~~Confidential~~

Helsinki, 13 April 2022

Addressees
Registrants of JS_203_983_6 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
04/12/2014

Registered substance subject to this decision ("the Substance")
Substance name: Dodecanal
EC number: 203-983-6

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

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 test performed for the information requirement of 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

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

1. 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)

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 appendix/appendices:

- Appendix entitled "Reasons common to several requests";

- Appendix/Appendices entitled "Reasons to request information required under Annexes VII to IX of REACH", respectively.

Information required depends on your tonnage band

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

- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa;
- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa;

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

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 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.)
- In vivo mammalian erythrocyte micronucleus test (Annex X, Section 8.4., column 2)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

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

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 five read-across justification documents in IUCLID Section 13.

In your dossier, you read-across between Heptanoic acid EC No: 203-838-7 (CAS 111-14-8) and also other aldehydes including undec-10-enal EC No: 203-973-1 (CAS 112-45-8), nonanal EC No. 204-688-5 (CAS 124-19-6), 2,6-dimethylhept-5-enal EC 203-427-2 (CAS106-72-9) and 2-methylhendecanal EC No. 203-765-0 (CAS 110-41-8) as source substances and the Substance as target substance.

You have provided the following reasoning for the prediction of toxicological properties: "*The Target Substance and Source Substance have been characterised using the categories and databases present in the OECD [Q]SAR Toolbox. From the profiling, it can be seen that the two substances share structural similarities and also 'mechanistic action' similarities which are both general and endpoint specific."* You also claim that " *The data (key physical chemical parameters and toxicological data available for both substances) although performed under slightly different test conditions and therefore cannot be directly compared, indicates that the results from the Source Substance are anticipated to be comparable to that of the Target Substance and are considered to be suitable for both classification and labelling and any required risk assessment"* You conclude that *" the output from the OECD [Q]SAR Toolbox shows that the profiles of the Target Substance and the Source Substance are sufficiently*

[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

similar such that available toxicological data from the Source Substance can be used to address the several endpoints in the REACH registration dossier for the Target Substance".

To support your read-across justification, you have provided in your dossier:
- Structural information on the Substance and the source substances,
- Information on physicochemical properties,
- An assessment of the structural characteristics and mechanistic alerts obtained from the QSAR Toolbox v2.3.0 for the Substance and for each of the source substances,
- Data on acute toxicity to compare the toxicological properties of the substances.

Based on the above, ECHA understands that you used the QSAR Toolbox for the identification of source substances and use information on these source substances to 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.
In your comment to the draft decision, you read-across between Undecanal (EC 203-972-6 (CAS 112-44-7) as source substance and the Substance as target substance. You have provided the following reasoning for the prediction of toxicological properties: *'the target substance and source substance have the same expected mode of action and similar physicochemical properties relevant for the read-across endpoints*'.

To support your read-across justification, you have provided:
- Structural information on the Substance and the source substance

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

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*" (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.). The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

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

While the information on acute toxicity of the substances available in your dossier may provide support that the source substances have similar properties as regards acute toxicity , these data do not inform on the genotoxicity, sexual function, fertility and developmental properties of the target and source substances. Therefore, this information does not provide relevant information for the Substance and the source substances to support your read-across hypothesis.
For the endpoints listed above, you have provided no bridging studies either in your dossier or in your comment allowing to compare the properties of the Substance and of the source substances.

In the absence of such information, you have not established that the Substance and 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.

B. Inadequate read-across hypothesis

A read-across hypothesis must be provided, establishing why a prediction for a toxicological or ecotoxicological 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 based on the structural similarity between the source substance(s) and the Substance, which you consider a sufficient basis for predicting the properties of the Substance.

However, there are structural differences between the Substance and source substances. The source substance 2,6-dimethylhept-5-enal (EC.No 203-427-2) is a branched and unsaturated aldehyde and the source substance Heptanoic acid (EC. No. 203-838-7) is an aliphatic acid whereas the Substance is a linear saturated aldehyde.

You did not discuss this dissimilarity between the source substances and the substance and the impact on the toxicological properties.

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

B. Conclusions on the read-across approach

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

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

1. 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 provided an adaptation according to Annex XI, Section 1.5 (Grouping of substances and read-across approach) together with the following studies:

i. *In vitro* gene mutation in bacteria ([redacted], 2007) as a key study, according to the OECD TG 471, GLP) with the source substance undec-10-enal EC. No 203-973-1 (CAS 112-45-8) with the following strains, TA 98, TA 100, TA 1535, TA 1537, and TA 102 which all gave negative results,
ii. *In vitro* gene mutation in bacteria ([redacted], 1999) as a supporting study, according to the OECD TG 471, GLP, with the source substance 203-765-0 / 2-methylundecanal EC.No 203-765-0 (CAS 110-41-8), with the following strains TA 98, TA 100, TA 1535, TA 1537, and TA 102 which all gave negative results.

We have assessed this information and identified the following issue:

For the reasons explained under the section 1, your adaptation according to Annex XI, Section 1.5 is rejected for the source subtances undec-10-enal EC. No 203-973-1 and 2-methylundecanal EC.No 203-765-0.

Therefore, the information requirement is not fulfilled.

In your comments to the draft decision, you state that information on *In vitro* gene mutation study in bacteria test is available in the Research Institute for Fragrance Materials (RIFM) database and that you will provide this information in an updated of your registration dossier. Please note that this decision does not take into account 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.

Study design

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

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* cytogenicity/chromosome aberration study in mammalian cells (Eckl. Et al. 1993), key study, no guideline, not specified GLP, with the source substance Nonanal EC. No 204-688-5
ii. An *in vivo* Mammalian erythrocyte micronucleus test ([redacted] 2007), according to OECD TG 474, GLP, with the source substance Undec-10-enal EC. no 203-973-1

ECHA has assessed this adaptation and identified the following issues:

1. Read-across rejection

For the reasons explained under the section 1 of the Appendix on Reasons common to several requests , your adaptation according to Annex XI, Section 1.5 is rejected for the source subtances Nonanal EC. No 204-688-5 and Undec-10-enal EC. No 203-973-1 (studies i and ii.)

2. Non-compliant study

In addition, 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 (OECD TG 473).
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 (OECD TG 473).

The reported data for the study i 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(OECD TG 473).
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 (OECD TG 473).

Therefore, the study i. does not have adequate and reliable coverage of the key parameters of the OECD TG 473.

Therefore, the information requirement is not fulfilled.

In your comments, you stated that information on *In vitro* Micronucleus study (OECD 487) and *In vivo* Micronucleus study (OECD 474) are available in the RIFM database and that you will provide this information in an updated of your registration dossier. Please note that this decision does not take into account 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.

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 1 the Appendices A and B.

The result of the requests for information in section 1 the Appendices A and 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

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), not GLP, with the source substance nonanal EC. No 204-688-5 (CAS 124-19-6)

ECHA has assessed this adaptation and identified the following issues:

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.

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 to perform the requested study.

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 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 in your dossier the following sources of information with source substances:

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

In your comment on the draft decision, you have provided brief summaries for the following additional sources of information:

iii. a screening study (no reference) OECD TG 422, GLP, with the source substance Undecanal EC. 203-972-6,
iv. a long term study (no reference), OECD TG 408, with the Substance.

You specify that your registration dossier will be updated to include the additional sources of information iii. and iv along with a read-across justification document for study iii. You also refer to "*the scheduled OECD 414 study that will be conducted by the lead registrant in rats with the registered substance*". However, this strategy relies essentially on data which is yet to be generated and/or provided, therefore it can not be considered as source of information in your weight-of-evidence adaption. 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).
Based on the presented sources of information, you argue that the available data gives sufficient information to conlude on the reproductive toxicity because: "*Valid studies are available for the source substances Heptanoic acid and 2,6-dimethylhept-5-enal . Dose levels of 200 mg/kg bw/day of heptanoic acid and of 300 mg/kg bw/day of the test material (2,6-dimethylhept-5-enal) had no significant adverse effects on the reproductive performance of female Sprague-Dawley rats or the growth or development of their offspring***."**

Annex XI, Section 1.2 states that there may be sufficient weight of evidence 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 adaptation. However, 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 investigated by the required study.

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.

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.

1) *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 level 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. The sources of information (iii - iv) only provide high level statements on the reproductive organs. In addition to this, the source of information (iv) describes some results on male fertility. the limited information provided in your comments to the draft decision I still not sufficient to report 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. Furthermore, the sources of information (i - ii) 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 deficiency:

- 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. Further, for study iii., you have not yet provided a read-across justification and therefore the validity of the read-across cannot currently be assessed. As a result, 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.

2) 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-iii) 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. The source of information (iv) does not provide information on those parameters.

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

3) 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. The source of information (iii) provide high level statement on those parameters and the source of information(iv) does not provide information on those parameters.

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

As a result of all these deficiencies relating to 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.

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[4] administration of the Substance.

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

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

1. 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.

According to Annex IX, Section 8.7., Column 2, third indent, the study does not need to be conducted if the substance is of low toxicological activity. This needs to be demonstrated with three concomitant criteria, two of them being :

- that there is no evidence of toxicity seen in any of the tests available;
- that it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure.

You justified your adaptation by stating that the Substance is of very low toxicity. You have substantiated your claim of low toxicity by referring to data obtained in the one generation study in rats with the source substances 2,6-dimethylhept-5-enal and Heptanoic acid.

We have assessed the information and identified the following issue:

As already mentioned under section B.3, the provided data for screening for reproductive /development toxicity are rejected. Therefore, they can not be taken into account in order to support the low toxicity of the Substance. Furthermore, you have not provided any toxicokinetic data to show that there is no systemic absorption.

Based on the above, your adaptation is rejected and the information requirement is not fulfilled.

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

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[5] administration of the Substance.

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 Dodecanal.

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

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

assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018).

Your adaptation is therefore rejected.

On this basis, the information requirement is not fulfilled.

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

Study design
The Substance is difficult to test due to the low water solubility (1.6 mg/L) and adsorptive properties Log Kow (4.9). OECD TG 211 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 211. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

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 Dodecanal.

We have assessed this information and identified the following issue:

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

Your adaptation is therefore rejected.

On this basis, the information requirement is not fulfilled.

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

Study design

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

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[6].

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[7].

[6] https://echa.europa.eu/practical-guides
[7] 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 from 18 to 27 months (best case) or up to 40 months (worst case) from the date of adoption of the decision. You justify the extension by referring to lab capacities of main Contract Research Organisations (CROs) and also to the fact that the substance is difficult to test. You further justify the need to extent the deadline to 40 months by referring to the ECHA Guidance on Registration, Section 7.2. You consider that "*an additional deadline of 12 month (after the final testing reports are received) should be applied as the requested data would trigger the rework of the current CSR*". However, the above section of the ECHA Guidance on Registration refers to relevant maximum deadlines for spontaneous update in relation to the conditions set out under Article 22(1) of REACH. Under Article 22(2) of REACH, an update of the registration dossier to provide the information required by the decision made in accordance with Artcile 40 must be provided within the deadline specified in that decision. Therefore, your request for an additional extension of 12 months is irrelevant.

ECHA has assessed the information provided as part of your justification and has granted the request and extended the deadline to 27 months.

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[8] 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)[9]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[10]

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[11]

[8] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[9] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[10] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[11] 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.