products is an information requirement under Annex IX of REACH (Section 9.3.2.).

You have adapted these information requirements under Annex IX, Section 9.2, Column 2 with the following justification: "*In accordance with column 2 of REACH annex IX, further degradation testing does not need to be conducted as the chemical safety assessment does not indicate a need for further investigation*". You have not provided further justification.

We have assessed this information and identified the following issue:

> This information requirement may be adapted under column 2 if the Chemical Safety Assessment (CSA) demonstrates and documents that risks arising from the Substance are controlled (Annex I, Section 0.1; Annex IX, Section 9.2, Column 2).
>
> To this end, you need to provide a justification as why there is no need to provide any further information on the identification of the degradation products taking into account the PBT/vPvB properties of the Substance itself and of any of its constituent, impurity or transformation/degradation product present in concentration ≥ 0.1% (w/w) (Annex I, Section 4). This information is also needed for the risk assessment of the Substance (Annex I, Section 6).
>
> You have not provided any justification as why the CSA does not indicate the need to provide information on the identity of degradation products.
>
> As already explained under Section B.6. the Substance may have PBT or vPvB properties. Without the information on relevant transformation/ degradation products, your CSA does not demonstrate that the risks of the Substance are adequately controlled because you have not demonstrated that this information is not needed for the PBT/vPvB assessment (Annex I, Section 4) and risk assessment (Annex I, Section 6). Therefore, your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

In your comments on the draft decision, you agreed to provide the requested information.

Study design

Regarding appropriate and suitable test method, the methods 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 Kow and potential toxicity of the transformation/degradation may be investigated. You may obtain this information from the degradation simulation study also requested in this decision or by some other measure. If any other method than the test requested under Section C.5 is used for 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 study according to OECD TG 309 (Section C.5) must be conducted at 12°C and at a test concentration < 100 µg/L. 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, *e.g.* 20°C) and at higher application rate (*i.e.* > 100 µg/L).

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[11].

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[12].

[11] https://echa.europa.eu/practical-guides
[12] 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. Testing strategy for aquatic toxicity testing

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

C. 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 synthetize its relevant constituents and/or fractions.

Appendix F: Procedure

The information requirement for an Extended one-generation reproductive toxicity study (EOGRTS; Annexes IX or X, Section 8.7.3.) is not addressed in this decision. This may be addressed in a separate decision once the information from the Sub-chronic toxicity study (90-day) requested in the present decision is provided.

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 23 January 2020.

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.

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[13] 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)[14]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[14]

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[15]

[13] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[14] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[15] 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 the corresponding information requirements applicable to them

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

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

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.