~~Confidential~~

Helsinki, 27 June 2022

Addressees
Registrants of JS_203_957_4 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
17/08/2021

Registered substance subject to this decision ("the Substance")
Substance name: Decanal
EC number: 203-957-4
CAS number: 112-31-2

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 ***2 April 2024***.

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

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

1. In vitro 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

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

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

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 VIII 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.

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 analogue read-across approach under Annex XI, Section 1.5.**

You seek to adapt the following standard information requirements by applying read-across approaches in accordance with Annex XI, Section 1.5:

- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)

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

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

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance R.6. and related documents[2,3].

A. Predictions for toxicological properties

You have provided a read-across justification documents in IUCLID Sections 7.5, 7.6 and 7.8.

You read-across between the structurally similar substances, nonanal (EC No. 204-688-5, CAS No. 124-19-6), dodecanal (EC No. 203-983-6, CAS No. 112-54-9), heptanoic acid (EC No. 203-838-7, CAS No. 111-14-8) and 2,6-dimethylhept-5-enal (EC No. 203-427-2, CAS No. 106-72-9) as source substances and the Substance as target substance.

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

- Nonanal (EC No. 204-688-5, CAS No. 124-19-6): "*[…] the output from the OECD [Q]SAR Toolbox shows that the profiles of the Target Substance and the Source Substance are sufficiently similar such that available toxicological data from the Source Substance can be used to address the following endpoints in the REACH registration dossier for the Target Substance.*"

- dodecanal (EC No. 203-983-6, CAS No. 112-54-9), heptanoic acid (EC No. 203-838-7, CAS No. 111-14-8) and 2,6-dimethylhept-5-enal (EC No. 203-427-2, CAS No. 106-72-9): "[…] *the target and source substances have similar human health profiles as a*

[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

result of structural similarity, the same expected mode of action and similar physicochemical properties."

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 predictions of toxicological properties.

1. *Inadequate read-across hypothesis*

A read-across hypothesis must be provided, establishing why a prediction for a toxicological property is reliable. Firstly, this hypothesis should be based on recognition of the structural similarities and differences between the substances (Guidance on IRs and CSA, Section R.6.). Secondly, it should also explain why the differences in the chemical structures should not influence the toxicological properties or should do so in a regular pattern, taking into account that variations in chemical structure can affect both toxicokinetics (uptake and bioavailability) and toxicodynamics (e.g. interactions with receptors and enzymes) of substances (Guidance on IRs and CSA, Section R.6.2.1.3).

Your read-across hypothesis is only based on the structural similarity, and to a limited extent the physicochemical (dis)similarities, between the source substance(s) and the Substance, which you consider a sufficient basis for predicting the properties of the Substance. However, your hypothesis does not explain why the structural differences between the substances do not influence the toxicological properties or do so in a regular pattern.

While structural similarity is a prerequisite for applying the grouping and read-across approach, it does not necessarily lead to predictable or similar human healthproperties. You have not provided a well-founded hypothesis to establish a reliable prediction for a toxicological property, explaining why the structural differences do not influence toxicokinetics and toxicodynamics of the substances.

2. *Supporting information*

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

Supporting information must include toxicokinetic information on the formation of the (common) compounds and bridging studies to compare properties of the Substance and source substances.

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

For the source substances, you provide the studies used in the prediction in the registration dossier. Apart from those studies, your read-across justification documents include data tables with limited information on the outcome of toxicological studies on the source substances and the Substance.

In the data table comparing the source substance nonanal with the Substance, you only provide bridging LD50 results for the endpoint acute toxicity. In addition, you indicate that the tests were performed under slightly different test conditions and therefore cannot be directly compared. Furthermore, the endpoint acute toxicity does not inform on genetic damage and can thus not be used to support a read-across on genetic toxicity. No other (results of) bridging studies were submitted to support the use of nonanal as a source substance.

In the data table comparing the source substance dodecanal with the Substance, only the results of two bridging Bacterial Reverse Mutation Assays (OECD 471) and acute oral toxicity studies are shown.

The registration dossier does not include any robust study summaries of the bridging studies mentioned above or descriptions of data for the source substance that would confirm that both substances cause the same type of effects. In addition, no comparison of the toxicokinetic profiles of the source substances and the Substance is made.

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.

3. Adequacy and reliability of source studies

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

- be adequate for the purpose of classification and labelling and/or risk assessment;
- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3);
- cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter.

Specific reasons why the studies on the source substances do not meet these criteria are explained further below under the applicable information requirement sections A.2, B.1, B.2 and B.4. Therefore, no reliable predictions can be made for these information requirements.

B. Predictions for ecotoxicological properties

i. Aquatic toxicity

You have provided the following reasoning for the prediction of aquatic toxicity: *"To address the toxicity to aquatic algae as part of the REACH registration of decanal (target sub-stance) it is proposed to read-across to nonanal (source substance). This is an analogue approach for which the read-across hypothesis is based on different compounds which have similar proper-ties. It is covered by scenario 2 in the ECHA Read-Across Assessment Framework [RAAF, ECHA 2017]."*.

You read-across between the structurally similar substances, nonanal, EC No. 204-688-5 (CAS No. 124-19-6) as source substance and the Substance as target substance.

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 based on a worst-case approach.

ECHA notes the following shortcoming with regards to prediction of aquatic toxicity.

In order to make an accurate prediction of ecotoxicological and toxicological properties all relevant information must be considered in the prediction. If not all information is considered in the read-across approach, bias can be introduced in the predictions which may result in an over/underestimation in the prediction (RAAF, 2017; Chapter 4.5.1.5.). Bias may be caused by incorrect/incomplete selection of source substance(s); or due to a particular selection of study(ies) performed on the source substance(s).

To justify the selection of source substances, you must provide documentation how the source substance(s) have been chosen, for example, what methods/tools have been used to map the field of potential source substance(s), which other substances have been considered and why they have been discarded (RAAF, 2017, Chapter 4.4.1.5/4.5.1.5). If there are structural analogue(s) not used as source substances and data show significantly different results for the properties to be predicted without any justification for setting aside these different results, then the proposed predictions are considered biased.

You report information from the following source substance: nonanal (CAS: 124-19-6; EC: 204-688-5). You have not provided any justification on the selection of this substance used to predict the properties of the Substance.

Another substance (undecanal, CAS: 112-44-7; EC: 203-972-6) has the following structure: linear saturated aldehyde, chain length 11 carbons.

The following study is provided on that substance showing the following effects:

Algae growth inhibition test according to OECD Guideline 201 (*Pseudokirchneriella subcapitata*), observed effective concentrations: EC50 (72 h; growth rate) = 132 µg/L; NOEC (72 h; growth rate and yield) = 23.5 µg/L (Study summary publicly available at: https://echa.europa.eu/registration-dossier/-/registered-dossier/10847/6/2/6).

This other substance is a structural analogue of the Substance and provides a more realistic prediction than the source substance that you have identified because higher toxicity to aquatic organisms is expected for linear aldehydes that have longer carbon chain. Therefore, a shorter chain aldehyde as the source source substance may underestimate ecotoxicity of a longer chain aldehyde as the target substance. The available data on this substance indicates significantly different results showing higher concern than the studies on the source substance you use to draw a conclusion on the endpoint. You have not justified why this source substance has not been considered.

Therefore, your predictions are biased and may underestimate the hazards of the Substance.

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 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.

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

You seek to adapt the information requirements for the following standard information requirements by grouping substances in the category and 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 vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)

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

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

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance R.6 and related documents.

A. Scope of the grouping

i. Description of the grouping

In your registration dossier you have performed categorisations through identification of 10 (*in vitro* gene mutation study in bacteria), 8 (*in vitro* cytogenicity study in mammalian cells) and 6 (*in vitro* gene mutation study in mammalian cells) nearest neighbours compared by prediction descriptors using OECD QSAR Toolbox. You have provided automated reports (2016) generated from the OECD QSAR Toolbox software in IUCLID Section 7.6.1.

You define the applicability domains of the categories based on:

- Group members listed in the two supporting documents entitled '*Prediction of Gene mutation for decyl aldehyde*', one of which including data generated in the absence of S9-mix and the other including data generated in the presence of S9-mix (information sources for in vitro gene mutation study in bacteria): "*Based on no alert found by DNA alerts for AMES, MN and CA by OASIS v.1.3. No alert found by DNA binding by OECD. Structural similarity of >10%.*"

- Group members listed in the supporting document entitled '*Prediction of Chromosome aberration for decyl aldehyde*' (information source for in vitro cytogenicity study in mammalian cells or in vitro micronucleus study): "*Based on no alert found by DNA alerts forCA and MNT by OASIS v.1.3. No alert found by DNA binding by OECD. Structural similarity of >50%.*"

- Group members listed in the supporting document entitled '*Prediction of gene mutation for decyl aldehyde*' (information source for In vitro gene mutation study in mammalian cells): "*No alert found by DNA binding by OECD. Structural similarity of 80%.*"

ii. Assessment of the grouping

ECHA notes the following shortcoming with regards to your grouping approach.

- *Applicability domain of the category*

According to the ECHA Guidance, a category (grouping) hypothesis should address "*the set of inclusion and/or exclusion rules that identify the ranges of values within which reliable estimations can be made for category members for the given endpoint" .*[4] Particularly, "*the applicability domain of a (sub)category would identify the structural requirements and ranges of physico-chemical, environmental fate, toxicological or ecotoxicological properties within which reliable estimations can be made for the (sub)category members*".[5] Therefore, to reliably predict properties within a category the applicability domain should be described including the borders of the category, for which chemicals the category does not hold and a justification for the inclusion and/or exclusion rules.

You describe the applicability domain of the substances covered by the grouping based on q limited set of profilers ("*no alert found by DNA alert for […]/binding*" and "*structural similarity of […] %.*" In more detail, the profilers used to specify the applicability domains specify the following classes of chemicals:

- "*Based on no alert found by DNA alerts for AMES, MN and CA by OASIS v.1.3. No alert found by DNA binding by OECD. Structural similarity of >10%":* Group members listed in the two supporting documents entitled '*Prediction of Gene mutation for decyl aldehyde*', one of which including data generated in the absence of S9-mix and the other including data generated in the presence of S9-mix (information sources for in vitro gene mutation study in bacteria)
- "*Based on no alert found by DNA alerts forCA and MNT by OASIS v.1.3. No alert found by DNA binding by OECD. Structural similarity of >50%":* Group members listed in the supporting document entitled '*Prediction of Chromosome aberration for decyl aldehyde*' (information source for in vitro cytogenicity study in mammalian cells or in vitro micronucleus study)
- "*No alert found by DNA binding by OECD. Structural similarity of 80%":* Group members listed in the supporting document entitled '*Prediction of gene mutation for decyl aldehyde*' (information source for In vitro gene mutation study in mammalian cells)

However, none of these general classifications introduce unambiguous inclusion/exclusion criteria for chemical structures allowed in the category substances. Furthermore, the provided applicability domain criteria based on above classification(s) cannot predict type of toxicity or the mode/mechanism of actions of the substances.

Therefore, this applicability domain does not introduce unambiguous inclusion/exclusion criteria which would identify the structural requirements and ranges of physico-chemical, environmental fate, toxicological properties within which reliable estimations can be made for the (sub)category members.

B. Predictions of properties

You have provided predictions based on category members using read-across from 10 (*in vitro* gene mutation study in bacteria), 8 (*in vitro* cytogenicity study in mammalian cells) and 6 (*in vitro* gene mutation study in mammalian cells) nearest neighbours compared by prediction descriptors using OECD QSAR Toolbox.

ECHA notes the following deficiencies with regards to predictions of toxicological properties.

i. Read-across hypothesis

[4] ECHA Guidance R.6, Section R.6.2.4.1
[5] ECHA Guidance R.6, Section R.6.2.1.2

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.[6] 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.

You have not provided a read-across hypothesis to establish a reliable prediction for the toxicological properties, based on recognition of the structural similarities and differences between the category members.

ii. 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 should:

- be adequate for the purpose of classification and labelling and/or risk assessment;
- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3); and
- cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter.

In addition, 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, among others, robust study summary(ies) of the study(ies) on the source substance(s).[7] A robust study summary must cover sufficient information to make an independent assessment of the study.[8]

However, to support your predictions, you have provided automated reports generated from the OECD QSAR Toolbox software. These reports contain the outcomes ("*positive*" or "*negative*") of "*Bacterial reverse mutation assay (e.g. Ames test)*", "*In Vitro mammalian chromosome aberration test*" or "*in vitro […] mammalian cell gene mutation assay*" performed with thecategory members. Therefore, you have not provided robust study summaries of the studies on the source substance(s).

In the absence of such documentation, ECHA cannot verify that the results to be read across meet the criteria above.

C. Conclusions on the grouping of substances and 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.

[6] ECHA Guidance R.6.
[7] ECHA Guidance R.6, Section R.6.2.6.2
[8] How to report robust study summaries Practical Guide 3, Version 2.0 – November 2012

3. Assessment of the weight of evidence adaptations under the requirements of Annex XI, section 1.2

You have adapted the following standard information requirements by applying weight of evidence (WoE) adaptation in accordance with Annex XI, section 1.2:

- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

Your weight of evidence adaptation raises the same deficiencies irrespective of the information requirement for which it is invoked. Accordingly, ECHA addressed these deficiencies in the present Appendix, before assessing the specific standard information requirements in the following appendices.

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

According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude that the Substance has or has not the (dangerous) property investigated by the required study.

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

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

Irrespective of the above mentioned deficiencies on the documentation, which in itself could lead to the rejection of the adaptation, ECHA has assessed the provided sources of information.

1. *Reliability of the read across approach*

Sections 1 and 2 of the present Appendix identify deficiencies of the read across approach used in your dossier. These findings apply equally to the sources of information relating to analogue substances submitted under your weight of evidence adaptations.

Additional issues related to weight of evidence are addressed under the corresponding endpoints.

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 provided the following information in the technical dossier, based on which you conclude that the Substance is not a skin sensitiser:

i. Human repeat insult patch test , study report, 1964.

ii. Open Epicutaneous test, not according to a specific guideline, study report, 1973.

iii. Draize test, not according to a specific guideline, study report, 1973.

iv. Guinea Pig Maximization test, not according to a specific guideline, study report, 1973.

v. Intradermal Freund's Complete adjuvant test, not according to a specific guideline, study report, 1973.

You have adapted this information requirement under Section 8.3.1, Column 2 using the following justification: adequate in vivo study is already available.

We have assessed this information and identified the following issues:

A) Assessment whether the Substance causes skin sensitisation

a) Adequacy of the study (i) for hazard identification

According to the ECHA Guidance[9], "*The evaluation of data quality includes assessment of adequacy of the information for hazard/risk assessment and C&L purposes*". The ECHA Guidance defines adequacy as "*the usefulness of data for hazard/risk assessment purposes*".

The study (i) seem to have been conducted on humans for the purpose of risk assessment and with the objective of identification of safe levels for specific intended uses.

Whilst the study (i) seems to have been designed to establish safe levels for specific intended uses, they do not investigate the intrinsic properties of the Substance as required for the purpose of hazard identification. In particular, the dose levels used in these studies are far lower (concentration of 5%) than the doses expected to be used for hazard identification purposes. Therefore, the study does not meet the information requirements and does not allow to make a conclusion whether the Substance causes skin sensitisation.

b) Study reliability (ii to v)

To fulfil an information requirement or be appropriate for an adaptation, a study must be reliable, i.e. assigned with a Klimisch score of 1 or 2 (ECHA Guidance R.4).

[9] ECHA Guidance R.4

You have provided four *in vivo* skin sensitisation studies (ii to v) which you assigned with reliability 4. We agree that these are unassignable and therefore cannot be used to conclude whether the Substance causes 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 a conclusion in cases where the substance is considered to cause skin sensitisation, the information provided must also 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.

In the comments to the draft decision, you "*agree with ECHA that a certain amount of data / information is needed to satisfy the data requirements for this substance and, therefore, agree to generate further data*". You have not provided specific comments for this endpoint. ECHA understands that you agree to provide this information.

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 a standard information requirement in Annex VII to REACH.

You have adapted this standard information requirements by applying weight-of-evidence approaches in accordance with Annex XI, Section 1.2.

In support of your adaptation you have provided the following sources of information with analogues:

i. an *in vitro* gene mutation study in bacteria, similar to OECD TG 471 with the analogue nonanal (EC No. 204-688-5, CAS No. 124-19-6) (1980);

ii. an *in vitro* gene mutation study in bacteria (1975), not according to a specific guideline with the analogue nonanal (EC No. 204-688-5, CAS No. 124-19-6);

iii. A prediction of gene mutation in bacteria, based on an *in silico* generated category of source substances (QSAR Toolbox);

As explained in the Appendix on Reasons common to several requests, it would be sufficient to reject your weight of evidence adaptation based on the fact that you have not submitted

any justification of your adaptation.

In any case, to fulfil the information requirement, normally a study performed according to OECD TG 471 must be provided. OECD TG 471 investigates gene mutations in bacteria as a key investigation using 5 different bacterial 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 sources of information you provided on gene mutations in bacteria do not cover all relevant and essential aspects as defined above.

The sources (i., ii. and iii.) of information provide information on some bacterial strains, but not on *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).

In addition, the reliability of these sources of information is significantly affected by the following deficiencies:

A. *Read-across adaptation (information sources i, ii and iii)*

   As explained in the Appendix on reasons common to several requests, you have not demonstrated that the applied read across for the Substance is adequate for the purpose of classification and labelling and/or risk assessment.

B. *The specifications of OECD TG 471, include the following:*

   a) The maximum dose tested must induce a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test dose must correspond to 5 mg/plate or 5 ml/plate.
   b) At least 5 doses must be evaluated, in each test condition.
   c) Triplicate plating must be used at each dose level.
   d) The number of revertant colonies per plate for the concurrent negative control must be inside the historical control range of the laboratory.

The reported data for the studies you have provided did not include:

a) a maximum dose of 5 mg/plate or 5 ml/plate or that induced a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance. (studies i, ii and iii)
b) the evaluation of at least 5 doses in each test condition. (studies i and iii)
c) triplicate plating at each dose level. (studies i, ii and iii)
d) a negative control with a number of revertant colonies per plate inside the historical control range of the laboratory. (studies ii and iii)

On this basis, the sources of information (i., ii., and ii.) were conducted at test concentrations that are too low and therefore do not provide reliable information to detect gene mutations in bacteria for the selected test materials. In addition, there are issues with the test conditions and/or reporting of these studies which significantly affect the overall reliability of the reported results. As a result, the provided studies cannot be considered as a reliable source of information that could contribute to the conclusion on the information investigated by the required study.

Taken together, the sources of information provide information on gene mutations but not in all required bacterial strains. In addition, their reliability is affected so significantly that they cannot be taken into consideration in a weight of evidence approach.

Therefore, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous property foreseen to be investigated in an OECD TG 471. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

In the comments to the draft decision, you "*agree with ECHA that a certain amount of data / information is needed to satisfy the data requirements for this substance and, therefore, agree to generate further data*". You have not provided specific comments for this endpoint. ECHA understands that you agree to provide this information.

Information on the study design

To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471) should be performed.

3. 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 adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

As explained in the Appendix on Reasons common to several requests section 1.B. your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

In the comments to the draft decision, you "*agree with ECHA that a certain amount of data / information is needed to satisfy the data requirements for this substance and, therefore, agree to generate further data*". You have not provided specific comments for this endpoint. ECHA understands that you agree to provide this information.

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

In vitro cytogenicity study in mammalian cells is a standard information requirement in Annex VIII to REACH. You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

In support of your adaptation, you have provided the following information:

i. an *in vitro* chromosome aberration study (1993), not according to a specific guideline with the analogue nonanal (EC No. 204-688-5, CAS No. 124-19-6);

ii. A prediction of chromosome aberration, based on an *in silico* generated category of source substances (QSAR Toolbox);

ECHA has assessed this adaptation and identified the following issues:

1. 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:

2. Non-compliant study

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must have 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 473. The criteria of this test guideline include for example

a) Two separate test conditions must be assessed: in absence of metabolic activation and in presence of metabolic activation.
b) The maximum concentration tested must induce 55+5% 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.
c) At least 300 well-spread metaphases must be scored per concentration.
d) One positive control must be included in the study. The positive control substance must produce a statistically significant increase in the response compared with the concurrent negative control.
e) The response for the concurrent negative control must be inside the historical control range of the laboratory.
f) Data on the cytotoxicity and the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures must be reported.

However, the reported data for the studies (i and ii) you have provided did not include:
a) two separate test conditions, but only in absence/presence of metabolic activation.
b) a maximum tested concentration of 10 mM, 2 mg/mL or 2 µl/mL, or that induced 55+5% of cytotoxicity compared to the negative control, or the precipitation of the tested substance.
c) the scoring of at least 300 metaphases per concentration.
d) a positive control that produced a statistically significant increase in the response

compared with the concurrent negative control.
e) a negative control with a response inside the historical control range of the laboratory.
f) data on the cytotoxicity and/or the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures. The studyi.) do not report data on cytotoxicity and the frequency of cells with structural chromosomal aberrations.

The information provided does not cover key parameters required by OECD TG 473.

Therefore, the information requirement is not fulfilled.

In the comments to the draft decision, you "*agree with ECHA that a certain amount of data / information is needed to satisfy the data requirements for this substance and, therefore, agree to generate further data*". You have not provided specific comments for this endpoint. ECHA understands that you agree to provide this information.

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 in Annex VIII to REACH 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 (weight-of-evidence) for an *in vitro* gene mutation study in bacteria, and an adaptation (read-across) 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 or *in vitro* micronucleus study provided in the dossier are rejected for the reasons provided in sections A.2 and B.1 of this draft decision.

The result of the requests for information in A.2 and B.1 of this decision 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 by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

In support of your adaptation, you have provided the following information:

i. In vitro gene mutation study in mammalian cells ([redacted], 1981), similar to other Guideline [redacted] (1975), with the source substance nonanal EC. No 204-688-5 (CAS 124-19-6)
ii. A prediction of gene mutation, based on an *in silico* generated category of source substances (QSAR Toolbox);

ECHA has assessed this adaptation and identified the following issues:

1. *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:

1. *Non-compliant study*

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must have 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 490. The criteria of this test guideline include for example

a) Two separate test conditions must be assessed: in absence of metabolic activation and in presence of metabolic activation.
b) 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.
c) At least 4 concentrations must be evaluated, in each test condition.
d) One positive control must be included in the study. The positive control substance must produce a statistically significant increase in the response compared with the concurrent negative control.
e) The response for the concurrent negative control must be inside the historical control range of the laboratory.
f) Data on the cytotoxicity and the mutation frequency for the treated and control cultures must be reported.

The reported study (ii) you have provided did not include an exhaustive datamatrix with details on any of the criteria listed above. You only list whether the studies on the source substances were negative or positive in the gene mutation assays, and what the associated $\log_{Kow}$ are.

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 or an *in vitro* micronucleus study provide a negative result.

In the comments to the draft decision, you "*agree with ECHA that a certain amount of data / information is needed to satisfy the data requirements for this substance and, therefore, agree to generate further data*". You have not provided specific comments for this endpoint. ECHA understands that you agree to provide this information.

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 a standard information requirement in Annex VIII to REACH. This information may take the form of a study record or a valid adaptation in accordance with either a specific adaptation rule under Column 2 of Annex VIII or a general adaptation rule under Annex XI.

You have provided an adaptation which ECHA understands is according to Column 2 of Annex VIII, Section 8.6.1. in your dossier.

In support of your adaptation, you have provided the following information:

i. an *in vivo* study (2012), according to OECD TG 408, with the analogue dodecanal (EC No. 203-983-6, CAS No. 112-54-9);

We have assessed this information and identified an issue (see Section C.1). Based on this, the information you provided does not fulfil the information requirement.

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 is a standard information requirement in Annex VIII to REACH.

You have adapted this standard information requirements by applying weight-of-evidence approaches in accordance with Annex XI, Section 1.2.

In support of your adaptation you have provided the following sources of information with analogues:

i. an experimental study One generation reproductive toxicity ([redacted] 1990, [redacted], 2001), no clear guideline, with the source substance Heptanoic acid EC. No 203-838-7.
ii. An experimental study toxicity to reproduction ([redacted] 1990, [redacted], 2001), no clear guideline, with the source substance 2,6-dimethylhept-5-enal EC. No 203-427-2

As explained in the Appendix on Reasons common to several requests, it would be sufficient to reject your weight of evidence adaptation based on the fact that you have not submitted any justification of your adaptation.

In any case, to fulfil the information requirement, normally a study performed according to OECD TG 421/422 must be provided. Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.7.3 at Annex VIII includes similar information that is produced by the EU B.63/OECD TG 421 or EU B.64/OECD TG 422. At general level, it includes information on the following key elements: 1) sexual function and fertility, 2) toxicity to offspring, and 3) systemic toxicity.

Sexual function and fertility

Sexual function and fertility on both sexes must include information on mating, fertility, gestation (length), maintenance of pregnancy (abortions, total resorptions), parturition, lactation, organ weights and histopathology of reproductive organs and tissues, litter sizes, nursing performance and other potential aspects of sexual function and fertility.

The sources of information (i-ii) provide only high statements and no detailed descriptions on mating, fertility, lactation and litter sizes. They do not provide information on the other parameters : organ weights and histopathology of reproductive organs and tissues, gestation (length), maintenance of pregnancy (abortions, total resorptions), parturition, nursing performance. Furthermore, the sources of information addressing the key investigations must follow the rules for the exposure duration as required in the information requirement (OECD TG 421, paragraph 29; OECD TG 422, paragraph 34) and be adequate for hazard classification and/or risk assessment as required by REACH. The studies (i.,ii.) do not have the required exposure duration according to the OECD TG 421 and OECD TG 422, because the exposure does not cover two weeks of premating and pregnancy and at least 13 days of lactation.

In addition, the reliability of these sources of information is significantly affected by the following deficiencies:

- Information from source substances can contribute to weight of evidence adaptation only if the read-across adaptation is acceptable. Studies (i-ii) are performed with source substances. However, for the reasons explained under section 1 of the Appendix on Reasons common to several requests, the provided studies performed on source substances cannot be considered reliable sources of information that could contribute to the conclusion on the key parameters investigated by the required OECD TG 421/422.

Toxicity to offspring

Information on pre- and perinatal developmental toxicity reflected by litter sizes, postimplantation loss (resorptions and dead foetuses), stillborns, and external malformations, postnatal developmental toxicity reflected by survival, clinical signs and body weights of the pups (or litters), and other potential aspects related to pre-, peri- and postnatal developmental toxicity observed up to postnatal day 13.

The sources of information (i-ii) provide only high level statements and no detailed description on litter size and body weights of the pups. They do not provide information on the other parameters: postimplantation loss (resorptions and dead foetuses), stillborns, and external malformations.

In addition, the reliability of these sources of information is significantly affected by the reliability issues as explained under section 1) above.

Systemic toxicity

Information on systemic toxicity include clinical signs, survival, body weights, food consumption, clinical biochemistry, and other potential aspects of systemic toxicity in the parental generation up to postnatal day 13.

The sources of information (i-ii) provide the required information on the following parameters: the clinical signs, survival, body weights and food consumption. They do not provide information on the other parameters: haematology, clinical biochemistry, organ weights and

histopathology of non-reproductive organs and other potential aspects of systemic toxicity in the parental generation up to postnatal day 13.

In addition, the reliability of these sources of information is significantly affected by the reliability issues as explained under section 1) above.

As a result of the defiencies affecting the relevance and reliability of the sources of information, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in an OECD TG 421 or 422 study with a design described in this decision. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

In the comments to the draft decision, you mention that "*the Screening for reproductive/developmental toxicity study does no need to be conducted if a pre-natal developmental toxicity is available, according to the REACH Regulation, Annex VIII, Section 8.7.1, Column II.*" As a a pre-natal developmental toxicity study at Annex IX has been proposed under testing proposal and accepted by ECHA (testing proposal draft decision issued on 18 February 2022), you question whether there is also the need to perform the screening for reproductive/developmental toxicity study at Annex VIII. You also claim that you will consider the inclusion of additional parameters on sexual function in the requested sub-chronic 90 day study (OECD 408).

REACH Annex VIII section 8.7.1., column 2 specifies that the screening for reproductive/developmental toxicity (OECD TG 421 or 422) does not need to be conducted if, for instance, a pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) is available. At present no pre-natal developmental toxicity study is provided in the IUCLID dossier, therefore no conclusion on the compliance can currently be made. Please note that this decision does not consider updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation). You remain responsible for complying with this decision by the set deadline.

Information on 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[10] administration of the Substance.

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

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

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

Sub-chronic toxicity study (90-day) is a standard information requirement in Annex IX to REACH. You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

In support of your adaptation, you have provided the following information:

i. an *in vivo* study (2012), according to OECD TG 408, with the analogue dodecanal (EC No. 203-983-6, CAS No. 112-54-9);

ECHA has assessed this adaptation and identified the following issues:

1. 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, the information requirement is not fulfilled.

Information on the design of the study to be performed (route/ species/ strain)

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.

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

2. Long-term toxicity testing on aquatic invertebrates

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

You have provided the following information:

- a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2. In support of your adaptation, you provided the following justification:

  Long-term daphnia toxicity testing as described in Annex IX of Regulation (EC) No 1907/2006 is not considered to be necessary as the chemical safety assessment demonstrates safe use of Decanal.

We have assessed this information and identified the following issue:

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

Your adaptation is therefore rejected and the information requirement is not fulfilled.

In the comments to the draft decision, you "*agree with ECHA that a certain amount of data / information is needed to satisfy the data requirements for this substance and, therefore, agree to generate further data*". You have not provided specific comments for this endpoint. ECHA understands that you agree to provide this information.

3. Long-term toxicity testing on fish

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

You have provided the following information:

- a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2. In support of your adaptation, you provided the following justification:

  Long-term fish toxicity testing as described in Annex IX of Regulation (EC) No 1907/2006 is not considered to be necessary as the chemical safety assessment demonstrates safe use of Decanal.

We have assessed this information and identified the following issue:

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

Your adaptation is therefore rejected and the information requirement is not fulfilled.

In the comments to the draft decision, you "*agree with ECHA that a certain amount of data / information is needed to satisfy the data requirements for this substance and, therefore, agree to generate further data*". You have not provided specific comments for this endpoint. ECHA understands that you agree to provide this information.

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: 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; due to the fact that the results from the 90-day study is needed for the design of the EOGRTS. Similarly the information requirement for a Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.) is not addressed in this decision; as the EOGRTS will cover the same parameters.

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 04 May 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 request(s).

In your comments on the draft decision, you requested an extension of the deadline to provide information. However, you have not specified how much extra time would be required not did you provide any supporting evidence for your request.

In order to be able to give due consideration to this extension request, ECHA requested you to specify the length of the extension time and to submit supporting documentary evidence. However, you did not reply to ECHA's request within given three week notification time, i.e. by 1 February 2022. Therefore, ECHA did not amend the original 18 month deadline for submission of the requested information in this decision.

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[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)[15]

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[16]

[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] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[16] 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.