~~Confidential~~

Helsinki, 05 November 2021

Addressees
Registrant(s) of JS_701-303-7_Full as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
19/09/2019

Registered substance subject to this decision ("the Substance")
Substance name: Oligomerisation products of sucrose with ethylene oxide and methyloxirane
EC number: 701-303-7
CAS number: NS

Decision number: Please refer to the REACH-IT message which delivered this communication (in format CCH-D-XXXXXXXXXX-XX-XX/F)

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of **13 May 2024**.

Requested information must be generated using the Substance unless otherwise specified.

Information required from all the Registrants subject to Annex VII of REACH

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

A. 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

4. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: OECD TG 203)

B. 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 request(s) are explained in the following appendices:

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

Information required depends on your tonnage band

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

- the information specified in Annexes VII, 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 Christel Schilliger-Musset, Director of Hazard Assessment

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

Appendix on Reasons common to several requests

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

You 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.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)
- Long-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1., column 2)

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

Grouping of substances and read-across approach

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

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

A. Scope of the grouping

In your registration dossier you refer to the sub-category 1 of Non Longer Polymers (NLP) category. You have provided in IUCLID sections 7.5.1. and 7.8.2, a document, entitled "[redacted]), referred to as justification document. In this document you have addressed chemical and structural considerations, toxicokinetics and (eco)toxicological properties of the substances. In addition, in section 13 of IUCLID, you have provided, as separate attachments, two documents, entitled "[redacted]). ECHA notes that in your justification document you refer to these documents as "*read across assessment reports* […] *previously completed* […]" and that "*This [2017] read across justification report aligns the original read across justifications with the new 2017 RAAF framework using available data and reports".* Therefore, ECHA solely based its evaluation on the information provided in the justification document (2017).

[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

In the read-across justification document you list the substances below as members of the sub-categoty 1 "Ether-linked substances":

- Sucrose, propoxylated (EC: 500-029-3) - hereafter referred to "source substance [1]"
- Sucrose, ethoxylated and propoxylated (EC: 607-907-6)
- D-Glucitol, propoxylated (EC: 500-118-7), hereafter referred to "source substance [2]"
- Pentaerythritol, ethoxylated (EC: 500-071-2)
- Pentaerythritol, propoxylated (EC: 500-030-9)
- Propylidynetrimethanol, ethoxylated (EC: 500-110-3)
- Propylidynetrimethanol, propoxylated (EC: 500-041-9)
- Ethane- 1,2-diol, propoxylated (EC: 500-078-0), hereafter referred to "source substance [3]"
- Propane-1,2-diol, propoxylated (EC: 657-256-7)
- 2,2'-Oxydiethanol, propoxylated (EC: 500-031-4)
- 2,2'-Oxybisethanol, ethoxylated and propoxylated (EC: 610-559-8)
- Glycerol, ethoxylated (EC: 500-075-4)
- Glycerol, propoxylated (EC: 500-044-5), hereafter referred to "source substance [4]"
- 2,2'-Iminodiethanol, propoxylated (EC: 500-085-9)
- 2,2',2''-Nitrilotriethanol, propoxylated (EC: 500-094-8), hereafter referred to "source substance [5]".

You have provided the following reasoning for the grouping:

All substances are UVCBs. "*The NLPs in this category are formed primarily from propoxylation or ethoxylation of the hydroxyl functionalities of the core molecules*". As a result, "*short chain oligomers formed from core molecules containing multiple hydroxyl or amino functional groups or a combination of the two"* are formed.

Further you state that the distinguishing feature among the NLPs within this category is the ether linkages between the core molecules and the ethoxy or propoxy repeating units. The core molecules are primarily sugars and small aliphatic polyols with an exception of two category members with an amine as the core structure (2,2'-Iminodiethanol, propoxylated (EC: 500-085-9) and 2,2',2''-Nitrilotriethanol, propoxylated (EC: 500-094-8). However, you state that since they form ether linkages, the two amines are part of the category.

You have reported the number of the repeating propoxylated and ethoxylated units as ranging from 1 to 18.

ECHA understands that this is the applicability domain of the sub-categoty 1 "Ether-linked substances" and your predictions are assessed on this basis.

In addition, for the Sub-chronic toxicity study (90-day) and for Pre-natal developmental toxicity study, you have provided information conducted with the analogue substance Ethylenediamine, ethoxylated and propoxylated (EC: 500-047-1), hereafter referred as "source substance [6]", that is not part of the sub-categoty 1 "Ether-linked substances".

B. Predictions for (eco)toxicological properties

For the sub-category 1 "Ether-linked substances", you have provided the following reasoning for the prediction of (eco)toxicological properties:

In the justification document you sate "*Since the reactive sites of all the molecules in this group are either ethoxylated or propoxylated, the formed oligomers are expected to have similar properties that are primarily determined by the nature of these alkoxyl repeating units"*. In addition, you claim that if absorbed, the category members are "*expected to be dealkoxylated to yield the core substances and ethylene glycol and propylene glycol".*

*Y*ou have supported your reasoning with assumptions for the toxicokinetic behavior (absorption, metabolism and excretion), based on the physicochemical properties of the category members. You further provide a high level summary for acute, repeated dose toxicity and genotoxicity of the core molecules of the category members. Based on this you state that "*this data confirms a pattern of similar physico-chemical, environmental, and toxicological properties amongst the category substances*".

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

You have not provided any justification for the source substance [6] (EC: 500-047-1).

ECHA notes that with regards to prediction(s) of (eco)toxicological properties there are issues that are common to all information requirements under consideration, common to some information requirements and also issues that are specific for these information requirements individually. Altogether they result in a failure to meet the requirement of Annex XI, 1.5. The common issues are set out here, while the specific issues are set out under the information requirement(s) concerned in the Appendices below.

(i) Missing supporting information to compare properties of the category members

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 other category members.

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

For the toxicological properties, ECHA notes that while the source substances within Category 1 "Ether-linked substances" provide information on the etoxylated and propoxylated moieties, they are largely structurally unrelated to the Substance when it comes to the core moiety – none of the source substances bear sucrose as a core substance. Therefore, supporting information would be needed to verify the hypothesis that the substances have the same type of effects or lack of effects despite their structural differences. The data set reported in the technical dossier does not include any experimental data of comparable design and duration

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

for the Substance to compare the genotoxicity in mammalian cells, systemic toxicity and reproductive toxicity properties between the Substance and the source substances.

Further, you indicated that upon absorption the substances are expected to be dealkoxylated to yield the core structure and propane-1,2-diol (propylene glycol) and/or ethane-1,2-diol (ethylene glycol) and provided information on the dealkoxylation metabolic sequence with alcohol ethoxylates (Drotman 1980, Talmadge 1994). However, you did not provide any supporting information characterising the rate of the dealkoxylation in physiological conditions. In addition, ECHA also notes that there are ether bonds not only between the core molecules and the ethoxy or propoxy repeating units but between the repeating units themselves. You did not discuss why breakage of the ether bonds along the repeating units is not expected. Due to above, you have not considered the potential impact on non-metabolised parent compound or metabolites other then the core molecules, propylene and/or ethylene glycol on the toxicity. Lack of this information further emphasises the need for the relevant, reliable and adequate information allowing to compare the properties of the category members.

For the ecotoxicological properties, while you provided data on aquatic toxicity with the source substances 1 and 2 both bearing an alcohol core, including sucrose for source substance 1, both of these substances contain only propoxylated moieties. Therefore, these substances do not inform on the properties driven by ethoxylated units present in the Substance bearing an alcohol core propoxylated and ethoxylated moieties.

Further, in your justification document you state that source substance 2 is identified "*as the most appropriate representative substance to address chronic aquatic toxicity (…) as it is a heavily branched polyol, which also exhibits high surface activity*."

ECHA notes that, the Substance, in contrast to source substance 2, exhibits no surface activity as indicated in the technical dossier ("*determined surface tension (…) was higher than 60 mN/m, the test item can be c1assified as not surface active*." Surface activity is a critical feature in regards to aquatic toxicity testing. You have not provided justification as to why prediction of the properties of the Substance is possible despite these differences in surface activity.

Therefore, you have not provided justification or supporting information on how and why the toxicity to aquatic organisms can be predicted based on these two source substances.

In the absence of information addressing the elements listed above, and without relevant, reliable and adequate information allowing to compare the properties of the category members, it is not possible to confirm that the Substance and the source substances cause the same type of effects.

(ii) Adequacy and reliability of source studies

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

Specific reasons why your source studies do not meet these criteria are explained further in Appendix C, Section 1. Therefore, no reliable predictions can be made for this information requirement.

(iii) Absence of documentation

Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide a justification for the read-across including a hypothesis, explanation of the rationale for the prediction of properties and robust study summary(ies) of the source study(ies).[5]

You have provided studies conducted with the source substance [6] (EC: 500-047-1), which is not part of the categoty 1 "Ether-linked substances". You have not provided documentation as to why this information is relevant for your Substance. In the absence of such documentation, ECHA cannot verify that the developmental toxicity properties of your Substance can be predicted from the data on the source substance [6].

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

For the reasons listed above, the predictions from source substance [6] fail.

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.

[5] ECHA Guidance, Chapter R.6: Section R.6.2.6.2

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

1. Growth inhibition study aquatic plants

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

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

i. Algal inhibition test (key study; OECD TG 201, GLP) performed with source substance [1]

As explained in the Appendix on general considerations your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

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

Study design

To fulfil the information requirement for the Substance, Freshwater Alga and Cyanobacteria, Growth Inhibition Test (test method OECD TG 201) is the most appropriate (ECHA Guidance R.7.8.2.).

For multi-constituents/UVCBs, the analytical method must be adequate to monitor qualitative and quantitative changes in exposure to the dissolved fraction of the test material during the test (e.g. by comparing mass spectral full-scan GC or HPLC chromatogram peak areas or by using targeted measures of key constituents or groups of constituents).

If you decide to use the Water Accommodated Fraction (WAF) approach, in addition to the above, you must:

- use loading rates that are sufficiently low to be in the solubility range of most constituents (or that are consistent with the PEC value). This condition is mandatory to provide relevant information for the hazard and risk assessment (ECHA Guidance, Appendix R.7.8.1-1, Table R.7.8-3);
- provide a full description of the method used to prepare the WAF (including, among others, loading rates, details on the mixing procedure, method to separate any remaining non-dissolved test material including a justification for the separation technique);
- prepare WAFs separately for each dose level (i.e. loading rate) and in a consistent manner.

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

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

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

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

i. *In vitro* chromosomal aberration test (OECD TG 473, GLP), performed with source substance [2], giving negative results
ii. *In vitro* chromosomal aberration test (OECD TG 473, GLP), performed with source substance [5], giving negative results

As explained in the Appendix on Reasons common to several requests, your adaptation in accordance with Annex XI, Section 1.5. is rejected. Therefore, the information requirement is not fulfilled.

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

Study design

To fulfil the information requirement for the Substance, both *in vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) and *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 a standard information requirement in Annex VIII to REACH in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

i. Triggering of the study

Your dossier contains (i) a negative result for *in vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.) and inadequate data for *in vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.), performed with the source substances which is rejected for the reasons provided in Appendix B, Section 1.

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

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

(i) *In vitro* gene mutation study in mammalian cells (OECD TG 476, GLP), performed with source substance [5], giving negative results.

As explained in the Appendix on Reasons common to several requests, your adaptation in accordance with Annex XI, Section 1.5. is rejected. Therefore, the information requirement is not fulfilled.

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

Study design

To fulfil the information requirement for the Substance, both the *in vitro* mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) and 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.

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

(i) Screening for reproductive/developmental toxicity study (key study; according to OECD TG 421, GLP) performed with source substance [5].

As explained in the Appendix of Reasons common to several requests, your adaptation in accordance with Annex XI, Section 1.5. is rejected. Therefore, the information requirement is not fulfilled.

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

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[6] administration of the Substance

4. Short-term toxicity testing on fish

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

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

i. Short-term toxicity to fish (key study; similar to OECD TG 203, non GLP) performed with source substance [1]

As explained in the Appendix on general considerations your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

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

Study design
To fulfil the information requirement for the Substance, fish acute toxicity test (test method OECD TG 203) is the most appropriate (ECHA Guidance R.7.8.2.).

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

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

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

A Sub-chronic toxicity study (90 day) is a standard information requirement under Annex IX to REACH.

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

(i) Short-term (28-day) repeated dose toxicity study in rats in rats (OECD TG 407, GLP) performed with source substance [5]

(ii) Sub-chronic (90-day) repeated dose toxicity study (OECD TG 408, GLP), performed with source substance [6]

We have assessed this information and identified the following issue(s):

A. You have adapted this information requirement by using a read-across approach under Annex XI, Section 1.5. As explained in the Appendix on Reasons common to several requests your adaptation is rejected.

As indicated in the Appendix on Reasons common to several requests, there are issue(s) with source study(ies).

B. To be considered adequate, the study has to meet the information requirement, a study must comply with the OECD TG 408 (Article 13(3) of REACH). The specifications of this OECD TG include, among other elements, that dosing of the Substance should occur daily for a period of 90 days until the scheduled termination of the study. The repeated dose oral toxicity (28-day) study you provided has an exposure duration of 28 days. Therefore, study (i) does not provide adequate to cover the information requirements.

In the comments to the draft decision you express your intention to "*take a step-wise approach to improve the dossier quality and grouping the NLP polyols*". As a first step you plan to perform an OECD TG 422 study with the Substance as well as with "*other representative substances*" of the NLP group which you intend to use as bridging information to strengthen the read-across/grouping approach and "*further inform which substances will serve as source substances in the NLP polyols group*". Based on this, as a second step, you will perform 90-day studies with the chosen source substances.

ECHA acknowledges your intentions to improve the toxicological profile of the Substance and your plans to refine your read-across approach. As indicated in your comments, this refined adaptation relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline

Based on the above, the information requirement is not fulfilled.

Study design

Referring to the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity, because the Substance is non volatile liquid (vapor pressure 0.0000119 hPa at 20° C). 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 by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. You have provided the following information

i. Pre-natal developmental toxicity study in rat (OECD TG 414, GLP), performed with source substance [3]
ii. Pre-natal developmental toxicity study in rat (OECD TG 414, GLP), performed with source substance [6]

As explained in the Appendix of Reasons common to several requests, your adaptation in accordance with Annex XI, Section 1.5. is rejected.

In the comments to the draft decision you express your intention to "*take a step-wise approach to improve the dossier quality and grouping the NLP polyols*" by performing bridging studies (OECD TG 422) which addressing both repeated dose toxicity and reproductive/developmental toxicity endpoints. You state that the "*results from the OECD TG 422 studies will inform on the way forward for the registered substance*".

ECHA acknowledges your intentions to improve the toxicological profile of the Substance and your plans to refine your read-across approach. As indicated in your comments, this refined adaptation relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

Therefore, the information requirement is not fulfilled.

Study design

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[7] 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 adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. You have provided the following information:

i. Daphnia magna reproduction test (key study; OECD TG 211, GLP) performed with source substance [2]

As explained in the Appendix on general considerations your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

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

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

Study design

To fulfil the information requirement for the Substance, the *Daphnia magna* reproduction test (test method OECD TG 211) is the most appropriate (ECHA Guidance R.7.8.2.).

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 Annex IX of Regulation (EC) No 1907/2006, it is laid down that long-term toxicity testing shall be proposed by the registrant if the chemical safety assessment indicates the need to investigate further the effects on aquatic organisms. According to Annex I of this regulation, the chemical safety assessment triggers further action when the substance or the preparation meets the criteria for classification as dangerous according to Directive 67/548/EEC or Directive 1999/45/EC or is assessed to be a PBT or vPvB. The hazard assessment of the test substance reveals neither a need to classify the substance as dangerous for the environment, nor is it a PBT or vPvB substance, nor are there any further indications that the substance may be hazardous to the environment. Therefore, and for reasons of animal welfare, a long-term toxicity study in fish is not provided."*

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.

In the comments on the draft decision, you do not agree to perform the requested study. Instead, you propose to provide an adaptation for this standard information requirement after performing the other aquatic toxicity studies also requested in this decision (requests A.1, B.4 and C.3). You indicate that, depending on the outcome of the hazard assessment using the existing and new aquatic toxicity studies, you intend to adapt this information requirement either 1) on the basis of *"no hazard identified";* or 2) under Annex XI Section 3.1 *"based on a measured L(E)C50 or NOEC"* and subsequent PNEC derivation, which "*may be compared with the results of an exposure assessment (which will be prepared at that stage, if this becomes necessary)*".You conclude that this approach "*is a promising way of avoiding an animal experiment*". Moreover, you refer in your comments to the principle of testing as last resort in Article 25(1) of the REACH Regulation.

ECHA has assessed the information provided in the comments on the draft decision and identified the following issues:

1) While you did not specify the legal basis for omitting the requested study based on a potential "no hazard" conclusion, ECHA understands that you refer to Column 2 Annex IX, Section 9.1. However, as explained above, the Column 1 information requirement cannot be

waived based on Column 2 referring to the Chemical Safety Assessment.

2) You further indicate your intention to alternatively adapt this standard information requirement based on exposure considerations, according to Annex XI, Section 3 of REACH regulation. In particular, if a PNEC can be derived from the results of the available and new aquatic toxicity studies with the Substance (requests A.1, B.4 and C.3), you propose to conduct a full and comprehensive exposure assessment and risk characterisation to demonstrate lack of risk to the environment.

The information in your comments is not sufficient for ECHA to make an assessment because you have only provided an intention to adapt, which relies on aquatic toxicity data which is yet to be generated and on an exposure assessment and risk characterisation that is not yet available.

In conclusion, the arguments provided in your comments are not appropriate to adapt the information requirement. When the conditions for an adaptation are not met, ECHA has the duty to request the missing study, which is a standard information requirement and ECHA does not breach the principle of testing as last resort in Article 25(1) of the REACH Regulation by requesting the study.

On this basis, the information requirement is not fulfilled. You remain responsible for complying with this decision by the set deadline.

Study design

To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (ECHA Guidance R.7.8.2.).

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[8].

B. Test material

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 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 identify all the constituents as far as possible as well as their concentration (OECD GLP (ENV/MC/CHEM(98)16) and EU Tests Methods Regulation (EU) 440/2008 (Note, Annex). Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods

This information is needed to assess whether the Test Material is relevant for the Substance.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[9].

[8] https://echa.europa.eu/practical-guides
[9] https://echa.europa.eu/manuals

Appendix E: General recommendations when conducting and reporting new tests for REACH purposes

A. Environmental testing for substances containing multiple constituents

Your Substance contains multiple constituents and, as indicated in ECHA Guidance R.11 (Section R.11.4.2.2), you are advised to consider the following approaches for persistency, bioaccumulation and aquatic toxicity testing:

- the "known constituents approach" (by assessing specific constituents), or
- the "fraction/block approach, (performed on the basis of fractions/blocks of constituents), or
- the "whole substance approach", or
- various combinations of the approaches described above

Selection of the appropriate approach must take into account the possibility to characterise the Substance (i.e. knowledge of its constituents and/or fractions and any differences in their properties) and the possibility to isolate or synthesize its relevant constituents and/or fractions.

Appendix F: 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 28 September 2020.

ECHA notified you of the draft decision and invited you to provide comments within the notification period.

ECHA took into account your comments and did not amend the request(s).

Deadline to submit the requested information in this decision

In your comments on the draft decision, you requested an extension of the deadline from 24 to 42 months from the date of adoption of the decision to provide the requested information.

You have provided a laboratory statement along with your comments in which you based your request for a deadline extension on the tier-testing approach, starting with the OECD 422 study, in order to "*corroborate the proposed read-across approach*", followed by the OECD 414 and OECD 408 study requests "if needed". For the OECD 422 study you claim that 18 months are needed, justified by the need *"for analytical method development, range-finding studies and conduct of the main study"*. For the repeated-dose and developmental toxicity studies you claim a period of 24 months, justified by the need to perform dose range-finding experiment for OECD 414 *"as well as the time period required for the performance of both definitive studies, including processing and evaluation of tissues, additional work arising from potential high-dose findings, discussion of results and reporting".*

Development of the analytical method

ECHA considers that 24 months is the default timeline for the conduct of the three studies mentioned above. It allows sequential testing of the OECD 422 and OECD 414/OECD 408, including the planning, range-finding studies, conducting of the tests, analysis of the results and preparation of the study reports. The PNDT and 90-day studies can be run in parallel.

However, based on the laboratory statement provided, ECHA notes that you have indicated a need for development of analythical method. Since the Substance is a UVCB and there is no animal experimental data available, ECHA acknowledges that extra time may be needed to develop a suitable analytical method and providing an additional 6 months is considered as sufficient for that purpose.

Intention to develop an adaptation

As indicated above, the deadline set in the decision allows for the development of the appropriate studies for fulfilling the standard information requirements addressed in the decision. As indicated in Appendix C, sections 1 and 2 above, you stated your intention to fulfil the information requirements under consideration by other means than by generating the requested information.

The timeline set in this decision allows for generating the required data on the Substance as a result of incompliances identified in the dossier submission identified in the header of the document. The objective of this compliance check is for you to fulfil the standard information

requirements by the set deadline. Therefore, a further extension of the deadline set in the decision to accommodate your statement of intention to provide an adaptation is considered unjustified.

In conclusion, ECHA sets the deadline to submit the information requested in this decision to 30 months from the date of the 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 G: List of references - ECHA Guidance[10] 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)[11]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[12]

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[13]

[10] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[11] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[12] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[13] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

Guidance document on transformation/dissolution of metals and metal compounds in aqueous media – No 29, referred to as OECD GD 29.

Guidance Document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption – No 150, referred to as OECD GD 150.

Guidance Document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD 151.

Appendix H: Addressees of this decision and 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]

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.