~~Confidential~~

Helsinki, 27 June 2022

Addressees
Registrants of OCTANAL JOINT as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
16/08/2021

Registered substance subject to this decision ("the Substance")
Substance name: Octanal
EC number: 204-683-8
CAS number: 124-13-0

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 October 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.; test method:

   - *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
   - Only if the *in vitro/in chemico* test methods specified under point A.1 .) 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)

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

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. 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

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

5. Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1.; test method: EU C.7./OECD TG 111)

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)

Reasons for the requests are explained in the following appendices:

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

Information required depends on your tonnage band

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

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

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

How to comply with your information requirements

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

You must follow the general testing and reporting requirements provided under the Appendix

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

Appeal

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

Failure to comply

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

Authorised[1] under the authority of Mike Rasenberg, Director of Hazard Assessment

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

Appendix on Reasons common to several requests

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

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

- 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.) Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Activated sludge respiration inhibition testing (Annex VIII, Section 9.1.4.)

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

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

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

A. Predictions for toxicological properties

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

You read-across between octanoic acid EC No. 204-677-5 (CAS 124-07-2) and also other aldehydes including melonal EC No. 203-427-2 (CAS 106-72-9), heptanal EC No. 203-898-4 (CAS No. 111-71-7), nonanal EC No. 204-688-5 (CAS No. 124-19-6) and decanal EC No. 203-957-4 (CAS No. 112-31-2) as source substances and the Substance as target substance.

You have provided the following reasoning for the prediction of toxicological properties:
As regards the read across from octanoic acid EC No. 204-677-5 you have provided the following statement: "[redacted]"

As regards the read across from Melonal EC No. 203-427-2 you have provided the following statement: "*The rate of hydrolysis for straight chain aldehydes tends to be greater than for branched-chain esters. The rate of oxidation increases with chain length and with the presence of additional double bonds (for example melanal). Branched chain aldehydes are prime substrates for aldehyde dehydrogenase and may be conjugated more rapidly or more readily*

[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

metabolised. Cleavage of functional groups around the double bond in melanal may occur more readily that breakdown of the straight chain alkyl aldehydes. However comparison of the endpoints in the table above indicates that, where direct comparison is possible, the toxicity of the straight chain aldehydes is not markedly different from that of melanal. Where differences do occur, melanal is more toxic that the remaining read-across candidates and these more conservative endpoints have been applied to octanal where read-across data is required. The use of melanal , with structural differences from the remaining straight chain substances is considered acceptable since the toxicity profile for melanal is not markedly more benighn than for the other read across candidates. The differences in some physicochemical parameters were not considered adequate to preclude the use of any of the candidates from the read-across group."

As regards the read across from the other aldehyde source substances you claim that:
" The toxicity profile established for a number of closely associated alkyl aldehyde substances has, where possible, been demonstrated to be similar to that of octanal, and based on the structural and physico-chemical similarities also found for the parameters tabulated in the document, it is considered justified to use data from the read-across candidates to supplement existing octanal data or address data gaps for the notified substance.".

ECHA understands that you predict the properties of the Substance using a number of read-across hypotheses. For the read across from Octanoic acid your hypothesis is based on the formation of common (bio)transformation products while for the other source substances your hypothesis is 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 predictions of toxicological properties.

A. Missing supporting information on the formation of common (bio) transformation products – Read across from Octanoic acid

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*"[4]. 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).

In order to confirm the formation of the proposed common hydrolysis product and to assess the impact of the exposure to the parent compounds your supporting information must include information characterising the rate and extent of the hydrolysis of the Substance and of the source substance(s). Supporting information must also include toxicokinetic information on the formation of the common compound.

However, you have only provided a hypothesis that, in general, aldehydes are readily oxidised to organic acids. You have not provided any experimental data or other adequate and reliable information about the (bio)transformation of your Substance.

Therefore, you have not shown that that (bio)transformation of octanal to octanoic acid is sufficiently rapid and complete so as to exclude systemic bioavailability and internal exposure to octanal itself.

In the absence of this information, you have not provided supporting evidence establishing

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

that the proposed common hydrolysis product is formed as assumed in your read-across hypothesis. Therefore, you have not provided sufficient supporting information to strengthen the rationale for the read-across.

B. Missing supporting information – Read across from other aldehydes

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 substance 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).

You claim that the toxicity profile between the source substances and the Subtance are similar. In order to support your reasoning, you have provided data from comparable studies on the source substances and the Substance for the following toxicological properties: acute toxicity, skin irritation, eye irritation, skin sensitisation properties and mutagenicity (*in vitro* gene mutation study in bacteria).

However, limited data on reproductive toxicity are available for melonal and octanoic acid and there is one repeated dose study with heptanal. However, for repeated dose toxicity and for reproductive toxicity there is no comparable data for the Substance. Similarly as regards mutagenicity (In vitro cytogenicity study in mammalian cells or in vitro micronucleus study and In vitro gene mutation study in mammalian cells) there is no bridging data available to allow a comparison of these properties.

Based on the above, there is insufficient data from bridging studies of comparable design and duration to support the predictions.

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

C. Read-across hypothesis contradicted by existing data

Annex XI, Section 1.5. provides that "substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances. The ECHA Guidance[5] indicates that "*it is important to provide supporting information to strengthen the rationale for the read-across*". The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substances. The observation of differences in the toxicological properties between the source substance(s) and the Substance would contradict the hypothesis that the properties of the Substance can be predicted from the data on the source substances. An explanation why such differences do not affect the read-across hypothesis needs to be provided and supported by scientific evidence.

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

The results of the information on repeated dose toxicity obtained with the source substances vary. Specifically, the No-observed-adverse-effect levels (NOAELs) reported in rats after oral exposure vary from 7 mg/kg (reported for nonanal and decanal) to 13 000 mg/kg (reported

[5] Guidance on information requirements and chemical safety assessment (version 6.0, July 2017), Chapter R.6, Section R.6.2.2.1.f

for octanoic acid).

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

B. Predictions for ecotoxicological properties

i. Aquatic toxicity

You have provided the following reasoning for the prediction of aquatic toxicity: *"The three substances are considered to be ecotoxicologically comparable based on structural, physiochemical and ecotoxicological information. It is therefore considered that the three read across materials provide data that can be used to fill data gaps in the octanal data set, therefore read-across is appropriate in order to meet the REACH Annex VII-IX data requirements.".*

You read-across between the structurally similar substances, heptanal EC No. 203-898-4 (CAS No. 111-71-7), nonanal EC No. 204-688-5 (CAS No. 124-19-6) and decanal EC No. 203-957-4 (CAS No. 112-31-2) as source substances 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 to be quantitatively equal to those of the source substance.

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

A. 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 information allowing a comparison of the 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 substance 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).

However, you have provided only effective concentrations (i.e. short-term toxicity in aquatic invertebrates and fish and also algae toxicity) for the source substances to demonstrate

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

similar toxicities to the target Substance. In addition, only effective concentrations of short-term toxicity to aquatic invertebrates and toxicity to algae were provided for the Substance to support your hypothesis on similar toxicities. For activated sludge respiration inhibition testing you have provided only the source study and no other information to support your hypothesis of similar toxicities. However, no further details (i.e. study summaries) on the reported studies were provided.

The data set reported in the technical dossier does not include relevant, reliable and adequate information for the Substance and of the source substance(s) to support your read-across hypothesis.

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.

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 weight of evidence adaptation under 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:

1. Skin sensitisation (Annex VII, Section 8.3)
2. *In vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1
3. *In vitro* cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
4. *In vitro* gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)

Your weight of evidence adaptation raises the same decifiencies 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.

In spite of this critical deficiency, ECHA has nevertheless assessed the validity of your adaptation. Your weight of evidence approaches have specific deficiencies . These deficiencies are set out under the information requirement concerned in the Appendices below.

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.

To fulfil the information requirement, as specified in the Annex VII, Section 8.3., Column 1 to the REACH Regulation, the following aspects must be covered: A) whether the Substance causes skin sensitisation, and B) whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A), in case, the Substance is considered to be a skin sensitiser.

You have adapted the standard information requirement mentioned above according to Annex XI, Section 1.2. of REACH (weight of evidence), based on which you conclude that the Substance is not a skin sensitiser. In support of your argumentation your have provided the following information:

i. in vivo skin sensitisation in guinea pigs, publication, 2001,
ii. in vivo skin sensitisation in guinea pigs, publication, 1985,
iii. in vivo skin sensitisation in guinea pigs, study report, 1973,
iv. Human repeat insult patch test, study report, 1964.

As explained in the Appendix on Reasons common to several requests your Weight of Evidence, 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.

A) Assessment whether the Substance causes skin sensitisation

Information that can be used to support weight of evidence adaptation for information requirement of Section 8.3 at Annex VII includes similar information that is investigated by *in vitro*, *in chemico* and/or *in vivo* test methods. These key investigations include:

- investigation of cell proliferation in the draining lymph nodes (local lymph node assay), investigation of local responses in animals or humans (guinea pig assays or human studies), or investigation of molecular interaction with proteins, inflammatory response in keratinocytes and activation of dendritic cells (*in vitro* and *in chemico* assays).

The sources of information (i. to iv.) provide relevant information, as they aim to provide information on the key investigations. The studies i. and iii. concluded that the Substance is a skin sensitiser, and the studies ii. and iv. concluded that the Substance is not a skin sensitiser. However, the sources of information (studies ii. and iv.) have the following deficiencies affecting their reliability.

i. Incompliant robust study summary for study ii.

Article 3(28) defines a robust study summary as a detailed summary of the objectives,

methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study minimising the need to consult the full study report. Information on the reporting needs are specified in the respective OECD test guidelines under section "Test report". Especially information on dose range finding study, concentrations used for induction and challenge, and detailed results are needed.

In the endpoint study report of study ii., you do not report results of the range finding study, therefore ECHA cannot verify whether appropriate concentrations were used for induction and challenge to conclude that the substance is not a skin sensitiser. Moreover, you state in the dossier that the induction concentration is not specified for the Substance. In addition, you only conclude that the Substance is not a skin sensitiser, however you have not provided detailed study results.

As the study ii. is missing critical elements of the study details, therefore this deficiency significantly affects the reliability of this source of information and therefore its ability to predict the properties of the Substance.

ii. Adequacy of the study iv. for hazard identification

According to the ECHA Guidance[7], "*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*". In the context of a weight of evidence adaptation of standard information requirements, the set of information provided must be adequate for hazard identification.

The study (iv.) seems 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, as it was stated in the dossier that "*The maximum user concentration for Aldehyde C-8 was* [redacted]*%, the concentration tested in HRIPT was* [redacted]*% giving a negative result*" (not stated in the study iv. but within the study ii. under section "*Any other information on results incl. tables*").

Whilst the study (iv.) seems to have been designed to establish safe levels for specific intended uses, it does not investigate the intrinsic properties of the Substance as required for the purpose of hazard identification. In particular, the dose levels used in this study is far lower i.e. [redacted]% than the doses expected to be used for hazard identification purposes. Therefore, the study does not allow to make a conclusion whether the Substance causes skin sensitisation.

Taken together, the relevant sources of information, as indicated above, show contradictory information on whether the Substance is a skin sensitiser. The studies ii. and iv. based on which you consider that the Substance is not a skin sensitiser have major reliability issues in regards to the assessment of intrinsic hazardous property, as either rationale for the dose level selection was missing (study ii) or the study has been performed for safety assessment instead of hazard identification (study iv). Therefore, the weight of the information from the studies i. and ii. are considered stronger in the weight of evidence, than that from studies ii. and iv. Therefore, based on the information provided you, it is not possible to conclude that the Substance is not a skin sensitiser.

Conclusion

[7] ECHA Guidance R.4

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 skin sensitisation studies.

Therefore, your adaptation is rejected and the information requirement is not fulfilled.

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.

Information on the study design

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

2. In vitro gene mutation study in bacteria

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

You have adapted this information requirement by using Weight of Evidence under Annex XI, Section 1.2 of REACH.

You have provided the following source of information to support your adaptation:

i. *In vitro* gene mutation study in bacteria (Florin 1980), equivalent or similar to OECD TG 471, not GLP) with the following strains, TA 98, TA 100, TA 1535 and TA 1537which all gave negative results.

ECHA has assessed this information and identified the following issue:

Annex XI, Section 1.2 states that there may be sufficient weight of evidence "*from several independent sources of information*".

However, you have provided only one source of information.

Irrespective of this deficiency, which in itself leads to the rejection of the adaptation, ECHA has assessed if the provided source of information could alone fulfill the information requirement and found the following deficiencies:

To fulfil the information requirement, the study has to meet the requirements of OECD TG 471[8] (1997).The conditions of OECD TG 471 specify that :

a) The test must be performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101)
b) 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.
c) At least 5 doses must be evaluated, in each test condition.
d) Triplicate plating must be used at each dose level.
e) The number of revertant colonies per plate for the concurrent negative control must be inside the historical control range of the laboratory.
f) The mean number of revertant colonies per plate must be reported for the treated doses and the controls.

The reported data for the study i. you have provided did not include:

a) the required fifth strain, *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).
b) 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.
c) the evaluation of at least 5 doses in each test condition.
d) triplicate plating at each dose level.
e) a negative control with a number of revertant colonies per plate inside the historical control range of the laboratory.
f) data on the number of revertant colonies per plate for the treated doses and the controls.

Therefore your adaptation according to Annex XI, Section 1.2 is rejected. In addition, the study submitted does not *per se* fufill the information requirement.

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, the *in vitro* gene mutation study in bacteria (OECD TG 471) is considered suitable

3. Growth inhibition study aquatic plants

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

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

[8] ECHA Guidance R.7a, Table R.7.7–2, p.557

For the reasons 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.

4. Short-term toxicity testing on aquatic invertebrates

Short-term toxicity testing on aquatic invertebrates is a standard information requirement in Annex VII to REACH.

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

For the reasons 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

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 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 source substances:

i. An *in vitro* cytogenicity ([redacted], 1984), equivalent or similar to OECD 473, not specified GLP, with a source substance Decanal (EC No. 203-957-4)
ii. An *in vitro* cytogenicity ([redacted] 1990), equivalent or similar to OECD 473, not specified GLP, with a source substance (EC No. 204-688-5)
iii. An *in vitro* mammalian cell micronucleus test ([redacted], 1993) , not specified GLP, with a source substance Nonanal (EC No. 204-688-5)

In spite of the critical deficiency explained in Section 2 of the Appendix common to several requests, Annex XI (absence of justification of weight-of-evidence), we have assessed your adaptation:

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.4.2. at Annex VIII includes:

- Detection and quantification of cytotoxicity and the frequency of cells with structural chromosomal aberration(s) or the frequency of micronuclei in cultured mammalian cells (in vitro) or in mammals (in vivo).

The sources of information (i-iii) provide some relevant information on cytotoxicity and the frequency of cells with structural chromosomal aberration(s) or the frequency of micronuclei in cultured mammalian cells.

However, the reliability of sources of information (i-iii) is affected by the deficiency identified and explained under section 1.A of Appendix on Reasons common to several requests (read-across).

In addition, sources of information (i-iii) also have the following deficiencies:

Testing in accordance with OECD TG 473 or OECD TG 487, respectively[9]. requires that the following specifications/conditions have to be met:

- Two separate test conditions must be assessed: in absence of metabolic activation and in presence of metabolic activation.
- 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.
- Data on the cytotoxicity and the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures must be reported.

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

- two separate test conditions,

[9] ECHA Guidance R.7a, Table R.7.7–2, p.557

- a positive control that produced a statistically significant increase in the responscompared with the concurrent negative control.
- data on the cytotoxicity and/or the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures.

In the absence of such information on those critical aspects of the specification/conditions of the provided studies, ECHA cannot evaluate the reliability of the conclusions on cytotoxicity and the frequency of cells with structural chromosomal aberration(s).

Conclusion

Taken together, even if these sources of information provide some information on cytotoxicity and the frequency of cells with structural chromosomal aberration(s) or the frequency of micronuclei in cultured mammalian cells, 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 whether your Substance has or has not the particular dangerous properties foreseen to be investigated *in vitro* cytotoxicity study in mammalian cells or *in vitro* micronucleus study.

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.

Study design

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

2. In vitro gene mutation study in mammalian cells

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

i. Triggering of the study

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

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

The result of the requests for information section section 2 of the Appendix A and section 1 of the Appendix B 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

For Annex VIII, 8.4.3., you have not provided any study with the Substance in your dossier. However, you have adapted this information requirement by using Weight of Evidence under Annex XI, Section 1.2 of REACH.

i. *In vitro* gene mutation study in mammalian cells ([redacted], 1981), equivalent or similar to OECD 476, not GLP, with a source substance Heptanal (EC No. 203-898-4)
ii. *In vivo* mammalian gene mutation test ([redacted]1994), equivalent or similar to OECD 486, not GLP specified, with a source substance Nonanal (EC No. 204-688-5)

In spite of the critical deficiency explained in Section 2 of the Appendix common to several requests, Annex XI (absence of justification of weight-of-evidence), we have assessed your adaptation:

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.4.3 at Annex VIII includes the information that is investigated by the OECD TG 476/490 and OECD TG 488. This includes:

- Detection and quantification of gene mutations (point mutations, frame-shift mutations, small deletions, etc.) including data on the frequency of mutant colonies in cultured mammalian cells (in vitro) or mutant frequency for each tissue in mammals (in vivo).

The source of information (i) provides relevant information on detection and quantification of gene mutation in cultured mammalian cells while the source of information (ii) does not provide this information However, the source of information (i) has deficiencies affecting its reliability as identified and explained under Section 1.A of the Appendix on Reasons common to several requests.

In the absence of such information on those critical aspects of the specification/conditions of the provided studies, ECHA cannot evaluate the reliability of the conclusions on the potential of the Substance to cause gene mutations.

Conclusion

Taken together, even if the source of information (i) provide some information on Detection and quantification of gene mutations, their reliability is affected so significantly that they cannot be taken into consideration in a weight of evidence approach.

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 vitro* gene mutation study in mammalian cells. 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.

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. 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 a standard information requirement under Annex VIII to REACH, if there is no evidence from analogue substances, QSAR or in vitro methods that the Substance may be a developmental toxicant. There is no information available in your dossier indicating that your Substance may be a developmental toxicant.

i. You have adapted the standard information requirement mentioned above according to Annex XI, Section 1.5. of REACH (read-across). In support of your adaptation, you have provided the following study record:One generation reproductive toxicity study ([redacted] 1990), equivalent or similar to OECD TG 421, GLP, with the source substance heptanal (EC No. 203-898-4).

We have assessed the information and identified the following issue:

For the reasons explained under the Section 1.A of the Appendix on Reasons common to several requests, your adaptation according to Annex XI, Section 1.5 is rejected for the analogue heptanal (EC No. 203-898-4).

In addition, to be considered compliant and to generate information concerning the effects of the Substance on male and female reproductive performance as well as specific target organ toxicity, the study has to meet the requirements of EU B.63/OECD TG 421 or EU B.64/OECD TG 422. The criteria of this test guideline include for example

- At least 10 male and 12-13 female animals for each test and control group. However, the study you have provided was conducted only with 10 females for each test group and no male.
- Dosing of the Substance for a minimum of four weeks for males and approx. 63 days for females to cover premating, conception, pregnancy and at least 13 days of lactation. However, in the study you have provided the animals were exposed daily from 7 days prior to cohabitation through to day 4 post partum. Therefore, the study does not have a required exposure duration according to OECD TG 421 because the exposure does not cover two weeks of premating and at least 13 days of lactation.
- Examination of parameters for sexual function and fertility such as duration of gestation, parturition, lactation and weight and histopathology of reproductive organs and tissues. However, those parameters have not been performed in the study you have provided.
- Monitoring of oestrus cycles. However, the oestrus cycles have not been monitored in the provided study.
- Examination of offspring parameters such as anogenital distance,number of nipples/areolae in male pups. However, those offspring parameters investigations have not been performed in the provided study.

Based on the above, the information you provided do not fulfil the information requirement.

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 requested as part of this decision, 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.

4. Activated sludge respiration inhibition testing

Activated sludge respiration inhibition testing is a standard information requirement in Annex VIII to REACH (Section 9.1.4.).

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.

5. Hydrolysis as a function of pH

Hydrolysis as a function of pH is a standard information requirement in Annex VIII to REACH (Section 9.2.2.1).

You have provided the following information:

i. an adaptation under Annex VIII, Section 9.2.2.1., Column 2 with the following justification for data waiving:

> "*Hydrolysis testing is not considered necessary as studies on biodegradability have indicated that the substance will degrade rapidly in the environment and is unlikely to persist.*"

We have assessed this information and identified the following issue:

This information requirement can be adapted according to column 2 of Annex VIII, if the substance is readily biodegradable, or if the substance is highly insoluble in water.

- Ready biodegradability is demonstrated via the results of a compliant OECD TG

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

301 or 310 (Article 13(3) of REACH) study.

The information you provided on Ready biodegradability (Annex VII, Section 9.2.1.1.) to support your adaptation under Annex VIII, Section 9.2.2.1., Column 2 describes the following:

1. the result of OECD 310: "*The test item attained 46% degradation after 28 days and therefore cannot be considered to be readily biodegradable"*
2. the result of OECD 302C: "*The test substance was found to be inherently biodegradable after achieving 77% degradation in an OECD 302C guideline study".*

The provided degradation information does not show that the Substance is readily biodegradable according to the OECD 301 or 310. Furthermore, the OECD 302C only provides information on the inherent biodegradability of the substance, not on its ready biodegradability.

As a result the substance is not shown to be readily biodegradable, and therefore, the applied adaptation is not applicable.

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.

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 a standard information requirement in Annex IX to REACH.

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

- One sub-chronic toxicity: oral (equivalent or similar to OECD TG 408, not specified GLP, Gaunt *et al.* 1983) with the source substance melonal EC No. 203-427-2

We have assessed this information and identified the following issues:

For the reasons explained under the Section 1.A of the Appendix on Reasons common to several requests, your adaptation according to Annex XI, Section 1.5 is rejected for the source substance melonal EC No. 203-427-2

In addition, to be considered compliant and enable concluding whether the Substance has dangerous properties and supports the determination of the No-Observed Adverse Effect Level (NOAEL), a study has to meet the requirements of OECD TG 408. The following key parameters of this test guideline include, among others

1. highest dose level should aim to induce some systemic toxicity, but not death or severe suffering

The highest dose level in the study did not induce any systemic toxicity. Therefore, the dose level selection was too low, and the study does not fulfil the criterion set in OECD TG 408.

Based on the above, the information you provided do not fulfil the information requirement.

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

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, because Substance is a liquid of low vapour pressure.

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

2. Pre-natal developmental toxicity study in one species

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

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

- One developmental toxicity (Narotsky MG. *et al.* 1993), no guideline, not specified GLP, with the source substance octanoic acid EC No. 204-677-5

We have assessed this information and identified the following issues:

For the reasons explained under the Section 1.A of the Appendix on Reasons common to several requests, your adaptation according to Annex XI, Section 1.5 is rejected for the source substance octanoic acid EC No. 204-677-5

In addition, In order to be considered compliant and enable assessing if the Substance is a developmental toxicant, the study has to meet the requirements of OECD TG 414. The criteria of this test guideline include e.g.

- testing of at least three dose levels and a concurrent control.

  However, the study you have provided was conducted only with two dose levels,

- 20 female animals with implantation sites for each test and control group.

  However, The study you have provided was conducted with 15 pregnant females in the control group, 11 at the low dose and 9 at the high dose.

- examination of the dams for weight and histopathology of the thyroid gland, thyroid hormone measurements, gravid uterus weight, uterine content, /body weight of the dams/clinical signs of the dams.

  However, in the study you have provided, the gravid uterus weight has not been measured and uterine content has not been examined.

- examination of the foetuses for sex and body weight, external, skeletal and soft tissue alterations (variations and malformations), number of resorptions and or live foetuses/, measurement of anogenital distance in live rodent foetuses.

  However, in the study provided, this examination has not been recorded and the anogenital distance in live rodent foetuses has not been measured.

Based on the above, the information you provided do not fulfil the information requirement.

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

Information on 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[11] administration of the Substance.

3. Long-term toxicity testing on aquatic invertebrates

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

You have provided the following information:

- 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:

  In accordance with REACH Regulation (EC) No 1907/2006, Annex XI, Section 3, exposure of aquatic organisms to octanal (CAS No. 124-13-0) is absent or not significant and the testing for chronic toxicity towards aquatic invertebrates is therefore omitted. The

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

registered substance is readily biodegradable (75% biodegradation after 28 days; OECD 301F), therefore octanal does not persist in the environment. The substance is only partially miscible in water (0.1 mass % over the temperature range from 0 to 90°C), therefore the aquatic environment is not expected to be a main pathway for exposure to this substance. In addition, the sorption to sediment, soil, and other organic matter is moderate, based on a predicted log Koc of 2.63 (QSAR), and the sediment/soil compartment is not expected to be a major route of exposure for this substance. The vapour pressure of the octanal is 148.29 Pa at 25 °C, thus air is a relevant compartment for the distribution of the compound. In fact, octanal is a fragrance substance incorporated into a variety of fragranced products. It is used in industrial, professional and consumer settings. Furthermore, octanal has a low potential for bioaccumulation based on a log Kow ≤ 4.5 (log Kow = 3.5) and an estimated BCF of 94.69 L/kg wet-wt (QSAR). Short-term aquatic toxicity data is available for all three trophic levels (fish, aquatic invertebrates, algae). The data either is for the registered substance itself or read across from the structural analogue substances heptanal and nonanal. The short-term toxicity to fish showed a moderate toxicity (LC50 (14-d) = 7.9 mg/L). Based on the aquatic data set, read across from heptanal and nonanal, the lowest acute effects were seen in aquatic invertebrates with an LC50 (48 h) of 1.54 mg/L for nonanal, which was used for the PNEC derivation. The toxicity study with algae showed an ErC50 (72 h) of 2.9 mg/L (heptanal) and a NOEC of 0.92 mg/L. The risk characterization for octanal indicated no risk to the aquatic environment (RCR < 1).

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).

For the sake of completeness, ECHA also evaluated your adaptation under Annex XI, Section 3.2(a) (Substance-tailored exposure-driven testing).

Under Annex XI, Section 3, this information may be omitted based on the exposure scenario(s) developed in the Chemical Safety Report. The justification must be based on a rigorous exposure assessment in accordance with Annex I, Section 5 and must meet the following criteria:

a) It can be demonstrated that all the following conditions are met:
   i. the absence or no significant exposure in all scenarios of the manufacture and all identified uses referred to in Annex VI, Section 3.5., and
   ii. a PNEC can be derived from available data, which:
      - must be relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes and therefore must be based on reliable information on the hazardous properties of the substance on at least three trophic levels;
      - must take into account the increased uncertainty resulting from the omission of the information requirement, in this case by selecting an appropriate assessment factor (AF) as described in ECHA Guidance R.10.3.
   iii. the ratio between the results of the exposure assessment (PECs) and the PNEC are always well below 1

For the reasons explained under request A.1 and A.2, your dossier does not include reliable information on the hazardous properties of the substance on at least three trophic levels.

Therefore, you have not demonstrated that an appropriate PNEC can be derived and your adaptation is rejected.

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.

4. Long-term toxicity testing on fish

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

You have provided the following information:

- 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:

  In accordance with REACH Regulation (EC) No 1907/2006, Annex XI, Section 3, exposure of aquatic organisms to octanal (CAS No. 124-13-0) not significant and the testing for chronic toxicity towards fish is therefore omitted. The registered substance is readily biodegradable (75% biodegradation after 28 days; OECD 301F), therefore octanal does not persist in the environment. The substance is only partially miscible in water (0.1 mass % over the temperature range from 0 to 90°C), therefore the aquatic environment is not expected to be a main pathway for exposure to this substance. In addition, the sorption to sediment, soil, and other organic matter is moderate, based on a predicted log Koc of 2.63 (QSAR), and the sediment/soil compartment is not expected to be a major route of exposure for this substance. The vapour pressure of the octanal is 148.29 Pa at 25 °C, thus air is a relevant compartment for the distribution of the compound. In fact, octanal is a fragrance substance incorporated into a variety of fragranced products. It is used in industrial, professional and consumer settings. Furthermore, octanal has a low potential for bioaccumulation based on a log Kow ≤ 4.5 (log Kow = 3.5) and an estimated BCF of 94.69 L/kg wet-wt (QSAR). Short-term aquatic toxicity data is available for all three trophic levels (fish, aquatic invertebrates, algae). The data either is for the registered substance itself or read across from the structural analogue substances heptanal and nonanal. The short-term toxicity to fish showed a moderate toxicity (LC50 (14-d) = 7.9 mg/L). Based on the aquatic data set, read across from heptanal and nonanal, the lowest acute effects were seen in aquatic invertebrates with an LC50 (48 h) of 1.54 mg/L for nonanal, which was used for the PNEC derivation. The toxicity study with algae showed an ErC50 (72 h) of 2.9 mg/L (heptanal) and a NOEC of 0.92 mg/L. The calculated PEC/PNEC ratios for the freshwater and marine compartment were < 1 for all uses. In conclusion, the environmental exposure assessment for the substance indicates no risk for the aquatic compartment (all RCR < 1; please refer to Chapter 9 and 10 of the Chemical Safety Report for detailed information).

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).

For the sake of completeness, ECHA also evaluated your adaptation under Annex XI, Section

3.2(a) (Substance-tailored exposure-driven testing).

Under Annex XI, Section 3, this information may be omitted based on the exposure scenario(s) developed in the Chemical Safety Report. The justification must be based on a rigorous exposure assessment in accordance with Annex I, Section 5 and must meet the following criteria:

a) It can be demonstrated that all the following conditions are met:
   i. the absence or no significant exposure in all scenarios of the manufacture and all identified uses referred to in Annex VI, Section 3.5., and
   ii. a PNEC can be derived from available data, which:
      - must be relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes and therefore must be based on reliable information on the hazardous properties of the substance on at least three trophic levels;
      - must take into account the increased uncertainty resulting from the omission of the information requirement, in this case by selecting an appropriate assessment factor (AF) as described in ECHA Guidance R.10.3.
   iii. the ratio between the results of the exposure assessment (PECs) and the PNEC are always well below 1

For the reasons explained under request A.1 and A.2, your dossier does not include reliable information on the hazardous properties of the substance on at least three trophic levels.

Therefore, you have not demonstrated that an appropriate PNEC can be derived and your adaptation is rejected.

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.

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[12].

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[13].

[12] https://echa.europa.eu/practical-guides
[13] https://echa.europa.eu/manuals

Appendix E: Procedure

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

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

The compliance check was initiated on 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 requests.

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 clarify your request and to submit supporting documentary evidence. However, you did not reply to ECHA's request within given three week notification time. Therefore, ECHA did not amend the original 24 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[14] 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)[15]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[16]

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[17]

[14] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[15] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[16] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[17] 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]

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.